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3rd International Workshop on HIV Pediatrics,
15 - 16 July, 2011, Rome, Italy
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ABSTRACTS
Oral Presentations
Abstract: O_1

Growing up with HIV

Sexual Risk Behavior among Perinatally HIV-Infected Youth in the US: Predictors and Implications for Intervention Development

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Background: Perinatally HIV-infected (PHIV+) children are entering adolescence, a time of sexual initiation and inconsistent adherence to antiretroviral medications (ARVs). Few longitudinal studies have evaluated predictors of initiation of vaginal or anal sex (sex), or associations with unprotected sex in PHIV+ youth. This information is needed to evaluate potential HIV transmission risk to sexual partners.

Materials & Methods: We evaluated 330 PHIV+ US youth (10-16 years old; 52% female at baseline) enrolled in the Pediatric HIV/AIDS Cohort Study (PHACS). Sexual behaviors were reported via audio computer-assisted interview; other information was collected via face-to-face interviews or medical chart abstraction. Longitudinal analysis of predictors of sexual initiation and cross-sectional analysis of factors associated with unprotected sex were conducted. Prevalence of ARV resistance and HIV disclosure to partners was summarized among subsets of sexually active youth.

Results: 92 youth (30% of males, 26% of females) reported sexual activity at either initial or follow-up visit (median initiation age=14.0 years); 52 (56%) reported unprotected sex.

Among 160 youth not sexually active by their initial visit, ARV non-adherent youth were more likely than adherent youth to initiate sex (HR=3.49, 95% CI=1.54, 7.93) (median follow-up=1.14 years). Among sexually active youth, anal sex was strongly associated with unprotected vaginal or anal sex (OR=5.13, 95% CI=1.73, 15.2). Among sexually active youth asked about partner disclosure (n=55), 28% had disclosed their HIV status to their first sexual partner prior to sex. Viral resistance testing was available for 14 of 51 sexually active youth with viral load >1500 copies/ml; 7 had resistance to NNRTI, 10 to NRTI, 6 to PI, and 5 to all 3 ARV classes.

Conclusions: PHIV+ youth are becoming sexually active with over half reporting unprotected sex, placing their partners at risk for HIV infection, including with drug-resistant strains. Interventions addressing non-adherence and unprotected sex are urgently needed.

No conflict of interest
Body composition and metabolic abnormalities of perinatally HIV-infected children in South Africa on long-term ARV treatment

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Introduction: Few studies have assessed metabolic and body composition alterations in young HIV-infected African children undergoing ARV treatment. We compared regional fat and metabolic profiles of children treated with a protease-inhibitor (PI)-based regimen (LPV/r/3TC/d4T) to those switched to a NNRTI-based treatment regimen (NVP/3TC/d4T).

Materials & Methods: This study evaluated 156 HIV-infected children exiting a randomized clinical trial assessing continued LPV/r-based therapy vs. switch to NVP-based therapy conducted in Johannesburg, South Africa (2005-2010). Anthropometrics, HIV-viral load (VL), fasting total cholesterol (TC), high-density lipoprotein (HDL), low-density lipoprotein (LDL), triglycerides (TG), and C-reactive-protein (CRP) were measured. Upper arm and thigh fat area estimates (UFE, UTFE) were calculated. Intent to treat analyses of the treatment groups (PI vs. NNRTI) were conducted. Outcomes were compared across treatment using the Wilcoxon rank sum test and t-test for continuous variables and chi-squared or Fisher exact test for categorical variables.

Results: 156 children aged 3.6-6.9 years (mean 5.1±0.8) were enrolled including 82 (53%) male. 85 (42 male) were randomized to the PI- and 71 (40 male) to the NNRTI-regimen. There were no differences in total years on ARV treatment (4.2±0.7 vs. 4.1±0.6), years since randomization (3.4±0.7 vs. 3.3±0.7), weight-for-age-z-score (-0.67 vs. -0.66), height-for-age-z-score (-1.02 vs. -0.93), or proportion with VL <50 cps/ml (84.7% vs. 91.5%) for the PI-and NNRTI-treated groups, respectively. However, several metabolic parameters differed between groups. The mean TC in mg/dL was greater among those in the PI group (171±39 vs. 161±31, p=0.05), as was the proportion with TC >200 mg/dL (18.8% vs. 8.5%, p=0.03). Significantly lower mean HDL levels in mg/dL (51±14 vs. 59±16, p=0.006) and higher mean LDL levels in mg/dL (100±34 vs. 88±27, p=0.018) were observed in the PI group. Additionally, a higher ratio of TC: HDL was observed in the PI group (3.6±1.1 vs. 2.9±0.9, p<0.001). The mean TG level in mg/dL was greater among those in the PI group (94±39 vs. 72±29, p<0.001), as was the proportion with TG >150 mg/dL (12.9% vs. 2.8%, p=0.04). Mean CRP levels in mg/L were lower in the PI group (3.5±6.1 vs. 9.6±21, p=0.0237) but the proportion of subjects with CRP levels ≥10 mg/L levels was not significantly different between the two groups (10.7% vs. 18.3%, p=0.177). Significantly greater UFE and UTFE (cm²) were observed in the PI group (5.9±4.7 vs. 5.2±1.7, p=0.03 and 15.7±6.0 vs. 13.6±5.3, p=0.01).

Conclusion: Unfavorable alterations in lipid profile and triglycerides, and differences in regional fat are detectable in young South African children receiving long-term PI-based regimens compared to those switched to NNRTI-based regimens. Future studies are warranted to determine how these alterations affect long-term cardiovascular disease risk.

No conflict of interest
Abstract: O_3

Growing up with HIV

Project Control: Evaluation of a brief HIV counseling video to improve teenagers risk reduction behavior

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Introduction: The United States Centers for Disease Control and Prevention has cited adolescents, particularly those of minority races and ethnicities, to be at persistent risk for HIV infection. It has recommended continual HIV prevention outreach and education efforts for this at-risk population. Brief behavioral interventions have been shown to help increase rates of condom use, as well as reduce risky sexual behaviors among adolescents. Yet, routinized prevention counseling is often viewed as time-consuming and burdensome in busy clinical settings. The use of video-based HIV prevention models minimizes strain on hospital resources. This study compared the effectiveness of a brief theory-based, youth-friendly HIV counseling video series with the standard practice (an HIV counselor) in improving risk reduction behavior among teens recruited in an urban Emergency Department (ED).

Material & Methods: A two-armed randomized controlled trial was conducted on a convenience sample of 203 non-critically ill, sexually active individuals aged 15-21 in an urban emergency department. Participants in the control (counselor) group received HIV information and counseling from a trained HIV counselor while those in the intervention (video) group watched a series of youth-friendly counseling videos tailored to patients stages of change. The video series was developed based on qualitative research with adolescent ED patients and applied the Theory of Reasoned Action through reinforcement of condom use as a positive behavior and demonstration of other peers views on using condoms as a positive behavior. The behavioral intervention video also demonstrated how to properly use a male and female condom and dental dams. All participants completed pre- and post-intervention measures on three mediating variables hypothesized to reduce unsafe sexual behavior: condom intention, condom outcome expectancy, and condom self-efficacy. HIV testing was optional for both arms.

Results: 203 patients were enrolled and randomized, 102 in the video group and 101 in the counselor group. The groups were similar with respect to age, gender, race, ethnicity, and sexual history. The video intervention performed as well as in-person counseling at improving several condom use measures. The mean difference between groups (video-counselor) in improvement over time (from pre- to post-counseling) in condom self-efficacy was 0.26, CI(0.03,0.50), in male outcome expectancy was 0.15, CI(0.02,0.28), and in female outcome expectancy was 0.20, CI(-0.01,0.40). Participants in the video group improved their condom use intention score significantly more than those in the counselor group, with a mean difference between arms for change over time of 1.02, p-value= 0.01, CI(0.24,1.80). The intervention effect on condom intention score did not differ by gender or ethnicity.

Conclusions: The use of a theory-based, youth-friendly video can be a valid means to provide post-test counseling education and prevention messages within an urban ED. The theory-based prevention messages can improve specific mediators representing risk reduction behavior among teenagers immediately following the intervention. Longitudinal studies are needed to evaluate the sustainability of these effects.

No conflict of interest
Abstract: O_4
Growing up with HIV
High drug resistance prevalence among vertically HIV-infected patients transferred from paediatric care to adult units in Spain


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Background: Antiretroviral treatment (ART) has contributed to increase life expectancy of HIV-1 infected children. In developed countries, an increasing number of children are reaching adulthood and are transferred from paediatric to adult units. These patients are usually more ARV-experienced, with more treatment switches and longer periods of treatment than adults. It can favour the developing of resistance mutations and immunological or clinical failure events, impacting in their clinical management.

Materials and Methods: This study analyzes clinical, virological and immunological features of HIV-1 vertically infected children at the time of transfer to adult units in the Madrid Cohort of HIV-infected children. All parameters were retrospectively collected from the HIV-1 infected children cohort database. Pol (protease and/or reverse transcriptase) sequences of the latest HIV-1 specimens recovered from each patient before the transfer to adult units where collected from routine genotypic resistance tests or newly performed from samples available at HIV-1 BioBank. HIV-1 variants were characterized by phylogenetic analysis. Resistance mutations were identified according to the IAS-2010 mutation list.

Results: Eighty-eight vertically infected patients were transferred to adult HIV units in different hospitals from Madrid between 1997 and December 2010. All were HIV-1 diagnosed at childhood (mean 2.09 years age), majority (94.3%) were born in Spain and only few (12.5%) were adopted. The mean nadir CD4+ T-cells count was 7%, by clinical stage: N (1.1%), A (25%), B (28.4%), C (44.3%), and by immunological status: 1 (2.2%), 2 (26.1%) and 3 (69.3%). The ART history showed that 62.5% of the patients started treatment with monotherapy, 21.5% with bitherapy, 12.5% of them started directly with HAART and 3.5% (3 patients) remain drug naive. Five was the mean number of ART regimens in the 85 pretreated patients, with at least 3 HAART regimens in 48% of them. By the time of transfer to adult units, the mean age of the study population was 18.39 years, the mean CD4+T-cells count was 626 cells/ml. A 7% presented less than 15% CD4+ T-cells and 67.4% more than 25% CD4+ T-cells. 83% received HAART, 3.4% combined therapy and 13.6% had stopped treatment. Among the 77 patients with available viral load data, 58.4% presented less than 500 RNA-copies/ml and 37.6% undetectable viraemia (<50 copies/ml). Pol sequences (PR and/or RT) were available from 40 patients. Phylogenetic analysis revealed that all patients were infected by HIV-1 subtype B variants. Global resistance prevalence among ARV-exposed patients was 42% for PI, 59.5% for NRTI and 27% for NNRTI. The main resistance mutations found at PR were: L90M (16.6%), M46I/V82A (each 13.8%). At RT for NRTI: D67N (42.9%), M41L (37.1%), T215Y/F (31.4%), K219Q (25.7%), T69D/M184V/L210W (each 20%) and K70R (11.4%). For NNRTI: G190A (11.4%), K103N/Y181C (each 8.6 %) and V108I (5.7%). No primary drug resistance mutations were found in the 3 nave subjects.

Conclusions: Despite of good immunological and virological control before transfer, we found a high prevalence of drug resistance mutations in HIV-1 infected children transferred to adult units, which could compromise future long-term ART and clinical management in vertically HIV-1-infected patients.

No conflict of interest
Abstract: O_5

Growing up with HIV

Routine HIV testing in adolescents and young adults presenting to an outpatient site in Durban, South Africa

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Background: Although adolescents and young adults are disproportionately affected by the HIV epidemic, they have poor access to HIV testing services. HIV testing opportunities can be improved by offering routine HIV testing as part of outpatient care. Our objective was to evaluate HIV testing uptake and prevalence among adolescents and young adults offered routine, voluntary HIV testing in an urban outpatient clinic in Durban, South Africa.

Methods: Adolescent and young adult patients (12-24 years) presenting for general medical outpatient services were offered routine, rapid HIV testing as part of the health services at no charge. Per South African guidelines, patients ≥12 years could consent without guardian approval. We performed a retrospective analysis of HIV testing records and determined the number of unique outpatient visits, HIV tests, and reactive HIV tests in adolescents (12-17 years) and young adults (18-24 years). We determined the HIV prevalence rate in adolescents and young adults presenting for HIV testing and compared these rates by sex.

Results: From February 2008 to December 2009, 3,350 patients 12 to 24 years registered for outpatient care. There were 998 adolescent (12-17 years) and of those 544 (55%) were female. Of the adolescent females presenting for outpatient services, 980 (66%) were HIV tested versus 543 (63%) young adult males (p>0.1). Among the 1,523 (65%) young adults who underwent routine HIV testing, the HIV prevalence was 19% (95% CI 17-21%). The HIV prevalence rate in young adult females was 22% versus 14% among young adult males (p<0.01).

Conclusions: Although the HIV prevalence rate in adolescents and young adults participating in a routine HIV testing program in an outpatient clinic is high, the uptake of HIV testing remains low, especially in adolescent males. There is an urgent need to offer comprehensive and age-appropriate routine HIV testing to adolescents and young adults presenting to outpatient services.

No conflict of interest
Abstract: O_6

Growing up with HIV

Screening of Adolescents and Young Adults for HIV in a Large Urban Pediatric Emergency Department: How to Do it Right?

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Background: In 2009, Childrens National Medical Center, Washington, DC, implemented an opt-out oral fluid rapid HIV screening in the Emergency Department (ED) for adolescents aged 13-24 years. This study aimed at quantifying the success of the programs implementation and at identifying barriers towards increasing its capture rate.

Methods: We prospectively studied the rates of HIV ED screening during the first 20 months of the program and investigated the barriers towards the HIV screening through structured interviews with staff, review of the ED database and program performance evaluations.

Results: From March 2009 through November 2010 there were 25,736 ED visits by adolescents and young adults aged 13-24 years. Of these, 7,060 (27.4%) were approached, of whom 4,726 (66.9%) did not opt-out, and 4,672 patients were tested (mean age=16.5 years (±2.1); 2,708 (58.0%) females; 1,963 (42.0%) males; 0 transgenders). Seven (0.15%) had a reactive test, and 4 (mean age=18.6 years (±1.5); 2 (50%) females) were confirmed HIV-positive and linked to care. During the 20 month study period, monthly screening rates increased >28 fold from 15 to 428 patients per month. The rates of screening were directly related to the presence of 2.5 full time dedicated testers (p<0.0001) and the implementation of a triage nursing order (p=0.0001).

Conclusions: The majority of adolescents and young adults accepted the oral rapid HIV screening in our pediatric ED. Increasing screening required dedicated support staff and implementation of a new procedure, which allowed nursing staff to order the test without consulting a physician. In order to transition HIV ED screening to a standard of clinical practice, the transfer of testing procedure to the nursing staff is required. An ongoing study is evaluating the most efficient mechanism of transition to nursing screening algorithm.

No conflict of interest
Abstract: O_7

Controversies in Pediatric Treatment

Predictive value of six-week viral load on mortality in HIV-infected Zimbabwean infants

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Background: Untreated mortality in HIV-infected infants is high, with no reliable markers to distinguish progressors and non-progressors. In European/US studies, viral load is less predictive of disease progression in infants than in older children or adults. The predictive value of viral load (VL) for mortality in sub-Saharan African infants remains unclear.

Materials and Methods: Data from the ZVITAMBO Vitamin A trial, conducted in Zimbabwe between 1997-2001, were used to determine the predictive value of VL, measured at 6 weeks of age. Mother-infant pairs were enrolled within 96 hours of delivery and followed up at 6 weeks, 12 weeks, then monthly to 12-24 months. HIV-exposed infants were tested by HIV DNA PCR and designated intrauterine (IU)-infected (PCR positive within 96h of birth) or intrapartum (IP)-infected (PCR negative at birth, positive by 6 weeks). VL was measured at 6 weeks of age using the Roche Amplicor HIV-1 Monitor test version 1.5 (lower detection limit 400 copies/mL) in infants for whom a cryopreserved plasma sample was available. Infant mortality was determined up to 12 months of age in the absence of cotrimoxazole prophylaxis or ART, which were unavailable at this time. Multivariate Cox models were used to assess the impact of VL and other covariates on mortality.

Results: Of 4495 HIV-exposed infants, 887 tested HIV DNA PCR positive by 6 weeks of age (382 [43%] IU, 505 [57%] IP). Six-week plasma samples were available for 461 infants (154 IU, 307 IP). Mortality risk in the first half of infancy (6 weeks to 6 months) almost doubled [HR 1.87 (95%CI 1.52, 2.30)] for each log₁₀ increase in VL. Infants with VL in the top two quartiles had a threefold increased risk of death by 6 months (HR 2.96-2.98; P<0.001). Among infants who survived to 6 months, plasma VL measured at 6 weeks of age was the only factor that predicted mortality by 12 months of age [HR 1.71 (95%CI 1.13, 2.58)].

Conclusions: This is the first study from sub-Saharan Africa to demonstrate that a single viral load measurement at 6 weeks of age is significantly and independently predictive of mortality throughout infancy in perinatally HIV-infected infants. Early diagnosis and initiation of ART is critical because of the risk of rapid disease progression during infancy. Since viral load impacts mortality, there is likely to be a survival benefit in achieving virological suppression as rapidly as possible after ART initiation.

No conflict of interest
Abstract: O_8

Controversies in Pediatric Treatment

Treatment efficacy in European children starting cART in infancy: factors associated with viro-immunological response and 1st-line therapy duration.

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Background: Guidelines recommend early ART for all HIV-infected infants. However, there are limited data on treatment response, duration of first line treatment and corresponding predictors among children starting treatment during infancy.

Methods: Data on ART-naive infants starting combination ART (cART) were pooled from 9 observational cohorts participating in the European Pregnancy and Paediatric HIV Cohort Collaboration (EPPICC). Logistic and linear regression models were used to explore predictors of virological and immunological responses at 12 months. Competing risk methods accounting for loss-to-follow-up and death were used to estimate cumulative probability of switching to second-line therapy and of treatment interruption (TI) and assess corresponding risk factors. Missing data for covariates were imputed using chained equation methods.

Results: 437 infants were followed for a median 5.9 (IQR 2.3-7.6) years after starting cART. Three-fifths (62%) suppressed viral load <400 copies/mL at 12 months. Although differences between NNRTI-based and PI-based regimens containing two NRTIs not being observed, infants starting 4-drug NNRTI-based regimens had better virological (adjusted OR=3.00, 95% CI 1.24-7.23; p=0.001) and immunological (coefficient 0.64, 95%CI 0.10-1.17; p=0.035) response at 12 months, compared with 3-drug NNRTI-based regimens. Around a fifth (18%, 77/437) of children switched to second-line therapy at some point. The cumulative probability of switching by 2 and 5 years from cART initiation was 10.2% (95%CI 7.5-13.4%) and 16.6% (12.9-20.7%) respectively. Children starting cART with either 4-drug NNRTI-based or boosted PI-based regimens were slower to switch (p=0.034), though data were sparse. Risk of switching decreased once a child had a viral load measurement <400 copies/mL (HR 0.23, 95% CI 0.14-0.37; p<0.001), and increased once a suppressed child had a confirmed virological rebound (HR 23.37, 95% CI 5.51-99.23; p<0.001). However, only 10.6% (95% CI 5.8-17.0%) switched within 12 months of their initial rebound. A third (129/437, 30%) of children underwent TI, with 108 (84%) interrupting first-line therapy. The probability of TI by 2 and 5 years was 13.1% (10.0-16.6%) and 26.7% (22.2-31.4%), respectively. Risk of TI was higher in the UK and Ireland (p<0.001), and compared with those starting 3 drug NNRTI-based regimens lower in 4-drug NNRTI-based (HR 0.36, 95% CI 0.16-0.80) and boosted PI-based regimens (HR 0.57, 95%CI 0.24-1.36) (p=0.024). It was also lower in children diagnosed with AIDS before cART initiation (HR 0.59, 95%CI 0.37-0.94; p=0.026), and higher after confirmed virological rebound (HR=2.60, 95%CI 1.57-4.30; p<0.001). By last follow-up, 64% (278/437) of children had neither switched to second-line nor experienced a TI, and 36% of these had been treated for at least 5 years. The estimated probability of remaining on first-line therapy without TI was 80.7% (95%CI 75.7-83.5%) and 64.2% (59.2-69.2%) by 2 and 5 years from cART initiation, respectively.

Conclusions: An effective and prolonged treatment response can be achieved in infants by starting treatment early, even outside of trial settings. Superior responses to 4-drug NNRTI compared with 3-drug PI or NNRTI-based regimens warrant evaluation in randomized trials. The use of NVP-based first-line regimens can be considered safe and effective in settings where protease inhibitors are still not available.

No conflict of interest
Abstract: O_9

Controversies in Pediatric Treatment

Predicting 1-year mortality using current CD4 percent and count in order to guide switching therapy in children on ART in Southern Africa.

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Introduction: In resource-limited settings, clinicians rely on clinical and immunological criteria to identify children requiring second-line, however these criteria perform poorly at identifying children with virological failure. In particular, the low positive predictive value of immunological failure for virological failure could lead to unnecessary switch to second-line in a virologically suppressed child. An alternative approach is to determine the short-term mortality risks for different CD4% and count thresholds, with thresholds below which mortality risk starts to increase rapidly indicating a need for therapy switch. We therefore aimed to determine the one-year mortality risk according to current CD4% and count while on antiretroviral therapy (ART) for children in different age strata.

Material and Methods: All children (<16 years) initiating ART with >180 days of follow-up after therapy initiation at International epidemiologic Databases to Evaluate AIDS (iDEA) Southern Africa collaborating sites were included. A person-intervals method was used: each CD4% or count measurement constituted an observation with time set at 0 and censored at the first of 365 days, date of death, date of transfer out or date of last visit if patient was lost to follow-up or remained in care at time of data transfer. Kaplan-Meier probabilities of death were estimated. Predicted probabilities of death were calculated using a Weibull model with independent variables of age category, CD4 count/percent and CD4 count/percent.

Results: Data from 17,173 children with median (interquartile range) age at ART initiation of 61 (25-107) months were included. Most children were severely ill at ART start with 71% and 70% having World Health Organization (WHO) Stage 3 or 4 disease and WHO-defined severe immune suppression respectively. The Kaplan-Meier estimates (95% confidence interval [CI]) of 1-year percentage mortality risk for children 24 to 35 months old according to CD4 percent category were 4.4% (1.4-13.0) (CD4%<10); 2.2% (0.7-6.5) (CD4%: 10-14.9); 1.3% (0.4-4.0) (CD4%: 15-19.9) and 1.3% (0.9-1.9) (CD4%≥20). Corresponding values for the same CD4 percent categories in children ≥36 months old were 4.6% (3.7-5.7), 1.9% (1.4-2.5), 0.9% (0.7-1.3) and 0.5% (0.4-0.6). Kaplan-Meier estimates (95% CI) of 1-year percentage mortality risk for children ≥36 months old according to CD4 count category were 8.6% (7.0-10.6) (CD4<100); 2.9% (2.2-4.0) (CD4: 100-199), 1.6% (1.2-2.1) (CD4: 200-349), 0.9% (0.7-1.3) (CD4: 350-499) and 0.4% (0.3-0.6) (CD4: 500-749). Predicted mortality from Weibull models increased exponentially with declining age and CD4% or count. For example, for a child of 24-35 months the 1-year mortality risk with CD4% of 20% was 1.6% and increased to 2.6%, 4.8% and 10.4% at CD4% of 15%, 10% and 5% respectively. For a child ≥36 months, the 1-year mortality risks were 0.8%, 1.3%, 2.4% and 5.0% for CD4% of 20%, 15%, 10% and 5% respectively.

Conclusions: These data suggest that in the absence of viral load measures, children 24-35 months old should be switched at CD4% <10, while lower thresholds could be considered for older children. For children ≥36 months, CD4 <200 cells/μl is associated with <5% 1-year mortality risk. Risk rises more steeply as CD4 drops.

No conflict of interest
Abstract: O_10

Controversies in Pediatric Treatment

Long-term consequences of planned treatment interruptions in HIV-infected children: results from the PENTA 11/TICCH trial

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Background: The PENTA 11, multicentre, randomised, phase II trial was conducted to evaluate clinical, immunological and virological consequences of CD4-guided antiretroviral therapy (ART) planned treatment interruptions (PTI) compared with continuous therapy (CT) in children with chronic HIV infection. No major clinical disadvantages were observed on the PTI compared to CT. Better CD4% recovery after PTI was observed in those with higher nadir CD4%- at the end of the trial in May 2008 all children were recommended to go back to CT. However, long term follow-up (LTFU) is needed to fully assess the risk and benefits of PTI in the management of chronic HIV infection in children.

Methods: 109 children with HIV-1 RNA <50 copies/ml and CD4%≥30% (2-6 years) or CD4 count ≥500 cells/µl (7-15 years) were randomized to CT or CD4-guided PTI. After trial end (2009), routine clinic data were collected annually in a planned 5-year follow-up study, along with additional neurodevelopmental, quality of life and immunological outcomes. Here we compare the proportion with HIV-1 RNA <50 copies/ml and changes from baseline in CD4% and lipids levels between arms at 1 and 2 years from trial end using regression analyses.

Results: 101/109 (50 PTI, 51 CT) children had follow-up up to 2 years after end of trial (79 Europe, 22 Thailand). Median duration of follow-up from trial enrolment was 4.6 (range 3.7-5.0) years. Time spent off ART before trial end was 45% in PTI versus 4% CT arms. After accounting for delay in restarting ART, 4.2% of time was spent off ART in PTI vs 1.3% in CT arm over the 2 years follow-up; 2 children in PTI and 4 in CT switched ART regimen for failure or toxicity, and 1 and 10 substituted drugs for simplification, respectively. During trial and follow-up, no child died or had a new CDC stage-C event, and only 1 child had a stage-B event (PTI, during main trial). The proportion with HIV-1 RNA <50 copies/ml was 77%(11/47) in PTI versus 90%(5/49) in CT arm at 1 year from end of main trial (p=0.07); corresponding proportion at 2 year was 82% (37/45) and 86% (6/53), respectively (p=0.57). Estimated difference in absolute CD4% between PTI versus CT from baseline was -3.5% (95% CI -6.3%, -0.7%; p=0.014) at 1 year and -1.6% (-4.5%, 1.3%; p=0.27) at 2 years after trial end. CD4% recovery after PTI was better among children with nadir CD4%>20% compared to <20%; estimated mean difference in absolute CD4% 4.8% (95% CI 1.5%, 8.0%; p=0.004). At 1 and 2 years, there were no difference in total, HDL and LDL cholesterol, and triglycerides. Neurocognitive and immunology substudies are ongoing from trial and follow-up.

Conclusions: There was no serious clinical outcomes in the overall study. Virological and immunological outcomes were similar between arms by 2 years after end of main trial. Nadir CD4 % remained associated with better long-term CD4 recovery. The role of PTIs in paediatric management requires further research, particularly given the recommendation to treat all HIV--infected infants.

No conflict of interest
Abstract: O_11

**Emerging issues in PMTCT**

**Infectious morbidity, mortality, growth of HIV-exposed, uninfected, formula-fed infants enrolled in NICHD/ HPTN 040/ PACTG 1043**

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**Background:** Formula feeding (FF) may be associated with adverse outcomes in resource-limited settings. NICHD/HPTN 040 was a randomized trial that enrolled FF-infants born to women with no prenatal antiretrovirals.

**Methods:** Infectious morbidities, mortality, and growth within a proportionally allocated random sample of 1000 HIV-exposed uninfected FF-infants enrolled between 4/2004 to 4/2010 in Brazil (N=766) and South Africa (SA) (N=234) were evaluated.

**Results:** Baseline parameters were: 90% > 37 wk. gestation; 77% black/mulatto maternal race; 67% prenatal care; median birth weight, 3.0 kg; median maternal CD4, 466 cells/mm³, median viral load (VL), 13580 copies/mL. 23% infants had at least 1 infectious serious adverse event (ISAE), rate of 60/100 infant-yrs (IY); rates were similar in Brazil and SA (61 vs. 59/100 IY, respectively) but varied by type of ISAE: gastrointestinal ISAE, 4.7/ 100 IY vs. 24.2/ 100 IY, and congenital infections ISAE, 21.8/100 IY vs. 3.6 100/IY for Brazil and SA respectively. 6 month Infant mortality was 22/1000 (±2.6 SD): 9.1 (±1.8 SD) in Brazil (median 53 days), 64.1 (±3 SD) in SA (median 54 days) (comparison 2006 countrywide 12 mo. IMR: Brazil 19, SA 56). Respiratory infections/sepsis were leading causes of death. Malnutrition (weight-for-age z-score < -2) at 6 months was present in 7.4% (6% Brazil, 11% SA). In multivariate analysis, infant mortality was associated with SA birth (p < 0.001), increasing maternal VL (p =0.048) and low birth weight (LBW) (p <0.004). ISAE was associated with fewer years of education (p <0.02) and maternal VL > 1,000,000 copies/ml (p=0.015).

**Conclusions:** Mortality in these HIV-exposed FF uninfected infants was lower than background country rates in Brazil but slightly higher in SA. Gastrointestinal ISAE and malnutrition were more common in SA. FF infants born in SA, to mothers with high VL or with LBW were at higher risk of death.

No conflict of interest
Abstract: O_12

Emerging issues in PMTCT

Mobile Text Messaging Improves PMTCT Follow-up in South African Public Setting

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Background: Interventions to increase follow-up testing rates of HIV-exposed infants are urgently needed. The Rahima Moosa Mother and Child Hospital in Johannesburg, South Africa, has a protocol in place in the delivery unit where all mothers unaware of their HIV status or with a negative result more than six weeks prior are offered repeat testing. Late maternal HIV diagnosis at delivery may exacerbate poor infant follow-up. This study aims to test whether mobile phone text messages (SMSs) improve infant follow-up rates, including for women who test late.

Methods: HIV-positive women were interviewed after their infant’s delivery and were offered inclusion in this (currently ongoing) study evaluating 10 weeks of SMS encouragement and reminders for infant PMTCT medication and PCR test appointments. Three groups were constituted: Women requesting enrolment in the SMS study, randomised (1:1) to either receive (group A1) or not receive SMSs (group A2) and those declining them (group B). Follow-up was tracked using clinical databases at two clinics, tracing PCR results through the national laboratory and by phoning women not found. Follow-up rates for infant PCR tests, PCR results and clinical statuses were compared between groups and additionally comparing the whole group of mothers to those only diagnosed with HIV for the first time at this delivery.

Results: Follow-up for PCR tests occurred at a median age of 46 days (IQR: 43; 52). Follow-up rates for PCR testing were 90.5% (CI: 86%-95%) in Group A1 (n=160), 78.2% (CI: 72%-84%) in Group A2 (n=177) and 63.0% (CI: 52%-74%) in group B (n=81). When considering only the 51 (12.2% of total) women newly diagnosed at the time of delivery, 86.7% (CI: 67%-100%) in group A1 (n=16), 41.7% (CI: 9%-74%) in group A2 (n=13) and 40.9% (CI: 18%-63%) in group B (n=22) brought their infants for testing. For both the whole group and women newly diagnosed at delivery, follow-up for PCR testing was significantly higher comparing A1 and A2 (p=0.003 and p=0.04 respectively). Return rates for PCR result were 67.3% (CI: 59%-75%), 61.9% (CI: 55%-69%) and 23.5% (CI: 14%-32%) for group A1, A2 and B respectively for the whole group and 67.7% (CI: 40%-94%), 33.3% (CI: 2%-65%) and 4.5% (CI: 0-14%) for A1, A2 and B where women were newly diagnosed at this delivery. The differences between follow-up for collection of PCR results was significant only in newly-diagnosed women (p=0.04, A1 vs. A2).

Conclusion: Text messaging improved infant follow-up rates in this urban South African context even for women only diagnosed HIV-positive at birth where higher early infant mortality and HIV transmission were concerning. Further work to implement these findings on a larger scale and to provide effective support to women newly diagnosed at delivery is required.

No conflict of interest
Abstract: O_13

Emerging issues in PMTCT

Impact of the national Prevention of Mother to Child Transmission (PMTCT) program on Mother-to-Child Transmission of HIV (MTCT), South Africa, 2010


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Introduction: The impact of national PMTCT programs on MTCT rates at the population level is unknown in most countries including South Africa where PMTCT was initiated in 2001.

Material and Methods: We conducted a national cross-sectional facility-based survey of infant-caregiver pairs attending the 1st infant immunization visit using a stratified multi-stage sampling design. Dried blood spot (DBS) specimens from 4-8 week old infants were tested for HIV antibodies. Infants were regarded as HIV-exposed if born to women who reported their HIV status as being positive and/or tested DBS antibody positive. DBS from HIV-exposed infants were tested for infant HIV infection by DNA PCR. Primary outcomes were (1) national MTCT rates at 4-8 weeks postpartum; and (2) significant factors associated with the MTCT. We calculated Odds Ratios and adjusted for covariates (AOR) using SAS 9.2

Results: Of 9610 enrolled infant-caregiver pairs, 2888 (30.1%; 95%CI 29.1%-31.0) HIV-exposed infants were identified. Among those, 79.6% (95%CI 77.9-81.2) HIV positive mothers received their CD4 test results; 59.8% (95%CI 57.8-61.7) received both maternal and newborn antiretroviral prophylaxis; 33.9% (95%CI 32.0-35.8) HIV-infected mothers received triple antiretroviral treatment and 22.9% (95%CI 21.3-24.4) reported exclusive breastfeeding. The national MTCT rate at 4-8 week postpartum was 4.0% (95%CI 3.3%-4.8%). The only risk factor associated with MTCT was unplanned pregnancy (AOR=1.7; 95%CI 0.9-2.9). Exclusive breast-feeding (AOR=0.6; 95%CI 0.4-0.9); and maternal triple antiretroviral treatment (AOR=0.4; 95%CI 0.2-0.8) were protective factors. The MTCT rates did not differ by socio-demographic characteristics; obstetric history; PMTCT knowledge and income.

Conclusions: After 9 years of implementing a national PMTCT program, the South African mother-to-infant transmission rate at 4-8 weeks postpartum was around 4%. Reducing unplanned pregnancies among HIV-infected women, and reducing mixed feeding might reduce MTCT rates even further.

No conflict of interest
Abstract: O_14

Emerging issues in PMTCT

Maternal and infant nevirapine for the prevention of mother-to-child transmission of HIV in women with <8 weeks of prenatal HAART: a Bayesian analysis

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Introduction: From 2008-2010, PHPT-5, a three-arm randomized clinical trial comparing maternal and infant peripartum nevirapine (NVP-NVP) versus infant only nevirapine (Placebo-NVP), and maternal lopinavir/ritonavir (LPV/r) in addition to standard zidovudine (ZDV) prophylaxis for the prevention of perinatal transmission of HIV (PMTCT) was conducted in Thailand. The trial was prematurely stopped and unblinded due to changes in national PMTCT guidelines recommending LVPr-based HAART in all HIV-infected pregnant women. At the time of unblinding, 404 women were enrolled with an overall transmission rate of 2.2%, with no significant difference between treatment arms. Factors independently associated with transmission were duration of ZDV prophylaxis (aOR 1.8 per week decrement; 95%CI: 1.3-2.4) and viral load at delivery (aOR 2.3 per log-10 increment; 95%CI: 1.1-4.8). We hypothesized that late presenter women with <8-weeks of prophylaxes had insufficient duration to suppress viral replication, and the addition of maternal and infant single dose nevirapine (sdNVP) would significantly decrease the risk of intrapartum transmission.

Material and Methods: Using transmission data from 3,876 women participating in the PHPT-1, 2 and 5 Perinatal HIV Prevention Trials (clinicaltrial.gov NCT00386230, NCT00398684 and NCT00409591, respectively) we applied Bayesian inference to model the risk of intrapartum transmission assuming that: 1) maternal prophylaxes duration has a direct effect on viral load at delivery (exponential decrease from baseline), 2) Viral load at delivery has a direct effect on the risk of intrapartum transmission (logistic regression adjusted for maternal viral load, gestational age, CD4 count at delivery and infant treatment duration).

Monte Carlo simulations were used to predict transmission rates with and without sdNVP in relation with maternal and infant prophylaxes duration, and to design future clinical trials.

Results: Assuming equal distribution of prophylaxis durations between 0 and 8 weeks, the model-based estimates of the intrapartum transmission rate in women receiving <8 weeks of prophylaxes was 2.6% (95%-Probability Interval= 0.5%-9.2%) with the standard of care (LPV/r based HAART during pregnancy and ZDV for the newborn), and 0.8% (95%-PI= 0.1%-2.9%) with maternal and infant sdNVP in addition to the standard of care, corresponding to a risk ratio of RR=3.9 (95%-PI= 2.1-9.7). Trial simulations showed that a single-arm study testing maternal and infant sdNVP in addition to standard of care with early stopping rules for efficacy or futility at N=58, 118, 275, and 410 has 78% (resp. 68%) probability of demonstrating statistical evidence that RR>1.3 (resp. RR>2).

Conclusions: This analysis suggests that maternal and infant sdNVP added to the standard of care can result in a 3-fold reduction in risk of intrapartum transmission among women with short duration of prenatal maternal HAART. Modeling based on historical trial data combined with optimal interim stopping rules enables the design of an ethically and scientifically sound single-arm trial to evaluate this hypothesis with <400 patients and limited type-1 and type-2 errors. In such a trial, observed transmission rates would then be compared to model-based historical estimates for women in the standard of care with the same distribution of prophylaxes duration.

No conflict of interest
Abstract: O_15

Emerging issues in PMTCT

HIV incidence in women during the first postpartum year: implications for PMTCT programs Francistown, Botswana, 2010

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Background: Incident HIV during pregnancy and breastfeeding is associated with high MTCT rates. In Botswana, >95% of pregnant women have routine HIV tests during antenatal care (ANC) and 67.5% test HIV-negative. We retested antenatally HIV-negative women one year postpartum.

Methods: All women with a recorded HIV-negative test during ANC presenting at immunization clinics with 9-15 month old infants were approached. We asked questions on sexual behavior, HIV testing, and infant feeding and provided HIV testing, counseling and referrals according to routine in Botswana.

Results: Of eligible women approached, 417 (98.3%) enrolled. Of these, 18 were HIV-positive (4.3%, 95%CI 2.7-6.9): two diagnosed postpartum but pre-study; 16 diagnosed in our study. A median 58 weeks was documented between the last negative test and the positive test. Of all women tested, 93% had a partner; 52% lived with their partner; 19% had >1 partner in the last 2 years; 17% always used condoms during and since pregnancy. The median period without sex during pregnancy and postpartum was at least 10 months (some women were still abstinent when surveyed). Only 0.7% of women reported having a positive partner, but 76% reported knowing their partners status. The only significant risk factor for incident HIV was having a partner of unknown status (p=0.015). All women breastfed, but 38% weaned their infant before study enrollment. DNA PCR performed for 17 HIV-exposed infants found 3 (17.6%) infected, and 6 uninfected but breastfeeding.

Conclusions: HIV incidence was high among women who tested HIV-negative during pregnancy despite reported prolonged abstinence from sex during and after pregnancy. Many women were vulnerable to incident HIV through risky sexual activity with partners of unknown HIV status. Breastfeeding infants in Botswana are at risk of HIV exposure; knowledge of partner HIV status and HIV testing of mothers in immunization clinics may mitigate this risk.

No conflict of interest
Abstract: O_16

Emerging issues in PMTCT

PMTCT drivers of loss and a novel programmatic response in Uganda

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Background: While sustained scale up of Uganda’s PMTCT program has led to increased access nationally, there remain significant barriers to the retention and follow-up of women and HIV-exposed infants (HEI) in the national PMTCT program. The Ministry of Health, with technical assistance from Clinton Health Access Initiative (CHAI), launched a comprehensive cohort study to better understand intra-facility linkages and drivers of patient loss throughout the PMTCT process, and in turn inform program strengthening.

Materials and Methods: Qualitative assessments and extensive data collection was undertaken at 6 facilities. Data for 419 HIV+ pregnant women (PW) with 1st ANC visit during March-Nov 2009 was retrospectively abstracted from 18 different types of registers and facility data tracking tools to identify the key drivers of loss along each point in the PMTCT-EID cascade. 45 Health care providers were interviewed and observed to learn about health system flows, and 3 focus group discussions were conducted with health providers at each facility to elicit potential solutions to gaps.

Results: Of the 419 HIV+PW in the data cohort, only 8% (n=32) made it through the entire cascade (i.e. mothers actively in-care post-pregnancy and babies tested via DNA PCR). Drop-offs were observed throughout the cascade. Notably only 43% of HIV+ PW attended more than one ANC visit. Only 26% (n=98) of HIV+PW received CD4-testing despite access to free CD4 services; of those received CD4, 56% (n=55) received their results and were initiated on the correct ARV regimen. At the five facilities with on-site ART clinics, only 21% of HIV+PW were linked to chronic care at the ART clinic. Clinical staging was conducted at only 45% of ANC visits and Cotrimoxazole was not given out at nearly one-third (34%) of ANC visits One-third (34%) of HIV+PW received no ante-partum ARVs, 16% received sd-NVP, 14% were on HAART, and 36% received AZT/3TC. Only 28% of HIV+PW delivered at a facility; resulting in only 24% of HEI receiving NVP syrup overall. Only 20% of HEI were brought back in for DNA PCR testing. Cross-cutting drivers of loss were identified through data analysis and qualitative assessments, they included: 1) Ineffective tracking tools for PMTCT (e.g. absence of longitudinal tracking); 2) weak mechanisms for cross-department linkages; 3) ineffective patient, sample, and data flow; 4) poor coordination and communication within facilities; and 5) poor knowledge and counseling skills among healthcare providers.

Conclusions: The review and its findings culminated in the Ministry of Health in collaboration with CHAI developing a novel programmatic package that targets the identified drivers of loss (The National PMTCT-EID Strengthening Program). This novel package which includes new patient tracking registers, innovative referral and follow-up tools, rationalized PMTCT clinic systems, new job aides and brochures, a comprehensive 5-day training curriculum, and a facility-level mentorship program has since been rolled out throughout the country.

No conflict of interest
Abstract: O_17

Emerging issues - Coinfection-Tuberculosis and Measles

Prevalence of HBV/HIV and HCV/HIV coinfections and HB vaccination in HIV-Infected children at the National Pediatric Hospital, Phnom Penh, CAMBODIA.

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Background: So far little was known on the epidemiology of hepatitis B, C with HIV infected people in Cambodia. Preventing Hepatitis B virus (HBV) infection by vaccination is essential for HIV-infected patients. In Cambodia hepatitis B vaccination was included in the National Immunization Program (NIP) since 2005. Our objective was to determine the response to HB vaccine in HIV-infected children. The aim of this study was determine the prevalence of HBV and HCV in the HIV positive children and to evaluate the response to hepatitis B vaccination in such cases and to correlate it to immunologic and/or virologic markers

Methods: This cross sectional study was conducted at HIV clinic of the National Pediatric Hospital (NPH) between April 2009 and March 2010. HIV-infected children were screened for HBV and HCV by detection of HBs-Ag HBs-Ab and HCV-Ab. HBV infection was defined by a positive HBV surface antigen (HBsAg), and HIV infection by a positive anti-HCV antibody. Immunization with Engerix-B 10mcg using a 0,1, 6-month schedule was administrated to eligible subjects (absence of HBs-Ag and HBs-Ab). Patients with severe OI and or very low CD4(<10%) were excluded for hepatitis vaccine. Quantitative testing for HBs-Ab (mIU/mL) was obtained 1 month after the 3rd dose. Children with Abs >100mIU/mL were considered as full protective level. Children with Abs 10-100mIU/mL were considered as partial response and need to provide an additional boosted dose as well. Computerized data were and analyzed using EPI INFO version 3.3.2

Results: 974 HIV-infected children (478 females) were consented and enrolled in the study. The prevalence of hepatitis B and C were 45/974(4.7%) and 9/974(0.9%) respectively.145 children who born after 2004 were received Hepatitis B vaccine through NIP from birth. Only 28/145 (19.3%) developed HBs-Ab. 236 children were reported that they were received hepatitits vaccine (three-doses) at private clinics and only 60/236 (25.4%) developed HBs-Ab on our screening. 789 of 974 met the criteria to receive HB vaccine in our study, median age was 8.6 years (IQR: 5.8-10.9).The response rate: 62.6% had HBs-Ab>100mIU/mL; 4.9% had 10-100mIU/mL and 32.5% were<10mIU/mL. The response rate among 40 children who had CD4<15% or <350cells/mL revealed that 70.0% did not respond at all (<10mIU/mL), 12.5% had a poor response (10-100mIU/mL) and only 17.5% produced a full seroprotection. 638 had HIV plasma VL value at the time of HB vaccination, 193 had VL>2.4Log/mL: 99/193(51.3%) were <10mIU/mL; 5/193(2.6%) were 10-100mIU/mL; 89/193(46.1%) were >100mIU/mL. For children with undetectable VL: 98/445(22.0%) were <10mIU/mL, 20/445(4.5%) were 10-100mIU/mL; 327/445(73.5%) were >100mIU/mL.

Conclusions: Prevalence of HBV-HIV coinfection was higher than HCV-HIV children (p<0.05). Response to HB vaccine through NIP is very low in HIV-perinatal infection and need to be evaluated after full course. HB vaccine response was significantly related to immunological and virological status (p=000), suggesting that HAART use before HBV vaccination could be helpful for immunosuppressed children.

No conflict of interest
Abstract: O_18

**Emerging issues - Coinfection-Tuberculosis and Measles**

**Dynamics of Epstein-barr virus in HIV-1-infected children in Uganda**

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**Introduction:** Epstein-Barr virus (EBV) is involved in a wide range of lymphoproliferative disorders and malignancies, particularly in immunocompromised subjects. In Africa, EBV primary infection occurs during early childhood, but in this context little is known about EBV viremia in HIV-1-infected children.

**Material and Methods:** Dried Blood Samples (DBS) from 187 HIV-1-infected children (0-14 years), 84 of whom were on antiretroviral therapy (ART), were collected at Nsambya Home Care. DNA was extracted and tested to quantify both EBV-type 1 and EBV-type 2 by multiplex real-time PCR, using primers and probes for EBNA2 gene. The reference curves were prepared by amplifying serial dilutions of two amplicons (EBV-1, nt 1083-1295 virus B95.8; EBV-2 nt 1080-1309, virus AG876); the multiplex assay had detection limit of 5 EBV-DNA copies, and showed a dynamic range from 5 to 2x10⁵ copies.

**Results:** 146 (78%) children, 61 of 84 (73%) on ART and 85 of 103 (83%) without ART, were found to be EBV-positive. EBV-1 and EBV-2 were detected in 17 (20%) and 14 (17%) children on ART, and in 24 (23%) and 20 (19%) without ART, respectively. Coinfection with both EBV types was observed in 30 (36%) children on ART and 41 (40%) without ART. Levels of EBV viremia were similar in children infected with EBV-1 (6621 [3011-12876] copies/ml) or EBV-2 (9932 [5203-21378] copies/ml), but higher in children coinfected with both viruses (14843 [9736-38509] copies/ml; p<0.001). Overall, no differences were found in EBV load between children on ART and without ART (10315 [5544-21572] vs 13760 [6631-31590] copies/ml). However, when children were stratified by age, in infants <5 years the EBV load was higher in ART-naive subjects compared to those on ART (16464 [8253-36261] vs 9993 [3791-15886] copies/ml; p=0.017).

**Conclusion:** These findings suggest that early treatment with ART, likely by limiting immune activation, may restrict EBV replication and expansion of EBV-infected cells during primary infection. Potential clinical implications remain to be investigated.

No conflict of interest
Abstract: O_19

Emerging issues - Coinfection-Tuberculosis and Measles

Bacteraemia in HIV-1 infected children on antiretroviral therapy in Uganda and Zimbabwe in the ARROW clinical trial

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Background: Bacteraemia is common in HIV infected children in Africa, including after start of antiretroviral therapy (ART), but there are limited data on bacteraemia pathogens and their antimicrobial sensitivity patterns in this population.

Methods: ARROW is a randomized trial investigating first-line treatment and monitoring strategies in 1207 previously untreated HIV-1-infected children initiating ART. Children developing febrile illnesses in follow-up were investigated for infections including blood culture and sensitivity done according to standard microbiological techniques. The patterns of the bacterial pathogens and their antimicrobial susceptibilities were determined.

Results: 848 blood cultures were obtained from 461 children, of which 123 (14.5%) from 105 children (median age 4 years, 51% girls) were positive, including 4 samples with 2 isolates. During the first year on ART there were 97 positive cultures in 1174 child/years of follow-up, an event rate of 8.3 per 100 child/years. Subsequently there were 30 events in 1866 child/years, 1.6 events per 100 child/years.

Pathogens and isolation rates were as follows: Streptococcus pneumoniae 36(28.3%), Staphylococcus aureus 11(8.7 %), other Staphylococcal species 12(9.4%), other Streptococcal species 10(7.9%), Klebsiella pneumoniae 6(4.7%), Pseudomonas aeruginosa 6(4.7%), Salmonella species 6(4.7%), Escherichia coli 5(3.9%), Enterococcus species 4(3.1%), Corynebacterium species 3(2.4%), Providentia species 2(1.6%), Moraxella species 2(1.6%) and Haemophilus influenzae 1(0.8%). Other bacteria and fungal species were isolated in 19(15.0%) and 4(3.1%) cases respectively. Most isolates were susceptible to ceftriaxone, vancomycin, amikacin and carbapenems. There were high rates of resistance to cotrimoxazole, penicillins, gentamicin, chloramphenicol and erythromycin.

Conclusions: High rates of proven bacteraemia were observed during the first year on ART in African HIV-infected children with Streptococcus pneumoniae most commonly isolated, suggesting a need for effective prophylactic antibiotics and/or pneumococcal vaccination. The high rates of resistance to commonly used antibiotics suggest that newer agents like ceftriaxone should be the drugs of choice when treating HIV-infected children with possible bacteraemia.

No conflict of interest
Abstract: O_20

Emerging issues - Coinfection-Tuberculosis and Measles

Virological outcomes in South African children co-treated with Highly-Active Anti-Retroviral Therapy (HAART) and anti-tuberculosis therapy

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Background: Rifampicin-based anti-tuberculosis therapy causes sub-therapeutic levels of protease-inhibitors (PI) in children receiving HAART, leading to virological failure. In South Africa, PI-based HAART remains recommended as first line in children <3 years of age. Although HAART partially reduces the risk of tuberculosis (TB) in HIV-infected children, the impact of TB co-infection on HAART outcomes requires better description.

Materials and Methods: Data were retrospectively collected from hospital records of HIV-infected children <13 years old who started HAART January 2003-December 2005 at Tygerberg Hospital, Cape Town, South Africa. Incident TB until December 2009 was captured. Virological outcomes were compared between children co-treated with HAART and anti-TB therapy (co-treated group) and not co-treated (HAART-only group). Co-treatment was defined as ≥2 weeks of rifampicin-based TB therapy and HAART. HAART regimens were classified as PI- versus non-nucleoside reverse-transcriptase inhibitor (NNRTI)-based. The PI, lopinavir/ritonavir (LPV/r), was replaced with ritonavir (RTV) for duration of co-treatment. Virological failure was defined as HIV viral load (VL) >5000 copies /ml on 2 consecutive 6-monthly measurements excluding baseline. Categorical and numerical data were analysed using Chi-squared and Wilcoxon sum-rank tests respectively. Chi-squared test for trend was used to analyse ordered categorical data, and rank test for Kaplan-Meier groupings.

Results: 218 children, 79 in co-treatment and 139 in HAART-only groups, were analyzed. Co-treated children were significantly younger (median 21 vs 36 months, p=0.0006) and more malnourished (median weight-for-age Z-score -3.27 vs -1.87, p<0.0001). There was no difference in baseline CD4 count and VL between groups. 72% in co-treatment vs 42% (p<0.0001) in HAART-only group had PI-based HAART. Co-treatment significantly predicted virological failure (unadjusted OR 2.73, 95% CI 1.31-5.73, p=0.003), even adjusting for age (OR 2.3, p=0.02) and HAART regimen (OR 2.6, p=0.01). Age and HAART regimen both modified the effect of TB co-treatment on odds of failure. PI-based HAART increased odds of failure 4.3 times (95%CI 1.5-12.9) in co-treated vs HAART-only group. Children who failed (43/218, 19.7%) were younger at baseline (15 months vs 35 months, p=0.0001) and had higher baseline VL (log 6.19 vs log 5.57, p=0.0026) than those who did not. By 12 and 18 months, 24.9% and 36.5% in co-treatment vs 5.6% and 9.2% in HAART-only group respectively had virological failure (p=0.002). Younger age and PI-based HAART, irrespective of TB, also significantly accelerated time-to-failure. In co-treated children, timing of TB (before or after starting HAART) did not influence odds of failing. Logistic regression revealed younger age and TB co-treatment to be strong independent predictors of failure.

Conclusions: The strong relationship between young age and virological failure in the presence of TB co-treatment is likely related to RTV as single PI. RTV augmented LPV/r performs better in young children with TB, but more data are needed. Aggressive strategies for the prevention of TB in this vulnerable population are urgently required.

No conflict of interest
Abstract: O_21

Emerging issues - Coinfection-Tuberculosis and Measles

Lack of Identification of Adult TB Contacts in Infants with Microbiologically Confirmed or Clinically presumed TB (MCCP TB) in Clinical Trial P1041

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Background: TB prevention in infants and children is a high priority in the developing world. P1041 was a randomized, placebo-controlled trial of isoniazid prophylaxis starting at age 3 months for 96 weeks in 1,328 HIV-infected (525) and exposed, uninfected (803) infants in South Africa. TB incidence was similar in INH and placebo groups, suggesting other prevention methods, including aggressive contact tracing, are needed to prevent TB in children.

Methods: As part of standard of care for P1041, all infants with MCCP TB had intensive contact tracing conducted to identify the source case of TB infection. We analyzed the prevalence, source and maternal and household factors of household contacts in children diagnosed with protocol-defined TB.

Results: 44 infants (3%) (21 HIV-infected and 23 exposed, uninfected) were diagnosed with MCCP TB during the study (31 from Johannesburg, 10 from Cape Town and 3 from Durban). 41% of infants were male; 91% of mothers reported no history of TB disease; 36% had more than 3 people living in room with index case; 24% of homes included a person over age 55 years. 11% mothers smoked and 2% breastfed. An adult household contact with TB could be identified in only 40% of infant TB cases in Cape Town, 39% in Johannesburg but none in Durban.

Conclusion: 60% of children with TB in this trial did not have a household TB source case identified despite intensive contact tracing. This indicates that the majority of TB exposures resulting in childhood TB in similar settings is due to exposure to infectious cases outside of the household. This markedly complicates preventing childhood TB through standard household contact tracing of adult TB cases in communities with a high TB incidence. Innovative strategies will be needed to prevent pediatric TB disease in such areas.

No conflict of interest
Abstract: O_22

Emerging issues - Coinfection-Tuberculosis and Measles

Divergent trends in HIV RNA levels in the cerebrospinal fluid of children and adolescents with central nervous system complications

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Background: The impact of various neurological comorbidities associated with HIV infection on cerebrospinal (CSF) HIV RNA load (VL) levels is unclear. We assessed the potential of CSF VL as a marker of HIV-related central nervous system diseases.

Methods: The VL was quantified in paired CSF-plasma samples (using Roche Amplicor and TaqMan assays with detection limits between 20 and 400 copies/ml) from 104 subjects with and 28 without neurological complications, in order to describe patterns of HIV-1 CSF viral burden in correlation with different neurological diseases. Intact blood-brain barrier (BBB) function was defined as an albumin index <9.

Results: Overall the CSF VL were lower compared to plasma (2.88 vs. 4.58 log10 copies/ml, p<0.001), and showed a positive correlation with albumin levels (rho=0.22, p=0.05) and pleocytosis (rho=0.51, p<0.001). Patients on cART with virological failure had significantly lower CSF VL compared to naive patients, regardless of their neurological condition. Two thirds of the patients with HIV encephalopathy (HIVE) had intact BBB. We describe two distinct patterns associated with specific neurological infections: 1) higher CSF compared to plasma HIV RNA levels in half of the 30 patients with HIVE (5.4 vs. 4.6 log10 copies/ml, p=0.002) and in 4 of 8 patients with cryptococcal meningitis; 2) significantly lower CSF compared to plasma VL in patients with PML and subacute measles encephalitis (3.2 vs. 4.9 log10 copies/ml, p=0.001 and 2.4 vs. 4.3 log10 copies/ml, p<0.001 respectively) similar to those from neurologically asymptomatic patients (2.55 vs. 3.23 log10 copies/ml).

Conclusions: In our group of children and adolescents high HIV RNA levels in the CSF are a good indicator of HIVE. Reduced HIV replication in CSF might be a marker for pediatric PML. The strikingly low HIV RNA levels in children with subacute measles encephalitis suggest an inhibitory effect of measles virus on CSF HIV replication.

No conflict of interest
3rd International Workshop on HIV Pediatrics
15 – 16 July 2011, Rome, Italy

ABSTRACTS
Poster Presentations
Abstract: PP_1

Poster presentation

Population pharmacokinetics of etravirine in HIV-1-infected treatment-experienced children and adolescents (6 to <18 years)

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Introduction: Etravirine is a non-nucleoside reverse transcriptase inhibitor approved for use in treatment-experienced HIV-1-infected adults at a dose of 200mg BID. A prior pharmacokinetic study (TMC125-C126) indicated that etravirine 5.2mg/kg BID (maximum dose 200mg BID) provided pharmacokinetic exposures in HIV-1-infected treatment-experienced children and adolescents (6 to <18 years) comparable to adults in the Phase III DUET-1 and DUET-2 trials with no new safety concerns. A Phase II open-label trial (TMC125-C213, PIANO; ClinicalTrials.gov identifier: NCT00665847) to evaluate the pharmacokinetics, efficacy and safety of etravirine 5.2mg/kg BID (maximum dose 200mg BID) in HIV-1-infected treatment-experienced children and adolescents (6 to <18 years) over 24 weeks is ongoing. For both trials, 25- and 100-mg tablets were used. The population pharmacokinetic model and interim pharmacokinetic results (Week 24) from PIANO are presented.

Materials & Methods: A pediatric population pharmacokinetic model for etravirine was developed based on a previously developed model in adults, supplemented with rich and sparsely sampled pharmacokinetic data from TMC125-C126 and PIANO, respectively. The model was then used to determine etravirine AUC12h and C0h for all subjects enrolled in PIANO up to Week 24. Sparse samples were collected at Weeks 4, 8, 12, 24 and 48 in the PIANO trial; at Week 24 two samples were collected, a trough and sample >1 hour after etravirine intake. Etravirine plasma concentrations were measured using a validated HPLC-MS/MS assay with a lower quantification limit of 2.00ng/mL. NONMEM VI compiled with Visual FORTRAN and R were used for model development and analysis. Models were fitted using the first order conditional estimation method.

Results: The population pharmacokinetic model consisted of a sequential zero- (D1) and first-order (KA) absorption with lag-time (ALAG1) and one-compartment disposition. A covariate effect of weight on apparent volume of distribution (V/F) and apparent clearance (CL/F) was included. The final estimates for ALAG1, D1, KA, V/F and CL/F were: 0.328 h, 2.24 h, 0.89 h⁻¹, 573 L and 45.9 L/h, respectively. Inter-individual variability was included on KA and CL/F. Parameters for the pediatric model were similar to the adult model. 476 sparsely sampled etravirine plasma concentration-time data were available from 101 subjects completing 24 weeks. The overall mean (SD) AUC12h and C0h were 5236 (4314) ng•h/mL and 347 (342) ng/mL, respectively. In children ≥6 to <12 years (n=41), AUC12h and C0h were 5764 (4044) ng•h/mL and 381 (321) ng/mL, respectively. In adolescents (≥12 to <18 years, n=60), AUC12h and C0h were 4834 (4483) ng•h/mL and 323 (357) ng/mL, respectively. The adult reference mean AUC12h and C0h are 5506 ng•h/mL and 393 ng/mL, respectively. Slightly lower exposures were observed in adolescents relative to adults although most of the adolescents were on the adult dose (i.e. 200mg BID).

Conclusions: A population pharmacokinetic model was built that adequately describes etravirine pharmacokinetics in the pediatric population. Etravirine when dosed 5.2mg/kg BID (maximum dose 200mg BID) in children and adolescents (6 to <18 years) provides comparable pharmacokinetics to adults receiving 200mg BID and is expected to be the recommended dose for this population.

Employee and stockholder of Johnson & Johnson
Abstract: PP_2

Poster presentation

24-week efficacy, safety, tolerability and pharmacokinetics of darunavir/ritonavir qd in treatment-naive adolescents aged 12 to <18 years in DIONE

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Background: DIONE (TMC114-C230; NCT00915655) is a Phase II, 48-week, open-label trial of darunavir/ritonavir (DRV/r) 800/100mg qd co-administered with zidovudine (ZDV)/lamivudine (3TC) or abacavir (ABC)/3TC in treatment-naïve, HIV-1-infected adolescents.

Methods: Patients aged 12 to <18 years, weighing ≥40kg, with HIV-1 RNA ≥1000 copies/mL were eligible. Efficacy, resistance and safety were assessed. For pharmacokinetic (PK) analyses, rich sampling was performed after 2 weeks and sparse sampling after 4 and 24 weeks of dosing.

Results: 12 patients (66.7% female; mean age 14.6 years) were enrolled. Mean baseline viral load was 4.72 log10 copies/mL, median baseline CD4 cell count and percentage were 282 cells/mm3 and 18.3%, respectively. Six patients each received ZDV/3TC and ABC/3TC. All patients were susceptible to DRV and background NRTIs at baseline. After 24 weeks, 11/12 (92%) patients achieved HIV-1 RNA <50 copies/mL (ITT-TLOVR); all achieved HIV-1 RNA <400 copies/mL. Mean CD4 count (NC=F) and percentage increased by 175 cells/mm3 and 8%, respectively. No patients discontinued therapy. Eleven (91.7%) patients reported ≥1 AE. The most frequently reported AEs (≥3 patients) were anaemia, nausea and vomiting (all n=3). Two (16.7%) patients had ≥1 AE at least possibly related to DRV (nausea [n=2], vomiting [n=1], diarrhoea [n=1], abdominal pain [n=1] and dizziness [n=1]); all were grade 1 or 2 in severity. Three (25.0%) patients each reported a grade 3–4 or serious AE; none of these were considered to be related to treatment. Grade 2–4 lipid-related laboratory abnormalities were observed for total cholesterol (n=2) and low-density lipoprotein (n=1); no grade 2–4 increases in triglycerides were observed. Median (range) darunavir area under the plasma concentration-time curve (AUC24h) was 87.9 µg•h/mL (34.6–128.0) and trough concentration (C0h) was 2196 ng/mL (510–3975). Median darunavir exposure was comparable to median exposure in treatment-naïve adults receiving DRV/r 800/100mg qd. All patients had darunavir C0h (corrected for protein binding) above EC50 for wild-type HIV (55 ng/mL).

Conclusions: Once-daily DRV/r 800/100mg in combination with 2 NRTIs was effective and well-tolerated for the treatment of HIV-1-infected, ARV-naïve adolescents, with comparable exposure to that observed in treatment-naïve adults.

Clinical Trial Agreements with Tibotec and Bristol Myers Squibb;
Abstract: PP_3
Poster presentation

Efavirenz plasma concentrations during 24 months follow-up post-ART in HIV-infected South African children

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Background: Efavirenz (EFV), a non-nucleoside reverse transcriptase inhibitor forms part of the recommended national first line antiretroviral treatment regimen for children >3 years and weighing >10 kg in South Africa. There is limited pharmacokinetic information on EFV plasma concentrations in sub-Saharan HIV-infected children available. EFV is primarily metabolized by CYP2B6 which is characterised by extensive inter-individual variability. The single nucleotide change, 516G>T, on the CYP2B6 gene has consistently been associated with elevated EFV plasma levels in adults in different populations. The recommended therapeutic range of EFV plasma levels is 1-4 µg/ml.

Method: In this prospective study cohort, 60 black children, both genders, with no prior exposure to antiretroviral therapy (ART) and eligible for ART were enrolled and followed up at 1, 3, 6, 12, 18 and 24 months post-ART initiation. They all attended the outpatient clinic at Harriet Shezi Children’s Clinic, Chris Hani Baragwanath Hospital, Soweto, South Africa.

Results: The median (IQR) EFV plasma concentrations when pooled significantly differed (P<0.00001) according to genotypes, 6.36 (3.47 – 7.28) for T/T, 2.55 (1.62 – 3.59) for G/T and 1.41 (1.02 – 1.74) µg/ml for G/G, respectively (P<0.00001). Analysis of the samples (n=649) taken during the mid-dose interval (1-24 months post-ART) showed that 29.5% of the patients had EFV plasma levels >4 µg/ml, 52.8% had levels within the therapeutic range (1-4 µg/ml) and 18% had levels <1 µg/ml.

Conclusions: A significant number of the samples (47.5%) were outside the accepted therapeutic range. The 18% proportion of children with concentrations <1 µg/ml would have an increased risk of developing viral resistance. Possible reasons contributing to this include genetic variation in drug metabolism and non-adherence. Bearing in mind that 23% of our study population were genotyped with the CYP2B6 516T/T allele, it is to be expected that a large (29.5%) number of the EFV plasma concentrations would be >4 µg/mL as was the case over the 24 months post-ART initiation. Therapeutic drug monitoring may be beneficial and serve as a tool to evaluate adherence more accurately.

No conflict of interest
Abstract: PP_4
Poster presentation

Maraviroc (MVC) pharmacokinetics (PK) in CCR5-tropic HIV-1-infected children aged 2-<18 years: preliminary results from Study A4001031

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Background: MVC is a potent CCR5 antagonist approved for treatment of CCR5-tropic HIV-1 in adults.

Materials & Methods: Study A4001031 is an ongoing, open-label, two-stage (stage 1: dose finding, stage 2: safety/efficacy), non-comparative, multi-center study in treatment-experienced HIV-infected children receiving MVC 40-450 mg twice-daily with optimized background therapy (OBT). MVC PK were determined at Week 2. Subjects infected with CCR5-tropic HIV-1 were enrolled and stratified into four age and MVC formulation cohorts: cohort 1: ≥2-<6 years (liquid); cohort 2: ≥6-<12 years (tablet); cohort 3: ≥6-<12 years (liquid); and cohort 4: ≥12-<18 years (tablet). Participants were dosed initially according to body surface area (BSA) and OBT based on interactions with MVC (adult-recommended doses with/without CYP3A4 inhibitors/inducers). Dose adjustment and PK re-evaluation occurred if average concentrations ($C_{avg}$) at Week 2 were <100 ng/mL. $C_{avg}$ was estimated from AUC (AUC/12) calculated from seven samples taken over 12 hours and summarized descriptively by cohort. AUC was calculated by standard non-compartmental methods.

Results: Twenty-nine subjects were enrolled (n=2, 10, 5, and 12 in cohorts 1, 2, 3, and 4, respectively), 45% of them were male. Six subjects were of Asian, 18 of Black, and five of Caucasian race. Of the 22 subjects taking MVC with a potent CYP3A4 inhibitor (all protease inhibitors), only one failed to meet the PK target with the initial dose (due to poor compliance). Conversely, all five subjects not receiving a potent CYP3A4 inhibitor (two nevirapine-based regimens; two raltegravir-based regimens; one NRTI-regimen) required at least doubling of the initial MVC dose. At the time of enrolment into Stage 2, one subject did not achieve the PK target after two dose adjustments but demonstrated good clinical response and was therefore included in the PK analysis. The geometric mean $C_{avg}$ for cohorts 1, 2, 3, and 4 were 178 ng/mL (n=2), 247 ng/mL (n=10), 221 ng/mL (n=5), and 242 ng/mL (n=9).

Conclusions: Preliminary data show that BSA-based MVC doses when co-administered with CYP3A inhibitors provide exposures ($C_{avg}$>100 ng/mL) associated with near-maximal efficacy in all cohorts. However, additional PK analyses are necessary to further evaluate the appropriate dose when MVC is administered without CYP3A4 inhibitors.

Employee of Pfizer Inc.
Abstract: PP_5

Poster presentation

Second-line highly active antiretroviral therapy in Asian HIV-infected children

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Background: The WHO recommends boosted protease inhibitor (bPI)-based highly active antiretroviral therapy (HAART) after non-nucleoside reverse transcriptase inhibitor (NNRTI)-based regimen failure. This study aimed to determine the efficacy and safety of this regimen in Asian HIV-infected children.

Methods: Data were retrospectively collected between July 1999 and June 2010 from five Asian countries through the TREAT Asia Pediatric HIV Observational Database (TAPHOD). The analysis included children who were <18 years of age at time of switching to bPI-based HAART after ≥24 weeks of non-nucleoside reverse transcriptase inhibitor (NNRTI)-based HAART. The efficacy was assessed at 48 and 96 weeks after switching by reviewing 1) WHO clinical staging, 2) immune recovery (CD4≥25% if age<5 years; CD4≥500 cells/mm3 if age≥5 years) and 3) proportion of children with virologic suppression (HIV-RNA <400).

Results: There were 153 children. 52% were female. The median (IQR) duration of NNRTI-based HAART was 2.6 (1.5-3.8) years. At the time of switching, the median (IQR) age was 10 (7-12) years, the percentage of children in WHO stage 1:2:3:4 was 7:25:42:26%, median weight for age z score (WAZ) was -1.9 (-3.0 to 1.1), median CD4 percentage was 12.5% (5.2%-20.0%), median CD4 cell count was 237 (90-466) cells/mm3, and median HIV-RNA was 4.6 (3.9-5.0) log10 copies/ml. Second-line regimens included lopinavir/ritonavir (83%), indinavir/ritonavir (16%), and atazanavir/ritonavir (1%). The most commonly used NRTIs were zidovudine/lamivudine (33%), zidovudine/didanosine (18%) and didanosine/lamivudine (17%). Ninety-six children (63%) had follow-up visits to 96 weeks (plus or minus 24 weeks). By 96 weeks after switching, two children died (one due to Mycobacterium avium complex and M. tuberculosis, and one from unknown causes) and another child progressed to WHO stage 4. Virologic suppression rates were 45/93 (54%) at week 48 and 30/48 (63%) at week 96. Immune recovery rates were 79/120 (66%) at week 48 and 57/79 (72%) at week 96. By multivariate analysis, predictors for virologic suppression at week 48 after switching were longer duration of NNRTI-based HAART (OR=1.7 per standard deviation, 95% CI 1.2-2.9), p=0.006), younger age (OR 0.8 per additional year, 95% CI 0.7-0.9, p=0.007), greater WAZ (OR=1.7 per standard deviation, 95% CI 1.1-2.7, p=0.020), and HIV-RNA at switching <10,000 copies/ml (OR 12.6, 95% CI 1.9-81.8, p=0.049). Statistically significant predictors of immune recovery at week 48 after switching were younger age (OR 0.8, 95% CI 0.7-0.9, p<0.001) and CD4 count at switching ≥200 cells/mm3 (OR 7.7, 95% CI 2.8-21.5, p=0.003). At week 96, fasting levels of total cholesterol and triglycerides were measured in a subset of children (n=50), high-density lipoprotein (HDL; n=34), and glucose (n=43); 36% had total cholesterol ≥200 mg/dl, 66% had triglycerides ≥130 mg/dl, 26% had HDL<35 mg/dl, and 5% had glucose ≥110 mg/dl.

Conclusion: Lopinavir/ritonavir-based HAART was commonly used as second-line treatment in this regional cohort. Hyperlipidemia was common. One-third did not achieve virologic suppression at two years, signifying a need for procurement of third-line regimens in national programs.

No conflict of interest
Abstract: PP_6
Poster presentation
Patterns of first-line antiretroviral regimen and switch to second-line in West African children on ART. The IeDEA paediatric West African Database.

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Background: Patterns of first-line regimen of antiretroviral treatment (ART) and switch to second-line need to be described in paediatric ART programs in Africa. We studied the 24-month durability of first-line regimen and the switch to a second-line ART according to their clinical and immunological response in the paediatric IeDEA West African collaborative database on AIDS.

Methods: A standardized data collection system was established for HIV-infected children enrolled in participating ART programs. Nine clinical centres from six countries contributed (Benin, Burkina Faso, Côte d’Ivoire, Ghana, Mali, Senegal). Inclusion criteria were: age ≤15 years, starting ART (≥3 drugs), with ≥1 measurement available on WHO clinical stage or CD4 cell count or CD4% during the first-line ART regimen. The 24-month probability of switching to a second-line defined as ≥1 a drug class change was estimated. Clinical failure was defined as the appearance or reappearance of WHO clinical stage 3 or stage 4 events after ≥24 weeks on ART in a treatment-adherent child. Immunological failure was defined as developing or returning to the following age-related immunological thresholds after ≥24 weeks on ART, in a treatment-adherent child. Study period was defined between the time of ART initiation and the date of switch or censorship. Follow-up was censored at the earliest date of the following: last clinical contact or transfer out or death.

Results: Between 06/2000 and 12/2009, 2,797 children were included. Baseline characteristics at ART initiation were: median age: 5 years; 54% with immunosuppression according to age. The most frequently prescribed first-line regimens were 2 NRTI + 1 NNRTI (61%), then AZT-3TC-NFV (13.9%). At 24-month post-ART initiation, 456 children had switched to a second-line ART (16.3%), 201 (7.2%) children had died, 17 were transferred out (0.6%) and 672 were lost-to-follow-up (24.0%). Over the 24-month period, children were classified as follows: 227 (8.1%) experienced a clinical failure alone, 120 (4.3%) had a documented immunological failure, and 2450 (87.6%) did not present either event. The 24-month probability of switch to second-line regimen was 23.3% (95% CI: 21.5-25.4) with differences across the ART-response strata: 25.3% 95% CI (23.2 -27.5), 26.4%, 95% CI (18.8-36.4), and 2.1%, 95% CI (0.8-5.5) in children with no failure, immunological failure and clinical failure alone, respectively. Median time to switch was 7 months (IQR: 3-16 months). Out of the 456 switched children, 285 (62.5%) had a first-line ART based on Nelfinavir, of whom 228 (80.0%) had to be switched to a NNRTI-based ART.

Conclusion: Switches practices were most often observed in children without any failure, probably due in part to the withdrawal of the Nelfinavir in 2007 and to the lack of access to Lopinavir pediatric formulations. Switches for clinical failure were rare and switches after an immunological failure were insufficient. Virological monitoring is still not available in routine in West Africa, but the immunological monitoring does not lead to consistent changes of ART. These gaps reveal that it is crucial to advocate for both access to monitoring tools but also to second-line ART regimen to provide adequate roll-out of paediatric ART programs.

No conflict of interest
Abstract: PP_7

Poster presentation

Community adherence support sustains improved outcomes for children on antiretroviral treatment: An evaluation in four provinces in South Africa

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Introduction: Adherence to treatment is a challenge for patients with chronic and acute illnesses, particularly for children as they are dependent on their households to ensure regular dosing. Loss to follow-up is also a considerable problem in paediatric antiretroviral therapy (ART) programs in low-income settings.

To address these challenges, a community-based adherence-support programme was implemented through patient advocates (PAs), who provide education, adherence and psychosocial support for caregivers of children on ART, through regular home visits to assess and address adherence challenges. Little data evaluating community-based support on children’s ART outcomes exists; this study evaluated the impact of PA-support in children in a low-income setting.

Methods: A retrospective cohort study of ART-naive children (< 16 years) starting ART between January 2004 and March 2010 using routine electronic data was conducted at 47 government ART facilities in four South African provinces. Children were eligible for the study if they initiated ART at least six months before site database closure. Outcome measures were death and retention in care (RIC). The vital status of patients lost to follow-up were compared with national death records, allowing corrected mortality estimates to be calculated using probability-weighted Kaplan-Meier and Cox functions. Sensitivity analyses were performed in a subgroup including only children enrolling at primary healthcare (PHC) facilities.

Results: Of 3563 children (49.3% female) evaluated, 323 (9.1%) received PA support; 3240 (90.9%) did not. Median treatment initiation age was 6.3 years (IQR: 3.3—9.5); with no differences in baseline clinical characteristics between the two groups. Children supported by PAs had significantly lower missing baseline immunological values (13.6% vs. 23.6%; P < 0.0005). The total observation time was 4670 person-years. RIC estimates after three years of ART were 91.5% (95% CI: 86.8—94.6) and 81.1% (95% CI: 78.7—83.3) in children with and without PAs, respectively (P =0.0006). Corrected mortality estimates at three years were 3.3% (95% CI: 1.6—6.8%) and 7.9% (95% CI: 6.4—9.7%) in children with and without PAs, respectively (P =0.034). In multivariate analyses adjusting for all available baseline variables, children with PAs had independently reduced mortality, AHR 0.36 (95% CI: 0.14—0.94; P=0.036), and independently reduced loss to care, AHR 0.49 (95% CI: 0.30—0.80; P =0.004). These trends remained apparent when including only children enrolling at PHC facilities; AHR for mortality 0.28 (95% CI: 0.08—0.95, P=0.042, n=1449); AHR for loss to care 0.58 (95% CI: 0.33—0.99; P=0.044, n=1507).

Conclusions: Children receiving community support had considerably better ART outcomes. The scale-up of this intervention as part of task-shifting may play an important role in the long-term success of paediatric ART programs in low-income settings.

No conflict of interest
Abstract: PP_8

Poster presentation

Adherence to Antiretroviral Therapy Among HIV-Infected Children in East Africa International Epidemiologic Databases to Evaluate AIDS (IeDEA)

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Introduction: Adherence to antiretroviral therapy (ART) is central to providing long-term HIV management that maximizes good health outcomes and minimizes the development of viral resistance. The objective of this analysis was to describe pediatric ART adherence within the clinic sites that are part of the East Africa IeDEA consortium and to investigate factors associated with increased risk of ART nonadherence.

Materials and Methods: This was a retrospective study from eight IeDEA clinical sites in Kenya, Uganda, and Tanzania. Patients included were seen between 1/2002 – 1/2009, <13 years of age, HIV-infected, had initiated ART, and had at least one ART adherence measure. Sites used 3 different adherence measures, including a 7-day quantitative recall, a 7-day categorical recall, and pill counts, collapsed into a binary measure of good vs. poor adherence per visit. Multiple adherence measures over time were averaged per person, and good mean adherence defined as ≥90% visits with good adherence. Adherence was described for various time periods after ART initiation, by site and by covariates. Enrollment time measures were censored for death or losses to follow-up using Kaplan-Meier. Mixed modeling analysis was done, fitting a generalized linear model with logit link, with good adherence as outcome, using demographics, including orphan status, as covariates, and weighted by number of children with adherence measures in each visit.

Results: Among 3,308 children, 51.9% were male. Mean age at ART initiation was 5.4 years (SD 3.4). For children with known parental status at ART initiation (N=1,962), 55.5% had one or both parents dead. Mean weight-for-age Z score (WAZ) was -2.4 (SD1.9) at ART initiation. 2,351 children had CDC classification, of which 38.3% were CDC Class C at ART initiation. Children were enrolled in HIV care for median 757.3 days (SD 473.2) and on ART for median 565.5 days (SD 436.9). 1.5% were on second-line ART at last visit. 88.2% of children had good mean adherence ≥90%, ranging from 75.7%-100% by site. Sites using pill counts to estimate adherence had the highest adherence rates. Describing adherence by time on ART, nonadherence was highest in the first 3 months on ART (11.3% nonadherence) and for after 12 months on ART (9.9-12.1% nonadherence). Poor mean adherence was more common among the youngest and oldest age groups (<12 months with 16.4% nonadherence and 11-12 year olds with 14.7% nonadherence, ages in between 10.2-12.1% nonadherence), orphans (14.8% vs. 10.5%), children on first-line ART (11.8% vs 10.5%), children with <180 days between HIV diagnosis and ART start (12.5% vs. 9.9%), children with worse nutritional status, and children with less severe disease staging. In sub-analyses modeling of mixed effects data by time on ART, orphans had persistently worse ART adherence than non-orphans.

Conclusions: For HIV-infected children on ART across East Africa, adherence remained high. Consistent adherence monitoring with validated measures and attention to vulnerable groups such as orphans are recommended.

Received support as part of a K23 award (Mentored Patient-Oriented Research Career Development Award) from NIH/NIMH (1K23MH087225-01)
Abstract: PP_9

Poster presentation

Retention of HIV Pediatric Patients Receiving Antiretroviral Treatment in Rwanda

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Background: By December 2010, 7,414 (67%) of the 11,000 estimated children in need of antiretroviral treatment (ART) in Rwanda had initiated ART. We performed a retrospective observational analysis to determine retention rates and factors associated with non-retention of pediatric patients (<15 years old) who started ART between January 2004 and September 2010 at 34 ICAP-supported sites in Rwanda.

Methods: As part of the Optimal Models of HIV Care in Rwanda Study, we used de-identified routinely-collected electronic patient-level data from 34 ICAP-supported sites (23 health centers, 8 district hospitals and 3 referral hospitals; 20/34 in rural settings). Patients received a comprehensive package of care at each monthly visit. Patients missing appointments were traced by phone or home visits to ascertain vital and transfer status, and, if found alive, to encourage re-engagement into care. Patients were considered lost to follow-up (LTF) if they were not known to have died or transferred out, and if they did not have a visit in the last 3 months of the observation period (October-December 2010). Transfers out were considered retained in care. Kaplan-Meier (KM) curves were used to assess the probability of LTF and non-retention (LTF+death) at 12 and 24 months. Cox proportional-hazards models were used to examine patient-level factors and site-level factors associated with LTF and death, accounting for clustering by site.

Results: Of the 3,784 children enrolled in HIV care at these sites, 2,371 (62.8%) children initiated ART between January 2004 and September 2010 (median age: 6.6 [interquartile range (IQR) 3.4-10.4] years old; 48.9% girls; 9.6% ≤18 months old). At ART initiation, 54.6% had a WHO stage III/IV and 21.4% were severely immunosuppressed. Among the 47.8% with a recorded weight at ART initiation, 482 (42.2%) had a CDC weight-for-age Z-score <-3. ART regimens at initiation were AZT/D4T+3TC+NVP (74.8%), AZT/D4T+3TC+EFV (13.3%) and ABC+3TC+NVP/EFV (10.5%). With a median time on ART of 2.5 years, [IQR 1.2-3.7], patient retention was 91.5%; including 427 (17.9%) that transferred to another health facility. Of those not retained, 112 (4.7%) were known deaths and 90 (3.8%) LTF. Additionally, KM estimates at 12- and 24-months for LTF were 1.8% and 2.8%, respectively, and were 5.0% and 7.0%, respectively, for non-retention. Factors at ART initiation associated with known death included younger age (AHR ≤18mPP_vs_≥5years = 4.3, CI [2.7-7.0]; AHR 18-59mPP_vs≥5_years = 1.7, 95%CI [1.1-2.7]), earlier year of ART initiation, low weight-for-age Z-score (AHR Zscore <-3_vs._Zscore_\geq -2 = 4.1, CI [1.4-11.4]), WHO stage IV (AHR stageIV_vs_I = 8.6, CI [3.2-22.7]) and severe immunodeficiency (AHR severe_vs._no evidence = 2.3, CI [1.4-3.9]). Factors associated with LTF included recent year of ART initiation and year program started providing HIV care and treatment services.

Conclusions: Retention of children with HIV who initiated ART was high at these Rwandan sites, highlighting the success of the HIV care and treatment program as well as an effective system that both documents patient outcomes (deaths and transfers) and encourages re-engagement for those LTF. Younger age, advanced HIV infection, severe malnutrition and earlier year of ART initiation were significantly associated with children’s mortality, highlighting the need for early diagnosis and treatment initiation in children with HIV.

No conflict of interest
Abstract: PP_10

Poster presentation

Prevalence, DEXA differences and risk factors for lipoatrophy among pre-pubertal African children on HAART

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Background: Lipoatrophy amongst children on HAART in Africa has not previously been investigated.

Method: We performed a cross-sectional study to determine the prevalence, DEXA differences and risk factors for lipoatrophy among pre-pubertal African children. The first 100, of 300 eligible (on HAART, 3-11 years old) clinic attendees were recruited. Lipoatrophy was graded by an expert HIV paediatrician using the European Paediatric Lipodystrophy Group classification. Durations of previous antiretroviral exposures were recorded. Dual Emission X-ray Absorbiometry (DEXA) was performed on 42 recruits and 34 HIV-uninfected controls.

Results: All 100 recruits and 34 controls were Tanner stage 1 or 2 (ie pre-pubertal). Lipoatrophy prevalence was 37% (95% confidence interval: 27.5% to 46.5%). Children with and without lipoatrophy had similar gender distribution (43% vs 52% female; p=0.41), ethnic distribution (49% vs 57% black; p=0.53), body mass index (15 vs 16; p=0.21), viral load (1.98 vs 2.23 log10 copies/mL; p=0.29) and mean CD4 (1296 vs 1223; p=0.48). Greater age (83 vs 66 months; p=0.002), overall time on HAART (56 vs 43 months; p=0.004), duration of stavudine exposure (41 vs 30 months; p=0.03) and duration of efavirenz exposure (p=0.01) were associated with lipoatrophy. A multivariable logistic regression model controlling for age and CD4% found that stavudine duration (OR=1.7 per 12months, p=0.003) was independently associated with lipoatrophy. 15 (36%) of the 42 recruits with DEXA scans, had lipoatrophy. There were statistically significant differences between children with and without lipoatrophy, as well as between children with lipoatrophy and HIV-uninfected children, in the following variables: Limb-fat-mass-to-limb-lean-mass ratio (overall p=0.004); Total extremity fat (p=0.005); Limb-fat-mass-to-total-lean-mass ratio (p=0.001); Limb-fat-mass-to-total-mass ratio (p<0.0001); Limb-fat-mass-to-body-mass-index ratio (p=0.002). There were no statistically significant differences between HIV-infected children without lipoatrophy, and HIV-uninfected children. Groups were well matched with regard to age, sex and ethnicity (p=0.24, 0.88, and 0.96 respectively).

Conclusion: Lipoatrophy was as common in pre-pubertal African children as reported among adults. Efavirenz may be associated with lipoatrophy in African children. HIV-infected children with and without lipoatrophy can be clearly differentiated by DEXA scanning. Children without lipoatrophy and HIV-uninfected children have indistinguishable DEXA findings. Given the high rate of lipoatrophy and the consequences of progression of lipoatrophy, regular screening and early switching of an offending antiretroviral is critical.

No conflict of interest
Non-Invasive Estimate of Liver Fibrosis Prevalence and Risk Factors in Latin American Perinatally HIV-infected Children

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Background: Chronic liver disease has emerged as an important cause of morbidity and mortality in adults with longstanding HIV infection in the HAART era. Little is known about the potential for liver dysfunction to develop in long-term survivors of perinatal HIV infection. APRI [aspartate aminotransferase (AST)-to-platelet ratio index] is a non-invasive measure validated for identifying significant hepatic fibrosis in HIV-hepatitis C (HCV) co-infected adults and in HIV-uninfected children with other liver disorders. APRI >1.5, a level correlated with liver fibrosis, occurs in 8% of HIV-infected adults without HCV or hepatitis B (HBV) infection. The current study uses APRI to assess for evidence of liver fibrosis in the NISDI [NICHD International Site Development Initiative] cohort of perinatally HIV-infected Latin American children.

Materials & Methods: NISDI has enrolled perinatally HIV-infected children up to 19 years old from 5 Latin American countries into an observational cohort from 2002-2009. Twice yearly study visits include medical history, physical exam and laboratory evaluation. Participants were eligible for this analysis at the first study visit for which an AST and platelet count were available. APRI was calculated as [(AST/AST upper limit of normal)/platelet count (10^9/L)] * 100.

Conclusions: Elevated APRI suggestive of liver fibrosis occurred in approximately 3% of perinatally HIV-infected Latin American children, even in the absence of HCV or HBV infection. PI-based ARV treatment appears protective while signs of inadequate HIV control appear to be risk factors for elevated APRI. More intensive evaluation, such as ultrasound transient elastography, may be warranted to validate the use of APRI as a clinically useful, non-invasive diagnostic tool, and to further characterize the presence and degree of subclinical, chronic liver disease in perinatally HIV-infected children with APRI > 1.5.

No conflict of interest

Results: Of 1032 perinatally HIV-infected children, APRI could be measured in 1012. APRI was >1.5 in 32 (3.2%, CI 2.2%-4.4%). Median (range) APRI was 0.29 (0.05-29.67). Two of 4 participants with history of HBV and 0 of 6 with history of HCV had APRI>1.5. Factors significantly associated with APRI>1.5 (compared to APRI≤1.5) included country (p<0.001), younger mean age (3.3 vs. 6.4 years, p<0.001), history of hepatitis B infection (p=0.006), use of hepatotoxic non-ARV medications (p=0.003), higher mean ALT (278 vs. 39 mIU/mL, p<0.001), higher mean log current viral load (5.2 vs 3.4, p<0.001) and log peak viral load (5.5 vs 4.6, p<0.001), lower mean current CD4 count (743 vs 1053 cells/mm^3, p<0.001) and nadir CD4 count (734 vs 1050 cells/mm^3, p=0.005), lower mean total cholesterol (122 vs. 155 mg/dL, p<0.001), and no prior antiretroviral (ARV) use (p=0.005). Rate of APRI>1.5 varied significantly by current ARV regimen (p<0.002), from no ARV (6.9%) to non-protease inhibitor (PI) regimens (3.2%) to PI-based regimens (1.6%). When cases of HBV and HCV were excluded, overall rate of APRI>1.5 was essentially unchanged at 30/1002 (3.00%, CI 2.0-4.3%).
Abstract: PP_12
Poster presentation

Incidence and risk factors for nevirapine related toxicities among HIV-infected Asian children randomized to starting ART at different CD4%


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Introduction: High baseline CD4 is a risk factor for nevirapine (NVP) toxicity in adults. This study compared the incidence of NVP toxicity between children who initiated ART when CD4 ≥15% versus CD4 <15% and identified predictive factors related to NVP-toxicity in children.

Methods: This is a substudy of the PREDICT study in which children were randomized to start ART at CD4 >15% versus <15%. Adverse events after ART initiation were collected. A multivariate logistic regression analysis was performed to assess potential risk factors.

Results: From March 2006 to October 2010, 201 HIV infected children initiated NVP-containing ART (137 started with CD4 15-24%). The median age, CD4% and HIV RNA at time of ART initiation were 7 years, 19% and 4.9 log10 copies/ml, respectively. Incidence of overall NVP-related toxicities, rash, hepatotoxicity and hypersensitivity were 32%, 14%, 22% and 7%, respectively. Median onset of NVP toxicity was 2.0 weeks (IQR: 1.64 – 8.4). 8.5% needed to substitute NVP with lopinavir/ritonavir, nefarnavir or efavirenz. Multivariate analysis showed that the overall NVP toxicity was 2.65 times higher among children with baseline CD4 ≥15% (95% CI: 1.29 to 5.45) and 1.87 times higher in Cambodians (95% CI: 1.02-3.45). The risk of NVP rash was 2.2 times greater in girls (95% CI: 0.93 to 5.18) and 2.58 times greater for children with CD4 ≥15% (95% CI: 0.92 to 7.20). Risk of NVP hepatotoxicity was 2.2 times greater for boys (95% CI: 1.06 to 4.55), 2.15 times greater for children with CD4 ≥15% (95% CI: 0.90 to 5.12) and 3.98 times greater among Cambodians (95% CI: 1.92 to 8.28).

Conclusion: One-third of HIV had NVP toxicity of which 8.5% needed ART substitution. Children who started ART when CD4 was ≥15% were at almost 5 times a higher risk for NVP toxicity. This risk should be carefully observed when implementing earlier ART treatment using NVP-based regimens.

No conflict of interest
3rd International Workshop on HIV Pediatrics
15 – 16 July 2011, Rome, Italy

ABSTRACTS
Posters
Abstract: P_1

HIV infection and adolescents

Designing a program to transition HIV-positive perinatally-infected adolescents from pediatric to adult care

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Introduction: With the scale-up of effective antiretroviral therapy (ART) programs for children in low-resource settings, HIV-infected children are surviving into adolescence and adulthood. At the Botswana-Baylor Children's Clinical Centre of Excellence (COE), the number of adolescents in care is growing. In December 2010 there were 392 13-to-15-year-olds, 249 16-to-20-year-olds, and five 21-year-olds receiving ART at the COE. Adolescents are a unique population negotiating the transition into adulthood while managing the complex stressors of HIV infection. The COE has a need for developing a process for transitioning teens into healthy adulthood and adult care.

Material & Methods: Separate focus groups were conducted with adolescents and their parents to investigate barriers to transition. Using an interdisciplinary team approach a transition plan was created.

Results: A two-phase transition plan was developed. In Phase-1 adolescents ages 13-16 will be followed to meet four goals: full disclosure, understanding of disease process, disease markers and prevention methods. Patients enter Phase-2 at age 16 if the above goals are completed and will be expected to meet Phase-2 goals: medication independence, maintain adherence ≥95%, undetectable VL, identification and enrollment in an adult HIV clinic. Achievement of these goals provides patients in Phase-2 with two options: transfer to an identified adult HIV clinic directly or transfer with interval visits at the COE. The long-term care plan for patients who decline transfer or are unable to meet Phase-1 and phase-2 goals by age 21 will be re-assessed by the COE's medical and mental health teams. For those unable to transfer despite assistance, continued care at the COE through an existing family model clinic is an option.

Conclusion: This plan represents one method of easing the transition of patients on ART from pediatric to adult care. It will be implemented with ongoing monitoring and evaluation to determine its success and adaptability to other settings.

No conflict of interest

Abstract: P_2

HIV infection and adolescents

Longitudinal evaluation of the weight of a cohort of Brazilian HIV infected children and adolescents

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Introduction: The slow weight gain is a common manifestation in children and adolescents infected with HIV, an important indicator of disease progression and also the effectiveness of antiretroviral therapy. However, the longitudinal profile and risk factors that interfere with weight gain of the Brazilian population are still poorly studied. The aim of this study was to assess longitudinally the weight of a cohort of children and adolescents infected with HIV and to identify potential risk factors that interfere with weight gain.

Material & Methods: Open cohort study conducted at a reference to assist the infected child, Faculty of Medicine, Federal University of Minas Gerais/Brazil. It was included 381 HIV-infected children and adolescents aged 0 to 19 years in regular follow-up from 1990 to 2008. The median follow-up was 75 months (0 to 199.8), with a median of 31 visits per child.
Children and adolescents accounted for 12,548 measurements of weight. We used the linear regression model with mixed effects adjusted for restricted maximum likelihood.

**Results:** The median age at diagnosis was 24 months (0.3 to 201.1), 51.7% were male, 93.4% were infected through vertical transmission. At admission, opportunistic infection and previous hospitalization were reported among 44.6% and 49.1%, respectively. Mortality was described among 11.5% of patients. None antiretroviral medication was reported by 307 (80.6%). The children who had antiretroviral therapy exposure: 48.7% did not use HAART at admission, 43.2% were using HAART with protease inhibitor (PI) and 8.1% were using HAART without PI. CDC94 C category was observed among 29.4%, followed by B category in 26.8%. The final model contains random effects in the intercept, the age and the age polynomial. The boys were heavier than girls over time. Children who were hospitalized or who died had a lower weight than those who were not hospitalized or the survivors in the same age. Those who had AIDS had smaller increases in body weight compared with the asymptomatic at admission and analysis after 5 and 10 years of follow-up showed difference in body weight of children with AIDS was 1.7 kg and 2.3 kg, respectively. After the age of 5 years, children in CDC94 B category of infection showed smaller increases in body weight compared with the asymptomatic. When compared with children and adolescents who did not use any antiretroviral therapy, children on HAART PI or without PI had smaller increases in body weight over time and have low weight after 5 years of follow-up.

**Conclusions:** The study confirmed the effect of multifatorial clinical and immunological variables that affect weight gain in children and adolescents infected with HIV. These results underscore the importance of a detailed anthropometric assessment in this pediatric population, confirming its importance in disease progression.

**No conflict of interest**

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**Abstract: P_3**

**HIV infection and adolescents**

**Host genetic determinants of innate immunity influence disease progression in HIV-1 infected children**

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**Introduction:** Defensins and Toll-Like Receptors (TLRs) play a crucial role in the host's innate immune response. While genetic polymorphisms in viral coreceptors and their ligands may influence viral entry into target cells, genetic variations in Defensins and TLRs may affect host-virus interactions and impact the disease progression.

**Material & Methods:** The study was performed in 120 perinatally HIV-1 infected children followed since birth. The median (interquartile) follow-up was 88(36-135) months. The end point was the onset of disease (stage C3) or the initiation of highly active antiretroviral therapy. Sixteen children developed early AIDS (C3 <24 months of age), 13 developed C3 from 24 to 84 months of age, and 14 developed delayed AIDS (C3 >84 months of age). The P1/P1 haplotype on the promoter of CCR5 coreceptor's gene was determined by heteroduplex analysis. Single nucleotide polymorphisms (SNPs) on Stromal Cell-derived Factor 1 (SDF1-3'G>A), Beta-defensin-1 (DEFB1 -44C>G; -52G>A), and TLR9 (1174G>A;1635A>G) genes were determined by TaqMan allelic discrimination assay.

**Results:** Genotype P1/P1 was associated with an aggressive clinical outcome, and its effect was strongest during the first 24 months of infection, being associated with a high risk of early AIDS [Odds ratio(OR) 7.3, 95% CI 2.1-12.5; p=0.002]. In contrast, SDF1 variants influenced only the late stage of infection, being the SDF1-3'GA genotype associated with a high risk of delayed AIDS [OR 4.3, 95% CI 1.2-7.8; p = 0.02]. Over time of infection, TLR9 1174AA and DEFB1 -44CG genotypes, and the DEFB1 -44G/-52G haplotype were
associated with delayed disease (p=0.030, p=0.031, p=0.047, respectively), while the TLR9 1635A/G genotype correlated with rapid disease progression (p=0.024).

Conclusions: Overall these findings suggest that effects of CCR5 and SDF1 variants depend on the coreceptor's usage of viral strains involved in rapid and delayed pediatric AIDS, while effects of DEFB1 and TLR9 genetic variants may be viral phenotype-independent.

No conflict of interest

Abstract: P_4

Complications of HIV therapy

United States Division of AIDS (DAIDS) Toxicity Tables Overestimate Neutropenia Among African HIV Exposed Uninfected Infants

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Background: Lower baseline Absolute Neutrophil Counts (ANC) values have been reported among healthy black African infants compared to other races. Use of the United States Division of AIDS (DAIDS) toxicity reference ranges which are based on non-African populations may overestimate neutropenia among African HIV-exposed uninfected (HIV-EU) infants participating in drug clinical trials.

Results: Neutropenia was overestimated at all age-bands, as high as 50% or greater in some instances. The percentage (95% Confidence Interval) of samples with 'normal' ANC according to age-band reference ranges increased with infant age: birth was 2%(2%-6%); 1-7 days was 9%(5%-13%); 8-21 days was 4%(2%-6%); 22-35 days was 10%(3%-20%); 36-56 days was 48%(42%-54%); 57-123 days was 57%(52%-62%); 124-159 days was 38%(23%-53%); and 160-200 days of age was 28%(23%-33%); chi square for trend = 88.24, p value <0.001. Similarly, these trends were observed in each of the three study drug cohorts: 6 month placebo; 6 month nevirapine and 6 week nevirapine.

Conclusion: Using the United States based DAIDS reference ranges to monitor adverse events in this drug clinical trial tended to overestimate neutropenia among these African HIV-EU infants. These findings emphasize the need to use population specific references while monitoring ANC among African infants.

No conflict of interest
Abstract: P_5

Complications of HIV therapy

Recovering of Lipodystrophy in Children after Substitution of Stavudine with Zidovudine in a NNRTI-Based Antiretroviral Therapy

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Objective: To study the improvement of lipodystrophy (LD) in HIV-infected children after substituting zidovudine (ZDV) for stavudine (d4T) in the prevailing NNRTI-based ART regimens.

Methods: We prospectively followed HIV-infected children enrolled in a prior LD study between August 2002 and October 2004 at Chiang Mai University Hospital, Chiang Mai, Thailand. Between February and September 2006, ZDV was substituted for d4T in all children. Children were evaluated by a clinical lipodystrophy check list modified from that of the European Paediatric LD study group together with waist/hip measurement at 24, 48, 72 and 96 weeks after substitution. The waist/hip ratios were converted to age- and sex-adjusted z-scores based on normal ranges among 6–15 year-old healthy Thai children.

Results: 45 LD children were enrolled. Cumulative number of children with complete improvement, partial improvement and no improvement from LD are shown in the table. By week 48 after substitution, all 9 cases with lipoatrophy had LD complete improvement, while only 11 of 26 (48%) of cases with lipohypertrophy did. But only 16 (36%) and 26 (58%) children achieved complete improvement from any type of LD at 48 and 96 weeks after substitution, respectively. At 96 weeks after changing to ZDV, 3 children did not have any improvement in their LD. In a univariate analysis, the use of a NVP-based regimen, the diagnosis of LD after >24 months of ART, and changing from d4T to ZDV within 18 months after diagnosis of LD were found to have significant association with rapid improvement; defined as having complete or partial improvement within 48 week after the substitution. In the multivariate logistic regression analysis, changing from d4T to ZDV within 18 months after diagnosis of LD was the only factor significantly associated with rapid improvement (OR 5.517, P=0.049). The use of ZDV in this setting was not found to be associated with any clinically significant hematologic effect.

Conclusion: This study demonstrated that changing from d4T to ZDV in an NNRTI-based ART among HIV-infected children and adolescents resulted in decreased severity or notable improvement.

No conflict of interest

Abstract: P_6

Complications of HIV therapy

Resistance-associated mutations among children on antiretroviral treatment in resource-poor settings: a systematic review

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Introduction: HIV-positive children are at high risk of acquiring drug-resistant viruses, which is a particular concern in settings where antiretroviral options are limited. This review explores resistance rates and patterns among children experiencing virological failure of antiretroviral treatment (ART) in developing countries.

Materials & Methods: We performed a systematic search of online databases and conference abstracts and included research papers reporting HIV-1 drug resistance after failure of first-line pediatric regimens in resource-poor settings. The proportions of
children with one or more HIV drug-resistance mutations were pooled using random effects models.

**Results:** We retrieved 1312 citations of which 30 studies reporting outcomes of 3241 children met the eligibility criteria. Among children with virological failure, virus with resistance-associated mutation(s) was isolated in 90% (95% confidence interval (CI) 88-93%). The prevalence of mutations associated with nucleoside reverse transcriptase inhibitors was 80%, with non-nucleoside reverse transcriptase inhibitors 88% and with protease inhibitors 54%. The pooled proportions of drug resistant HIV among children failing treatment varied from 75% in Central- and West Africa (95% CI 67-82%) to 96% in Asia (95% CI 91-100%). Among children receiving ART for less than a year, 76% (95% CI 69-83%) had at least one mutation at time of treatment failure. For children who failed after the first year of treatment, this proportion increased to 97% (95% CI 94-99%). The various thymidine analogue and protease mutations occurred most frequently in Latin-America.

**Conclusions:** Children experiencing virological treatment failure harbor high rates of drug-resistant virus. Our subgroup analysis points to higher resistance rates in regions with more extensive antiretroviral exposure (i.e. Asia, Latin-America). Within the protease drug class, both nelfinavir and single-dose ritonavir are associated with a higher risk of resistance development. Methods to prevent therapy failure, including adequate pediatric formulations and frequent monitoring, are urgently needed. Furthermore, donor agencies and policy makers should be pressed to prioritize the development of affordable second-line and salvage pediatric treatment options.

_No conflict of interest_

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**Abstract: P_7**

**Complications of HIV therapy**

**High prevalence of low bone mineral density among perinatally HIV-infected Thai adolescents receiving antiretroviral therapy**

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**Background:** Low bone mineral density (BMD) has been reported among 10-54% of HIV-infected adolescents and adults in developed countries. This study aimed to determine prevalence of and risk factors associated with low bone mineral density (BMD) among perinatally HIV-infected Thai adolescents.

**Materials and methods:** A cross-sectional study of lumbar spine (L2-L4) BMD as measured by dual-energy X-ray absorptiometry (DEXA) was performed using either a Hologic or Lunar machine. Clinical data, dietary consumption and levels of 25-hydroxyvitamin D level were collected at the same time. Low bone mass defined as BMD z-score ≤ -2. Vitamin D deficiency defined as 25-hydroxyvitamin D level < 20 ng/ml. Risk factors for low bone mass was analyzed using multivariate logistic regression analysis. Correlation between bone mineral density and dietary intake and vitamin D level was analyzed using Pearson Correlation Coefficient.

**Results:** From October 2010 to February 2011, 101 adolescents, 50% male, with a median age of 14.3 (range, 12.0-19.5) years were enrolled. The median body mass index (BMI) was 17.7 (range, 11.8-25.8) kg/m² with 26% had BMI < 5 percentile. Thirty-two adolescents (32%) were in Tanner stage 1-2. Median (IQR) dietary and calcium intake were 1540 (1266-1875) kcal/day and 583 (390-869) mg/day. Median (IQR) duration of receiving ART was 83.9 (52.2-104.2) months. Current
ART regimens were 50% NNRTI-based, 48% PI-based, 2% both NNRTI and PI-based, and 15 adolescents received tenofovir. Within the past 6 months, the median CD4 count was 646 (range, 159-1999) cells/mm$^3$ and 90% of adolescents had plasma HIV RNA < 50 copies/ml. The median BMD z-score was -1.8 (range, -5.5 to 2.1). The proportion of adolescents with BMD z-score ≤ -1.5, ≤ -2.0, and ≤ -2.5 were 58 %, 43 % and 27 %, respectively. The median of 25-hydroxyvitamin D level was 24.8 (range, 6.9-46.9) ng/ml and 25% had 25-hydroxyvitamin D level < 20 ng/ml. In the univariate analysis, Tanner stage 1-2 (vs Tanner 3-5), WHO clinical classification prior ART in stage 4, BMI < 5 percentile, plasma HIV RNA ≥ 50 copies/ml, receiving a PI-based regimen, and receiving tenofovir were associated with lower spine BMD z-score. In multivariate analysis, only BMI < 5 percentile, WHO clinical classification prior ART in stage 4, and receiving a PI-based regimen were associated with BMD z-score ≤ -2.

There was no correlation between serum 25-hydroxyvitamin D level, dietary intake, calcium intake with bone mineral density (p=0.363, p=0.058, p=0.736, respectively).

**Conclusion:** Almost half of perinatally HIV-infected Thai adolescents have low bone mineral density. However, low bone mass was not associated with current dietary intake and vitamin D deficiency. Further study to elucidate pathogenesis of low bone mass among HIV-infected adolescents is warranted. Preventive measures to prevent osteoporosis should be incorporated in routine care for these adolescents.

No conflict of interest

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**Abstract: P_8**

**Complications of HIV therapy**

**Kidney tubular damage in the absence of glomerular defects in HIV-infected pediatric patients on highly active antiretroviral therapy**


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**Background:** The identification of kidney disease as an important comorbidity among human immunodeficiency virus (HIV)-infected pediatric patients receiving highly active antiretroviral therapy (HAART) emphasizes the critical importance of early identification of patients at risk for kidney disease. Use of urine as a diagnostic medium may allow the noninvasive detection of incipient nephropathy in these patients.

**Aim of the study:** To evaluate renal tubular dysfunction in HIV positive pediatric patients on HAART therapy, with no evidence of renal glomerular dysfunction.

**Methods:** Design: Cross sectional study

Subjects: 20 pediatric HIV patients with normal serum creatinine and 20 healthy age and sex matched controls were enrolled in the study.

Methods: Urinary Neutrophilic gelatinase associated lipocalcin (NGAL), N-acetyl-β-D glucosaminidase (NAG), IgG, Transferrin, β2-microglobulin, α1-microglobulin were measured as indices of tubular damage, which was diagnosed when urinary concentrations of at least three tubular biomarkers exceeded the reference range.

**Results:** Tubular damage was identified in 13 patients (65%). The use of tenofovir, the most likely tubulotoxic agent, was not used in any of the patients. Proteinuria was found in 16 patients (80%). Urinary NAG and urinary NAG to creatinine ratio were elevated in 13 patients (65%). Tubular damage directly correlated to the duration of disease and inversely related to CD4 counts.
Conclusions: More than half of HIV-infected patients receiving HAART had subclinical tubular damage, which was associated with a higher incidence of proteinuria. This is the first study in medical literature on pediatric HIV patients documenting this important observation. Periodic monitoring of urinary biomarkers might facilitate the early identification of HAART patients predisposed to significant kidney disease.

No conflict of interest

Abstract: P_9

Complications of HIV therapy

Bone mineral density and clinical parameters in adolescents perinatally infected by HIV-1

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Background: We had previously shown that more than 1/3 of vertically-HIV infected adolescents, followed-up at the University Hospital of Federal University of Rio de Janeiro, have a lower body mineral density (BMD) than expected for age. The 1 year follow-up of a small group of patients (34 patients) showed that protein (g/kg/day) and vitamin D intake were positively correlated with Δ in body mineral content (BMC) of lumbar spine (LS) and total body (TB). Δ BMC LS and TB were also directly correlated to Δ weight and Δ height. The aim of this study was to assess the correlation between low BMD and clinical and immunological parameters.

Methods: 65 perinatally HIV-infected adolescents were studied. LS and TB BMD were estimated by dual energy X-ray absorptiometry (DXA). Low BMD was considered for Z-score ≤ -2. Pearson’s coefficients between the variables were calculated. Clinical and immunologic parameters analyzed were: time between birth and initiation of ARV therapy, time of undetectable viral load and CD4 > 500 cell/mm³, time of exposure to tenofovir (TDF), previous exposure to 2 NRTIs, a CD4> 500 cell/mm³ and an undetectable viral load at the time of the DXA evaluation. Analyses were conducted with the SPSS.

Results: Mean age was 17.4 ± 1.8 yrs; 55.4% females. At the time of the densitometry evaluation, six patients were not using ARV, one was being treated with 2 NRTIs, 11 with HAART + NNRTI and the remaining with HAART + PI. The majority (50 patients) had previous exposure to 2 NRTIs and 29 were currently using TDF (mean time 2.9±1.3 yrs). Mean age for ARV therapy initiation was 6.4 ± 3.9 yrs and on treatment was 11.0 ± 3.6 years. Twenty-four had an undetectable viral load (mean time 3.8 ± 2.5 yrs) and 29 had CD4+ > 500 cell/mm³ (mean time 5.7 ± 3.9 yrs). Patients that have already used TDF showed a significant lower BMD Z-score for LS (-1.82 ± 1.14 versus -1.23 ± 0.95, p=0.020) and for TB (-1.46 ± 1.05 versus - 0.79 ± 1.04, p=0.015), and there was a trend between the time of exposure to TDF and an indirect correlation with BMD Z-score for LS (r= -0.360; p=0.060) and TB (r= -0.370; p=0.052). Comparisons between groups that have already used 2 NRTIs, CD4+ > 500cell/mm³, or had an undetectable viral load didn’t show any relation to BMD. Time of CD4+ > 500cell/mm³ was positively correlated to BMD Z-score for TB (r= 0.371; p=0.048) but not with LS (r= 0.205; p=0.285). Others clinical parameters such as time between birth and initiation of treatment, time of ARV treatment and time of undetectable viral load were not correlated with BMD Z-score.

Conclusions: Patients using TDF have a significant lower BMD Z-score. Immune reconstitution, but not a virological control, have a direct impact in BMD z-score for TB.

No conflict of interest
Abstract: P_10

Comprehensive Pediatric HIV care

Non-vertical transmission of HIV in children: more evidence from the Western Cape, South Africa

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Background: In 2004 14 cases of unexplained HIV transmission were described from the Western-Cape, South Africa. Sexual abuse and contaminated blood products were excluded. Iatrogenic hospital related causes or household contact with an HIV-infected individual were implicated. We describe a further 10 cases of probable non-vertical HIV transmission.

Method: A retrospective descriptive series of 10 cases of non-vertical, non-sexual transmission of HIV to children identified by clinicians at the Tygerberg Hospital HIV Family Clinic between 2004 and 2010.

Results: One child born to HIV-infected parents was confirmed to be HIV-uninfected on DNA-PCR at 6 weeks and again at 5 months of age in the absence of breastfeeding and subsequently found to be HIV-infected. Premastication of food given to this infant by the father was reported. Nine cases had confirmed HIV-uninfected mothers, and 7 confirmed HIV-uninfected fathers. Sexual abuse was excluded by experienced clinicians. Two children were never hospitalised prior to HIV diagnosis, one of these had 2 HIV-infected household contacts. Eight cases had been hospitalised across 7 hospitals prior to HIV diagnosis, 3 as neonates. Six of 8 received intravenous antibiotics during hospitalisation and one had a tonsillectomy performed. At diagnosis, the median age was 66 months with 8 of 10 classified as WHO stage 3, and 1 each as WHO stage 2 and 4. There was significant morbidity, including 2 cases of chronic lung disease, MDR-Tuberculosis complicated by treatment-related hearing impairment, antiretroviral complications (lipodystrophy and abacavir hypersensitivity) and marked psychological impairment.

Conclusion: Nosocomial transmission not related to contaminated blood transfusions and household transmission is sporadically but repeatedly reported. Children infected with HIV via non-vertical routes are diagnosed at an advanced stage of disease and experience severe morbidity. There is a need for more extensive epidemiological studies.

No conflict of interest

Abstract: P_11

Comprehensive Pediatric HIV care

School performance of HIV infected children in care and antiretroviral treatment (ART) at the Kigali University Teaching Hospital (CHUK) in Rwanda

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Background: HIV is a neurotrophic virus and can impact children’s developmental and cognitive outcomes. We report on HIV infected children’s academic performance and compare it with national average.

Methods: We analyzed clinical, socio-economic and 2009 academic performance data of HIV infected children enrolled for comprehensive care and ART at CHUK from 2007 and 2009. Children’s package of care included regular clinical and biological monitoring, ART, opportunistic infection prophylaxis, monthly education on HIV and positive living. Extremely poor families received a school package (fees and supplies). We computed the average school promotion rate and compared it with the 2009 national average for Rwanda using Chi-square test.

Results: We included 110 HIV-infected children. 55% female; median age: 12 years
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(IQR: 9-13.75); 87% on ART; median follow-up: 23 months (IQR: 15.5-29); 55% were WHO stage 3 or 4; median baseline CD4 count: 413 cells/mm$^3$ (IQR: 198-668); median missed school days in 2009: 4 days (IQR: 3-6); 56% were older than the admitted normal ages for respective school levels in Rwanda. 90% attended primary and 10% attended secondary schools. There was no school dropout. 45 children (41%) received the school package. CHUK children's promotion rate for primary school was 70% vs 73.8% nationally (p=0.45) and 91% vs 94% nationally (p=0.6) for secondary school. Average promotion rate of children enrolled at WHO stage 1 or 2 and stage 3 or 4 was 83.7% and 62.3% respectively vs 76.5% nationally (p=0.2; p=0.01). Children’s promotion was associated with WHO stage 1/2 (83.7% vs 62.3%), p=0.001; attending monthly HIV education (78.2% vs 47.8%), p<0.001; <4 missed school days (81.4% vs 60.8%), p<0.001; age >12 years (77.6% vs 65.4%), p=0.04; better family economic status (87% vs 62%), p<0.001. CD4 cell count, ART and parents as caretakers were not associated with promotion.

Conclusion: CHUK school age HIV infected children had similar school promotion rates as the national average in 2009. However, advanced stage of the disease by the time of enrolment appeared to be associated with lower school promotion rate. While multiple factors influence educational achievement, providing comprehensive services to HIV-infected children can positively contribute to their educational success.

No conflict of interest

Abstract: P_12

Comprehensive Pediatric HIV care

Telling children their status: a systematic review of pediatric HIV disclosure in resource-limited settings.

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Introduction: In resource-limited settings, child HIV disclosure and its impact are not well understood. This systematic review aims to estimate the prevalence of child disclosure in resource-limited settings and to examine barriers to disclosure, current disclosure processes, and impact on patient outcomes.

Material & Methods: Bibliographic databases, including MEDLINE (January 1, 1966 - November 8, 2010), were systematically searched using strategy: hiv AND disclos* AND (child* OR adolesc*). Two reviewers selected all studies conducted in low- or middle-income countries (using World Bank criteria) that involved informing individuals ≤18 years of their own HIV status. Data extracted included prevalence of disclosure, associated child and caregiver characteristics, reasons for and against disclosure, and outcomes.

Results: Searches yielded 834 titles; 18 met selection criteria. Eight interviewed only caregivers and/or healthcare professionals, while ten included children. Six calculated disclosure prevalence, which ranged from 0%-30%. Child characteristics associated with disclosure included age, education level, medication responsibilities, ART duration, clinic enrollment duration, perceived ability to understand, CD4 and puberty. Barriers to child disclosure included fear child would disclose to others (9 studies), subsequent stigma (6 studies), concerns for child's emotional or physical health (7 studies), believing child unready (8 studies), and unpreparedness for questions (3 studies). Reasons favoring disclosure included improving adherence (10 studies), improving care (11 studies), increasing age (5 studies), child's questioning (4 studies), and child's right to know (3 studies). Studies endorsed disclosure models involving both caregivers and healthcare professionals. Youth reported mostly positive effects post-disclosure, with fewer long-term emotional difficulties. Three studies found adherence improved post-disclosure.

Conclusions: Though caregivers in resource-limited settings worry about child disclosure and few disclose, studies suggest positive effects for children. More research is needed to implement age- and culture-appropriate disclosure.

No conflict of interest
Abstract: P_13

Comprehensive Pediatric HIV care

Prevalence of HIV status disclosure among HIV infected children and its associated factors

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Introduction: The availability of Antiretroviral Treatments (ART) has increased the survival of the number of children who are reaching adolescent age. One of the greatest challenges that care takers and health care providers of perinatally HIV infected children face is disclosure of HIV serostatus to their infected children, a critical issue which can influence psychosocial health of the child and adherence to appointment as well as treatment either positively or negatively.

Objective: To assess the rate of HIV status disclosure of children infected with HIV and associated factors. Second, to evaluate health professionals’ and care givers’ perspective’s towards the disclosure in University of Gondar and Felegehiwot Hospitals, Amharic regional state, Northern Ethiopia.

Method: A cross-sectional hospital based study supplemented with qualitative in depth interview was conducted at Pediatrics ART units of University of Gondar and Felegehiwot Hospitals during May and July of 2009. A sample of 293 care takers of HIV infected children aged 5-15 years old were assessed. A pre-tested structured questionnaire was used to collect data, which was then analyzed using the statistical package called SPSS (Version 16.0).

Result: Most of the children were between the ages of 5 and 9, and nearly 50% were female. One-fifth of children (18.4%) learned of their HIV diagnosis around the age of 9.57. Five variables were found to be associated with children’s HIV status disclosure: (1) children who are older than 10 years old (Adjusted OR, 3.80; 95% CI, 1.77–8.11); (2) children who study at primary school level (Adjusted OR, 3.97; 95% CI, 1.08–14.55); (3) children who are on ART (Adjusted OR: 8.39: 95% CI, 3.02-23.27); (4) children who are more likely to be disclosed about their diagnosis than their counterparts; and (5) care takers who are illiterate (unable to read and write)(Adjusted OR: 8.82; 95% CI 2.28-34.06) and who are on ART (Adjusted OR: 3.59; 95% CI, 1.39-9.27) are more likely to disclose HIV status of their child to the child him/her self than their counterparts. Most of the care takers and health care providers reported that disclosure has advantages.

Conclusion: HIV status disclosure to the HIV infected children is less commonly practiced by care takers as well as health care providers in our country as that of similar studies in other countries. Factors related to children, such as age older than 10 years, children at primary school, those on ART and related to care takers who are illiterate played their role on encouraging HIV status disclosure for children who are infected. Hence, this finding can be used as a basis for further studies and design of HIV status disclosure for infected children guidance by ministry of health.

No conflict of interest

Abstract: P_14

Comprehensive Pediatric HIV care

Establish the prevalence and correlates of psychiatric illnesses among children in selected Comprehensive Centers in Kenya

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Introduction: The U.S. Department of Health and Human Services(1999) revealed that at least one in five (20%) children and adolescents had a mental health disorder at some point in their life from childhood to adolescence. The expanding literature base indicates the incidence and prevalence of emotional/behavioral problems in young children is increasing. Psychiatric disorders frequently occur in HIV infected patients but the reported prevalence rates differ considerably between studies, depending on
the stage of infection and the study population. Various factors are associated with psychiatric disorders. Psychiatric disorders affect the well-being of the HIV infected individuals and may also result in poor adherence to therapy. There are limited published data on Psychiatric disorders among infected children. The main objective of this study was to establish the prevalence and correlates of psychiatric illnesses among children in selected Comprehensive Care Centers (CCC) in Kenya.

Materials and Methods: This was a cross sectional study conducted in selected Comprehensive Care Centers in Kenya. Care takers and children were recruited. All patients were screened and scored for psychiatric disorders using the tool. WHO HIV staging, CD4 counts, and ARVs regiments were obtained from the patients records. Data was analyzed using SPSS version 16. Various statistical tests such as binary logistic regression, chi square test of association and multivariate analysis were used and P < 0.05 was considered to have significant association between variables.

Results: The prevalence of psychiatric illnesses in CCC in Kenya was 45.1%. Common types of psychiatric disorders were anxiety (29%), traumatic stress (12%), Somatisation (11%), Mood disorder (5%), defiant disorder (2%) and Obsessive compulsive disorder 1%. There was significant association between the WHO HIV staging and type of disorder P < 0.05.

Conclusion: Mental disorders are a prevalent among clients at the Comprehensive Centers in Kenya and interventions need to be put in place. Health care workers need to be equipped with relevant skills and knowledge for effective early diagnosis and management of among HIV infected psychiatric children. Proper Government policies, guidelines and strategies need to be put in place to be able to effectively manage the clients. Health care workers must endeavor to reduce the incidence and prevalence of psychiatric illnesses in Kenya. Families and communities, working together, can help children with mental disorders. A broad range of services is often necessary to meet the needs of these children and their families though services for young people with serious emotional disturbances are unavailable, unaffordable, or inappropriate.

No conflict of interest

Abstract: P_15

Comprehensive Pediatric HIV care

Routine pediatric HIV testing in an outpatient department in Durban, South Africa

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Introduction: Limited access to HIV testing for children impedes early diagnosis and access to ART. Testing opportunities can be increased by offering routine HIV testing as part of outpatient care. Our objective was to evaluate the uptake, acceptability, and yield of routine pediatric HIV testing in an urban outpatient clinic in Durban, South Africa.

Materials and Methods: We assessed the number of psychiatric patients (0-15 years) who underwent HIV testing upon physician referral during a ‘baseline’ period. We then implemented a routine, voluntary HIV testing program for patients, regardless of symptoms. Parents/caretakers were offered free rapid fingerstick HIV testing for their child. For patients <18 months, the biological mother was offered HIV testing and HIV DNA PCR was used to confirm the infant’s status. Children known to be HIV-infected and those presenting without a parent/primary caretaker were ineligible.

Results: From May-September 2010, 953 patients registered for outpatient care during the baseline period. Of the 124 (13%) patients who underwent HIV testing upon physician referral, 21 (17%) were HIV-infected. From October-December 2010, 314 eligible patients registered for care during the routine testing period. Of these, the parents/caretakers of 248 (79%) patients were approached for testing and 186 (75%) enrolled. Among those who underwent HIV counseling, 152 (82%) accepted testing for their child or themselves (biological mothers of infants <18 months). There were 12 (7.9%) newly-identified HIV-infected children (median 6.5yrs, 42% female).
Abstracts

The estimated HIV prevalence in patients who would not have been tested without a routine HIV testing program was 3.5%. Routine testing identified 6 new HIV cases per month compared to 4 during the ‘baseline’ period (p=0.06).

Conclusions: Routine HIV testing in an outpatient clinic has high testing uptake, is acceptable, and is a high yield strategy for identifying HIV-infected children in an epidemic area. Efforts should be made to scale-up pediatric HIV testing in outpatient clinics.

No conflict of interest

Abstract: P_16

Comprehensive Pediatric HIV care

Neuropsychiatric manifestations and cognitive functioning in South Indian children with HIV/AIDS

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Introduction: Although HIV infection is well known to cause neuropsychiatric manifestations and cognitive dysfunction, studies among Indian children are scarce. In the HAART era, concerns regarding long term morbidity have assumed prime importance.

Methods: The study was a descriptive study conducted at the Pediatric HIV clinic of the Institute of Maternal and Child Health, Calicut in Kerala, South India over a period of one year from October 2009. Children in the age group of 6 to 12 years were evaluated after a diagnosis of HIV infection was made using standard diagnostic guidelines. Data was entered in a semi structured proforma after the parents / care givers had given written valid consent. Detailed neurological evaluation was done. Psychiatric diagnosis was done based on DSM IV TR diagnostic criteria. General intellectual functioning was assessed using the Seguin formboard. The Academic performance was evaluated in three domains using the Academic Evaluation Scale. Data was analyzed using SPSS version 10 software.

Results: A total of 42 HIV positive children including 20 girls were enrolled in the study. All children had acquired HIV infection perinatally. HIV encephalopathy was present in 33% of children. The common neurological manifestations included developmental delay, regression of acquired milestones, microcephaly and focal neurological deficits. cerebellar signs were present in 4% of children. 21% of children had features of ADHD and 33% had learning disorder. Even though general intellectual impairment was seen only in 15% of children, 90% of them did not have age appropriate reading ability and none of them had age appropriate writing or mathematical ability. A positive correlation between neuropsychiatric manifestations and duration of illness and duration of ART was observed.

Conclusion: Neuropsychiatric manifestations are common in children with perinatally acquired HIV infection. Majority of these children have poor academic performance. Pediatricians looking after these children should be able to identify and treat neuro-cognitive problems at the earliest.

No conflict of interest

Abstract: P_17

Comprehensive Pediatric HIV care

Health system strengthening: A strategy for increasing Pediatric uptake of HIV services in rural areas

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Background: This paper aims to describe the effectiveness of health systems strengthening in increasing uptake of pediatric HIV services in rural settings of North central Nigeria. Management sciences for Health (MSH) currently delivers prevention, care and treatment services for HIV/AIDS through USAID funding in the rural and hard to reach communities of Kwara state, North central Nigeria. Pediatric uptake of services in these
rural clinics experience challenges which include poor synergy between HIV and child health programs, low community awareness, few trained health workers in the area of pediatrics HIV, poor follow up of HIV positive women and their babies, poor coordination of ART clinic appointment system with adult caregivers and lack of child friendly centers. Thus the need to strengthen health systems for increased uptake of pediatric HIV services.

Method: As part of its effort to increase uptake of pediatric services, MSH supported the state government to build the capacity of health care workers in Pediatric HIV services. Community volunteers were also trained on home base care with orphans and vulnerable (OVC) service delivery, aimed at empowering the volunteers to assess children and make referrals accordingly during home visits. Community outreaches were also conducted within 23 communities to create awareness on prevention of mother to child transmission. Health facilities were also mentored on integration of Pediatric HIV care into routine Child care services. There is also a bi-monthly activity known as children health day where mothers in the community bring their children to the health facility for health checks during which mothers are counseled on care of their children. A child friendly room was also established and furnished with toys, games and audio visual materials to serve as a relaxation center for the children and also to ease the stress of mothers and other care givers while they are waiting to be attended to by clinicians. The appointment dates of mothers and other caregivers were harmonized with that of their children as this will help children adherence to clinic appointments. The tracking system was further strengthened for proper follow up of HIV positive mothers and their children at the point of enrollment and also during home visits.

Results: Over a period of twelve months, 30 health care workers were trained on infant feeding and early infant diagnosis, 20 volunteers were also trained on HBC/OVC service delivery, 115 children were tested for HIV during the bimonthly children health day. The appointment dates of mothers and other caregivers were harmonized with that of their children as this will help children adherence to clinic appointments. The tracking system was further strengthened for proper follow up of HIV positive mothers and their children at the point of enrollment and also during home visits.

Conclusions: Increasing pediatric uptake of services in rural settings needs a multi model approach which includes integration, strengthening of community-facility linkages and capacity building for health care workers and volunteers.

No conflict of interest

Abstract: P_18

Comprehensive Pediatric HIV care

Prematurity is not a risk factor for early mortality in HIV-infected infants on antiretroviral therapy.

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Background: Maternal immunosuppression, delayed initiation of HAART, and low baseline CD4% are associated with early mortality in HIV-infected infants. We investigate the effect of prematurity (birth before 37 weeks gestation) on mortality of HIV-infected infants receiving ART in Soweto, South Africa.

Methods: A cohort study was undertaken of all HIV-infected infants born in 2009 who initiated HAART in infancy (age less than one year) at a treatment access clinic in Soweto. Data was collected on demographics, infant baseline CD4 and viral load (VL), infant HAART initiation, infant feeding, maternal CD4 count between 24 weeks gestation and 3 months postpartum, maternal PMTCT and estimated infant gestational age. Infant mortality and loss-to-follow-up were assessed at one year of age. Statistical analyses included two-sample t-test, chi-square test of proportions and logistic regression.

Results: Over a period of twelve months, 30 health care workers were trained on infant feeding and early infant diagnosis, 20 volunteers were also trained on HBC/OVC service delivery, 115 children were tested for HIV during the bimonthly children health day. The appointment dates of mothers and other caregivers were harmonized with that of their children as this will help children adherence to clinic appointments. The tracking system was further strengthened for proper follow up of HIV positive mothers and their children at the point of enrollment and also during home visits.

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Comprehensive Pediatric HIV care

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Results: During 2009, 145 of 168 eligible HIV-infected infants were initiated on HAART and 22% (n=32) had been born premature. Median
age at HAART initiation was 9.7 weeks (IQR:7.8-13.9). Premature infants had a significantly lower baseline CD4% compared with term infants (26.6% vs. 31.5%, p=0.025). There was no difference in baseline VL (p=0.89), age at HAART initiation (p=0.22) and the proportion of those formula fed (premature 80%, n=24; term 79%, n=88 p=0.93). Interestingly most mothers with CD4 <200cells/ul had a term baby (22/27 (81%)) 12 (8%) infants were lost-to-follow-up and mortality was 8% (12/145: term 6/95(6%); preterm 4/32 (13%); unknown gestational age 2/18 (11%) Median age at death 20.5 weeks (IQR: 14.2-27.4) There was no difference in the odds of mortality between premature and term infants (OR:1.9, CI:0.5-6.7). None of the variables: Infant gestational age, baseline CD4/VL, infant feeding method, maternal CD4, maternal PMTCT, predicted mortality.

Conclusion: With early ART initiation, premature HIV-infected infants in Soweto, South Africa are not at increased risk of mortality compared to term babies. Further research is required to determine mortality risk factors.

No conflict of interest

Abstract: P_19

Comprehensive Pediatric HIV care

Factors Affecting Disclosure Of Serostatus To Children Attending Jinja Hospital Paediatric HIV Clinic, Uganda

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Background Disclosure is an important public health strategy that offers benefits to the infected individual and public. Identifying factors that affect disclosure of serostatus in children will help improve the process of disclosure.[e1] Objective of the study was to determine prevalence of and factors affecting disclosure of HIV sero status to children attending Jinja Hospital Paediatric HIV clinic.

Methods and statistical analysis: A cross sectional study was carried out among 174 caretakers of children aged 5 to 18 years. 20 children disclosed to were interviewed and key informant interviews conducted for ten health workers. Data was collected on socio-demographic factors, disclosure status, health facility factors, fears and perceived benefits of disclosure by administering a questionnaire. Prevalence of disclosure was expressed as a percentage[e2] . Frequency distribution, cross tabulation and logistic regression was done with disclosure as the dependent variable. Thematic based analysis was done for data collected from health service providers.

Results: Overall prevalence of disclosure was 56.3%, complete disclosure was 43%. Among those not disclosed to, non-disclosure was 19% and deception 14%. Factors associated with disclosure of serostatus to a child were age of child (X² 37.4 df 1 p< 0.001), child being on antiretroviral therapy (OR 2.0 CI 1.1-3.6 p=0.024), duration on ART (X² 8.6 df 3 p 0.03), child attending a psychosocial support group (OR 7.4 CI 3.6-15.3 p < 0.001) and primary caretaker having tested for HIV (OR 2.8 CI 1.4-5.6, p=0.005). Average age at disclosure was 9.2 years. Common reasons for disclosure were being advised by health worker, attending psychosocial support groups and being asked by the child. Reasons for non disclosure were child being too young, fears of stigma and that child may disclose. Main problem encountered in disclosing was caretaker not knowing what to say. Perceived benefits were improved adherence (87%) and relief of knowing the truth. There were no appropriate guidelines on disclosure and only half of health providers had training on disclosure of HIV serostatus to children.

Conclusion: The overall prevalence of disclosure was low complete disclosure was 43.1%. The factors that were significantly associated with disclosure were age, attending psychosocial support group, being on ART and primary caretaker having tested for HIV. The guidelines on disclosure are very brief, and are poorly disseminated to health workers, and only close to 50% of the health workers had actually been trained on disclosure to children.

No conflict of interest
Abstract: P_20

Comprehensive Pediatric HIV care

Scale up of Early Infant Diagnosis and pediatric ART: Systematic analysis of the EID data and implementation of specific interventions to increase ART

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Introduction: Early Infant Diagnosis (EID) of HIV-infected infants is crucial in order to initiate antiretroviral treatment (ART) and decrease mortality. Although Tanzania has made considerable progress in scaling up PMTCT, an estimated 14,000 infants annually are still HIV-infected (of which, less than 1,000 are identified). To address this problem, the Elizabeth Glaser Pediatric AIDS Foundation, in collaboration with Ministry of Health, implemented EID services integrated into child health clinics at 165 sites in four regions from 2008 to 2010.

Methods: Routine EID data (uptake, turn-around time (TAT) from sample collection to result received at site, results given to parents/guardians, referral, enrollment and ART initiation of infected infants) were collected and analyzed. Baseline quarterly cohort analysis showed TAT of >2months, low report back rates to parents as well as poor initiation of infected infants on ART. The following interventions were implemented to address these issues:
- Q3 2009: Delegating sample/result transportation from district authorities to a courier service.
- Q1 2010: Staff sensitization on the importance of reporting results to caregivers and initiating ART.
- Cooperation with Central Laboratory to reduce TAT in two regions (database, data clerk, technical support implemented).

• Since Q3 2009: Implementation of a clinical mentoring system in primary health facilities, focusing on treatment of young children. Experienced HIV clinicians selected as mentors from district hospitals received didactic and hands-on training in comprehensive pediatric HIV treatment as well as mentoring. District authorities received support for transportation of mentors to LLHF

Results: Program performance between July 2009 and September 2010 was evaluated indicating that EID uptake increased (952 to 1385 exposed infants/quarter or 24.7% to 36.6% of all exposed infants), TAT reduced to two weeks in central lab supported-regions (four-six weeks in other two regions), percentage of guardians/parents receiving positive DBS results increased from 43.2% to 60.7% (following implementation of site-sensitization and clinical mentoring the rate increased to 71.6% (higher in regions with short TAT)) (89.3:67.6%). The overall transmission rate was 9% with a slight decrease over time. Most positive children were enrolled into care (320/324) and clinical mentoring increased percentage of infants receiving ART from 48% to 97.4%.

Conclusion: The critical review of indicators allows development of specific intervention. A combination of services increases quality of care for infected infants. Especially structural efforts will be needed to link follow-up of women with HIV and their infants to EID programs(decentralization of EID services) and to care and treatment services.

No conflict of interest
Abstract: P_21

Comprehensive Pediatric HIV care

An approach towards enhancing Mother Support Groups outreach in an urban setting.

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Background: According to 2009 sero-behavioral study, Sofala province has one of the highest HIV prevalence in Mozambique (13.1% among age group 15-24 years). Overall under-five mortality in the country also remains high (141/1000) as well as in Sofala province (138/1000). The 2008 child mortality study showed that 9.9 per cent of deaths among 0-5 years old were due to AIDS. Expansion of HIV-positive mother support groups is an integral part of the PMTCT programme developed by the Ministry of Health since 2004, with support from UNICEF and partners in the effort to reduce the cases of pediatric HIV. The aim is to provide psychosocial support to pregnant women and mothers living with HIV/AIDS, helping them to cope with the socio-cultural barriers, stigma and discrimination, and to follow antiretroviral treatment. Poor adherence is a major predictor of treatment failure, progression to AIDS and death. Urban settings face greater challenges in tracking HIV patients together with health system constraints related to organizational and human resource capacity. In this context, some of these groups are involved in the active search of women and children who are defaulting from services

Material and Methods: Since 2008, there has been a program to support a Community based organizations’ (CBO) of peer to peer mothers later called Kuplumussana (meaning‘helping each other’) to strengthen the activities of Pediatric day Hospital in Beira City. In 2010 the program expanded following the decentralization of ART treatment targeting 2 more health centers in Beira City. With the aim to evaluate the impact of interventions implemented by this HIV mother support group (MSG) and learn how they could enhance their activities to pediatric HIV care and treatment and its linkages with PMTCT, a review was conducted based on 2010 annual report of the association to analyze its contribution to the identification and tracking of defaulter HIV exposed children.

Results: A MSG composed of 29 mothers have enhanced their activities by actively tracking defaulters, conducted regular visits to HIV exposed children who defaulted for more than 3 months in the “At Risk children consultation” (RCC). As a result, from January to December 2010, a total of 2,692 home visits were conducted to catchment areas of 3 health facilities, resulting in 1767 children identified in the community. Among these, 414 are children who were lost for follow up due to several reasons (death, transferred to other health facilities or districts, or discharged for due to confirmation of HIV negative status). Of the remaining 1,353 children, 732 (54.1%) were reintegrated and actively participating in the RCC.

Conclusion: The MSG Kuplumussana experience has shown that good coordination of CBO with health facilities and supporting NGO can be a strategic way to recover defaulters. This demonstrates that MSG can add value for boosting care and support for pediatric HIV in Health facilities. Additionally these groups can evolve into associations and play a much higher role in supporting the involvement of PLWHA into the response to the epidemics and in building self-sustainability.

No conflict of interest

Abstract: P_22

Comprehensive Pediatric HIV care

Neurodevelopmental delay among HIV-infected preschool children receiving antiretroviral therapy in Soweto, South Africa.

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Background: Neurodevelopmental delay has been documented in up to 97.5% of HIV-infected children (18-36 months) in Soweto who were not yet on ART. With growing numbers of children in South Africa being successfully treated with antiretroviral treatment (ART), the effects of ART on neurocognitive functioning in children require investigation. The objective of this study was to determine the extent of neurodevelopmental delay in stable HIV-infected preschool children (aged 5-6 years) receiving ART and compare it to an apparently healthy (unconfirmed HIV-negative) group of preschool children.

Methods: This was a cross-sectional comparative study. Thirty HIV-infected preschool children (virologically and immunologically stable on ART for >1 year) were conveniently sampled from 350 eligible children on ART at the Harriet Shezi Children's Clinic in Soweto, Johannesburg. The comparison group comprised thirty well-nourished preschool children attending the Lillian Ngoyi Primary Health Care Clinic in Soweto (Johannesburg) for routine immunisations. Each child was assessed using the Griffiths Mental Development Scales-Extended Revised Version (GMDS-ER), at a single point in time. Six domains (Locomotor, Personal-Social, Hearing and Speech, Eye-Hand, Performance and Practical Reasoning) were examined and individually scored. An overall raw score and General Quotient (GQ) was derived from the average of the individual scores.

Results: Both groups were similar in age, gender, geographical area and socioeconomic status. However, there was a significant difference between primary caregiver type in the two groups; 70% of the HIV-infected children had either one or both parents as the primary caregiver compared to 93.3% in the comparison group. The overall developmental z-scores on GMDS-ER were <-2 (indicating severe delay) in 27 (90%) children in the HIV-infected group compared to 23 (76%) in the comparison group (p=0.166). Although, the comparison group of apparently healthy children performed far below expected levels, they scored consistently better than the HIV-infected group. Mental handicap (overall GQ<70) was evident in 46.7% of children in the HIV-infected group compared to 10% in the comparison group (p=0.002). There was a 7.88-fold increased likelihood of severe delay in the HIV infected group. The HIV-infected group and comparison group had significantly different (p=0.001) mean overall GQ scores of 70 (95% CI: 66.0-74.0) and 78 (95% CI: 75.6-80.5), respectively, with lower mean scores in the HIV-infected group in all individual domains. Both groups performed worst in the language and visual-spatial domains.

Conclusion: Although HIV-infected children performed worse than their apparently healthy peers in Soweto, both groups are likely to have significant problems at school. Early initiation of ART in HIV-infected infants may improve cognitive functioning among this group, however, intervention strategies which optimize early cognitive development for all children in the area, need to be urgently considered.

No conflict of interest

Abstract: P_23

Comprehensive Pediatric HIV care

Children living with HIV in Ukraine: establishing a new paediatric cohort study

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Background: Ukraine is the epicentre of the HIV epidemic in Eastern Europe, with the world’s most rapidly accelerating HIV epidemic. However, data are lacking on the natural and treated history of HIV infection in children living in this lower middle income country.

Materials and methods: Enrolment in this new prospective paediatric HIV cohort study started in February 2011. HIV-positive children (<18 years old) cared for at five HIV/AIDS Centres in Ukraine are eligible for enrolment, with informed parental consent. At enrolment, anonymised retrospective and current visit data are collected, from medical note review dating back to HIV diagnosis, including socio-demographic, clinical, treatment and laboratory
test data. Follow-up data will be collected at subsequent visits.

**Results:** By April 2011, 206 children had been enrolled (50% female), of whom 199 (97%) acquired HIV vertically and 3 (1%) via contaminated blood products (4 unknown). Median age at enrolment was 7.2 years (IQR 4.1, 10.0). All but two children had been born in Ukraine. Among the vertically-infected, median age at HIV diagnosis was 20.4 months (range, 2 months to 13.5 years). A quarter of children (43/164) were known to have mothers with an injecting drug use history and 16% (15/96) had mothers with diagnosed HIV/HCV coinfection; overall, 4.2% (5/118) children aged >18 months were HIV coinfected, but a third had not been tested. The mothers of 64 (32%) vertically infected children were known to have received antiretroviral prophylaxis/treatment (39 ZDV, 12 sdNVP, 11 ZDV+sdNVP, 2 HAART); 43% (85/199) of children had received neonatal prophylaxis (21 sdNVP, 50 ZDV and 14 both). Nearly a quarter of children (23%, 44/193) had received an AIDS diagnosis, at a median age of 6.1 years (IQR 1.5, 8.3); the most common AIDS indicator diseases were HIV encephalopathy (n=14), PCP (n=6) and extrapulmonary TB (n=6). WHO clinical stage was available for 142 children to date: 30 (21%) were at stage 1, 27 (19%) at stage 2, 41 (29%) at stage 3 and 44 (31%) at stage 4. At their most recent measurement, 20% of children (40/195) had a CD4 percentage below 25%, 56% (106/190) had a viral load ≤50 copies/ml and 32 (17%) had a viral load between 50 and 999 copies/ml. Most (90%, 177/196) children were currently receiving ART and median age at ART initiation was 3.9 years (IQR 1.3, 6.4); 41% (73/177) children had switched ≥1 regimen to date. Most (58%, 117/206) children were living with their parents, with four living in institutions and the remainder with other family members.

**Conclusions:** These preliminary findings demonstrate that nearly half of the children were infected despite PMTCT prophylaxis, that one in four has AIDS and that most are receiving ART. This raises concerns regarding the quality of ARV prophylaxis for PMTCT and adherence that need to be further studied. Enrollment and follow-up are continuing and will allow us to characterise this population for the first time, including HIV disease progression, treatment, growth and co-infections.

**No conflict of interest**

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**Abstract: P_24**

**Comprehensive Pediatric HIV care**

**HIV-infected Ugandan children suffer high rates of malnutrition and minimal recovery following the initiation of antiretroviral therapy.**


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**Background:** HIV-infected children in Africa suffer high rates of wasting and stunting, but there are limited longitudinal data about what factors lead to improvements in growth. We sought to characterize the extent of growth recovery that followed the initiation of ART in a cohort of rural Ugandan HIV-infected children.

**Materials & Methods:** Subjects were HIV-infected children from an ongoing clinical study in Tororo, Uganda that were either ART-suppressed (HIV RNA < 400 copies/ml) on first line therapy or ART-naive and initiating ART per WHO guidelines. Weight-for-age (WAZ), height-for-age (HAZ), and weight-for-height (WHZ) Z-scores were calculated monthly; CD4 count and percentage, HIV RNA and hemoglobin levels were obtained every 12 weeks. A measure of socioeconomic status (SES) was generated using principal components analysis of household assets. Associations between WAZ, HAZ or WHZ and enrollment age, CD4 count and percentage, HIV RNA and hemoglobin levels were obtained every 12 weeks. A measure of socioeconomic status (SES) was generated using principal components analysis of household assets. Associations between WAZ, HAZ or WHZ and enrollment age, CD4 count and percentage, HIV RNA and hemoglobin levels were obtained every 12 weeks. A measure of socioeconomic status (SES) was generated using principal components analysis of household assets. Associations between WAZ, HAZ or WHZ and enrollment age, CD4 count and percentage, HIV RNA and hemoglobin levels were obtained every 12 weeks. A measure of socioeconomic status (SES) was generated using principal components analysis of household assets. Associations between WAZ, HAZ or WHZ and enrollment age, CD4 count and percentage, HIV RNA and hemoglobin levels were obtained every 12 weeks. A measure of socioeconomic status (SES) was generated using principal components analysis of household assets. Associations between WAZ, HAZ or WHZ and enrollment age, CD4 count and percentage, HIV RNA and hemoglobin levels were obtained every 12 weeks. A measure of socioeconomic status (SES) was generated using principal components analysis of household assets. Associations between WAZ, HAZ or WHZ and enrollment age, CD4 count and percentage, HIV RNA and hemoglobin levels were obtained every 12 weeks. A measure of socioeconomic status (SES) was generated using principal components analysis of household assets. Associations between WAZ, HAZ or WHZ and enrollment age, CD4 count and percentage, HIV RNA and hemoglobin levels were obtained every 12 weeks. A measure of socioeconomic status (SES) was generated using principal components analysis of household assets.
Abstract: P_25

Comprehensive Pediatric HIV care

Improving record of anthropomorphic measures in clinical records of HIV infected children in Mozambique

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Introduction: Routine monitoring of weight and height of HIV infected children is essential for good clinical care. Missing data on weight and height is a significant challenge in efforts to identify malnourished HIV infected children in health facilities in Mozambique. ICAP, which provides technical support and HIV services in Mozambique, developed a tool to improve recording of anthropomorphic measures in pediatric patient charts as a strategy to improve identification of malnourished children.

Material & Methods: In efforts to support the National Nutrition Program for HIV infected children, ICAP implemented a “package” of support to Health Facilities (HF) including training and staff mentoring, providing job aids, registry books and pediatric scales. Despite those efforts it was noted that recording of anthropometric data was still a challenge. To address this issue, ICAP supported the development of a sticker to register weight and height data on the exterior of the clinical chart for all newly enrolled HIV infected children. The HIV clinic nurses responsible for measuring and weighing children were trained on how to fill in the sticker and it was added to the file at the enrollment visit. Data from the patient charts at ICAP sites are entered into a site level electronic database. Completeness of weight and height measurements for newly enrolled children in health facilities in Mozambique was assessed from the period before and after implementation of the support package at a rural health facility in Gaza Province, Mozambique.

Results: In the 3 months prior to the use of the sticker, the percentage of children newly
enrolled in care with registered height and weight data was 18% (8 of 44 patients) and 68% (30 of 44) respectively. After the strategy implementation, registered height and weight percentage among children newly enrolled in care were 79% (30 of 38 patients) and 95% (36 of 38) respectively.

Conclusion: Regular recording of anthropometric data is an important step to improve identification and treatment of malnourish children and consequently improving ART outcomes. The use of a sticker for recording height and weight measures at the enrollment visit appears to improve the completeness of these data for children entering HIV care and treatment services.

No conflict of interest

Abstract: P_26

Comprehensive Pediatric HIV care

Effect of baseline immunodeficiency on growth recovery after starting combination antiretroviral therapy in HIV positive South African children

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Introduction: Growth failure is common among HIV-infected children. We determined the effect of severe immunodeficiency at initiation of combination antiretroviral therapy (cART) on growth recovery in the first 2 years of treatment.

Materials & Methods: We analyzed routine data on children age <15 years who were underweight (weight-for-age z-score [WAZ] <-2) and/or stunted (height-for-age z-score [HAZ] <-2) at time of cART initiation. All children initiated cART between April 2004-March 2008 at Harriet Shezi pediatric outpatient HIV clinic in South Africa. Growth recovery was defined as achieving a WAZ or HAZ >-2 SD. Degree of immunodeficiency at cART initiation was defined as “severe” or “not severe” according to the 2006 WHO guidelines. The CD4 thresholds for severe immunodeficiency were <25% for children ≤11 months, <20% for children 12-35 months, and <15% for children >35 months. We used the Kaplan-Meier estimator to generate survival functions and fit a Cox proportional hazards model stratified by degree of baseline growth failure (z-score <-3 ‘severe’ and z-score between -2 and -3 ‘moderate’) and adjusted for age, viral load and TB treatment. Children were followed until 2 years of cART, death, loss to follow-up (LTF) (>3 months without clinic visit), or March 31, 2008. In a sensitivity analysis, we quantified the association between WHO clinical stage (4 versus < 4) at cART initiation and growth recovery.

Results: Of the 2406 children who initiated cART, 1467 (61%) had growth failure at time of cART initiation. Most children (907, 38%) were underweight and stunted, 125 (5%) were only underweight, and 435 (18%) were stunted with normal weight. Eighty percent of underweight children achieved normal weight within 2 years of follow-up, with a median time to recovery of 270 days; 90 died and 110 were LTF. Among stunted children, 58% achieved length/height recovery, with a median recovery time of 686 days; 84 died and 164 were LTF. In unadjusted analyses, severe immunodeficiency at cART initiation was not associated with weight recovery (hazard ratio (HR) 1.06, 95% CI 0.85-1.33) or length/height recovery (HR 1.07, 95% CI: 0.84-1.35). Adjustment for confounding did not change the associations: HR 1.08 (95% CI: 0.87-1.36) for weight recovery and 1.09 (95% CI: 0.86-1.38) for length/height recovery. Modification by degree of growth failure at cART initiation was not significant: adjusted HRs 1.04 (95% CI: 0.78-1.37) and 1.28 (95% CI: 0.88-1.86) for moderately and severely underweight children, respectively; 1.29 (95% CI: 0.96-1.73) and 0.96 (95% CI: 0.65-1.42) for moderate and severely stunting, respectively. Using clinical stage as the exposure confirmed the lack of association between severe immunodeficiency and growth recovery: unadjusted HR 1.10 (95% CI: 0.90-1.34) for weight recovery and 1.08 (95% CI: 0.85-1.38) for length/height recovery.

Conclusions: Despite two years of cART, a substantial proportion of children fail to achieve growth recovery, particularly length/height recovery. This highlights the need for early initiation of cART, prior to presence of growth

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failure. Our analysis does not support an association between severe baseline immunodeficiency and growth recovery. Further research to determine risk factors for failure of growth recovery on cART is needed to design appropriate intervention.

No conflict of interest

Abstract: P_27

Comprehensive Pediatric HIV care

Lipid changes in HIV-infected, HIV exposed uninfected (EU) and HIV unexposed control infants during the first year of life

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Background: HIV infection has been associated with changes in lipid levels, specifically decreased total cholesterol (TC), high density lipoproteins (HDL), low density lipoproteins (LDL) and increased triglycerides (TG). However, there are few longitudinal data regarding lipid changes in HIV-infected, HIV-exposed uninfected and unexposed children.

Methods: In this prospective analysis, lipid levels in HIV unexposed, HIV exposed uninfected (EU) and HIV-infected treated infants recruited in Nairobi at between 1999-2005 were assessed using cryopreserved specimens. Total cholesterol (TC), high density lipoprotein (HDL), low density lipoprotein (LDL), and triglycerides (TG) were measured at 6 months and compared between the three cohorts. Changes in lipids since baseline were assessed using paired t-tests. Differences between cohorts at each time point were assessed using linear regression.

Results: There were 35, 103 and 65 infants in the unexposed, EU and HIV-infected cohorts respectively. The median birth weight was 3.2kg (IQR 2.8, 3.5), 3.3kg (IQR 2.9, 3.5) and 3.0kg (IQR 2.8, 3.4), respectively and did not differ significantly between the groups. At birth, mean lipid levels of the unexposed were higher than either the EU or HIV-infected. The TC was 139.2 vs 65.5 vs. 64.8 mg/dl; in the unexposed vs EU vs HIV-infected respectively. HDL was 29.4 vs 18.7 vs 17.5 mg/dl; LDL 83.4 mg/dl vs 39.4 vs. 38.1 mg/dl; and TG was 98.9 vs 38.1 vs 41.7 mg/dl. For each lipid outcome, the levels of the HIV infected and EU were comparable (all p-values>0.4); the unexposed had significantly higher levels of each lipid than either the EU or HIV infected (all p-values<0.001). Between birth and 6 months the rate of change in lipid levels differed significantly within and between cohorts. Among the 15 unexposed infants with 6 month follow-up there was an increase in mean lipid levels in TC to 177.9 mg/dl (p=0.7), LDL to 112.6 mg/dl (p=0.115), HDL to 69.7 mg/dl (p=0.003), and decrease in TG to 77.3 mg/dl (p=0.027). Among 103 EU infants all measures increased significantly: TC to 141.6 mg/dl (p<0.001), LDL to 86.4 mg/dl (p<0.001), HDL to 27.6 mg/dl (p<0.001) and TG 139.3 mg/dl (p<0.001). Among the 28 HIV-infected infants with 6 month follow-up, similarly all measures increased significantly: TC to 133 mg/dl (p<0.001), LDL to 73.3 mg/dl (p<0.001), HDL to 47 mg/dl (p<0.001) and TG 179 mg/dl (p<0.001). At 6 months, the infected and EU had comparable TC (p=0.134), and HDL (p=0.3) and these levels were both lower than in the unexposed (p<0.001). LDL levels, in the HIV-infected were lower than in the EU (p=0.017) and unexposed (p=0.003); triglycerides levels, in the unexposed were lower than in the HIV-infected (p<0.001) and EU (p=0.003).

Conclusion: At birth the mean lipid levels of HIV unexposed control infants were significantly higher than EU and HIV-infected infants. However, there were marked increases in lipid levels during the first 6 months of life in EU and HIV-infected infants. Both HIV-exposure and infection may influence early lipid levels. It will be important to further characterize the influence of nutrition, growth, HIV, and ART on lipid metabolism during infancy.

No conflict of interest
Abstract: P_28
Treatment of pediatric HIV infection
Evaluation of viral load thresholds for predicting new WHO Stage 3 and 4 events in HIV-infected children receiving combination antiretroviral therapy

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Introduction: Determining the viral load (VL) threshold that predicts HIV-related clinical illness in children on antiretroviral therapy (ART) may guide the VL detection level that pediatric ART programs should use in monitoring therapy. Our prior analysis demonstrated that VL>5000, but not >400 copies/mL, predicted new WHO stage 3 or 4 events (WHO events), independent of adjustment for CD4 immunologic status (CD4), hemoglobin level (Hgb) and other significant covariates in a cohort of Latin American children on combination ART (cART) for at least 6 months. The present analysis explored VL thresholds between 400 and 5,000 copies/mL in the same data set to identify the cut-point for the best fitting model for predicting new WHO events.

Materials & Methods: Cox proportional hazards modeling was used to assess the time to WHO events as a function of time-varying CD4, VL, and Hgb and time-fixed covariates. Models were fit using different VL cutpoints between 400 and 5000 copies/mL, with the best fitting model identified on the basis of a standard model fit statistic (minimum Akaike Information Criterion [AIC] value).

Results: Models were fit on 550 subjects, 67 who experienced a WHO event. The AIC declined from a high of 731.15 for a VL cutpoint of 400 copies/mL to a minimum of 727.43 for a cutpoint of 2600 copies/mL. The VL cutpoint of 2600 copies/mL was also associated with the largest estimated hazard ratio among all VL cut-points evaluated; subjects with VL at or above this cutpoint had more than a two-fold higher risk of WHO events compared to those whose VL was below this level (p=0.015).

Conclusions: The current analysis suggests that it may be clinically important for HIV treatment programs to be able to detect VL somewhat lower than the threshold of ≥5,000 copies/mL as part of routine monitoring of children on stable cART.

No conflict of interest

Abstract: P_29
Treatment of pediatric HIV infection
Impact of Selenium and Zinc level on antiretroviral treatment outcomes in Thai HIV-infected children

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Introduction: Deficiencies in antioxidants during HIV infection may facilitate the development of oxidative stress that contributed to immune dysregulation and HIV replication.

Methods: Treatment-naive, HIV-infected Thai children ages 1-12 years old with CD4 15-24%
were enrolled. Selenium and zinc levels were measured by graphite furnace atomic absorption spectrometry at baseline and week 48. The deficiency cutoff was defined as selenium level <0.1 μmol/L and zinc <10.7 μmol/L. C-reactive-protein(CRP) and ferritin were measured at week 0 and 48. No micronutrient supplement was allowed.

Results: 141 enrolled children had a median(IQR) age of 7.3(4.2-9.0) years, 38.3% were male, %CDC N:A:B were 2:62:36%. Median(IQR) Z score weight-for-height (W/H) was -0.1(-0.8 to 0.4). Median(IQR) CD4% and HIV-RNA were 20(16-22.6)% and 4.6(4.1-5.0) log10 copies/mL. 70 children were started HAART at week 0. At baseline, none had selenium deficiency with a median (IQR) level of 0.9 (0.7-1.0) μmol/L. There was a positive associate between selenium level with age [Coefficient 0.03, p<0.001] and a negative association with HIV-RNA [Coefficient 0.89, p<0.001] to selenium. All 141 children had zinc deficiency with median level of 5.9 (4.8-6.9) μmol/L. No associations between zinc level and age, clinical symptoms, CRP, ferritin, CD4%, and HIV-RNA were found. After 48 weeks of HAART, 99% had HIV-RNA <50 copies/ml and median(IQR) CD4 gain was 11(7-14)%. In the 70 treated, the mean change of selenium level was 0.04 μmol/L (p=0.08). Zinc level significantly increased 0.5 μmol/L (p=0.007) but 97% still deficient. No association between baseline zinc and selenium levels and changes in W/H, CD4% or HIV-RNA.

Conclusion: Zinc deficiency was present in all Thai children in this study who had mild to moderate HIV disease while none had selenium deficiency. Without receiving supplements, zinc deficiency corrected in only 3% of children after HAART. No association between these micronutrients and HAART outcome was seen.

No conflict of interest

Abstract: P_30

Treatment of pediatric HIV infection

Significant CD4 depletion and advanced HIV disease in infants initiating HAART before 3 months of age

Background: Early initiation of HAART is essential in HIV-infected infants because maximal mortality occurs in the first few months of life. Early HIV diagnosis and treatment is integrated at the Perinatal HIV Research Unit (PHRU) in Soweto and decentralized in the Cape Town (CT) northern sub-district. We describe the characteristics at HAART initiation of infants successfully initiated on HAART by 3 months of age in these two regions of South Africa.

Method: We performed a manual search of antiretroviral registers in 12 public clinics in CT and extracted data from the Paeds Wellness database at PHRU. Demographic characteristics, pre-HAART immunological and clinical stage and outcomes of infants who started HAART at <3 months of age between June 2007 and September 2010 were analyzed descriptively and compared using a two proportion and two-sample t-test.

Results:

Table: Characteristics of infants initiating HAART <3m of age in 2 centers

<table>
<thead>
<tr>
<th>Variable</th>
<th>CT N=99</th>
<th>PHRU N=315</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age at HAART initiation (weeks)</td>
<td>10.1 (IQR:8.2-11.7)</td>
<td>8.6 (IQR:7.7-10.0)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CD4% ≥25% and WHO 1 or 2</td>
<td>11 (11%)</td>
<td>139 (44.1%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Pre-HAART CD4% &lt;25%</td>
<td>46 (46%)</td>
<td>104 (33%)</td>
<td>0.0152</td>
</tr>
<tr>
<td>WHO stage 1 or 2</td>
<td>12 (12%)</td>
<td>241 (77%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>WHO stage 3 or 4</td>
<td>42 (42%)</td>
<td>58 (18%)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

(3 infants from CT and 16 from PHRU had no CD4 or WHO stage recorded)

Only 11(11%) of infants at CT and 139(44%) of infants at PHRU initiated HAART under “optimal” conditions (CD4% ≥25% and WHO 1 or 2). Mortality at CT and Soweto was 10(10%) and 18(6%) respectively at time of review. LTFU was 7(7%) and 25(8%) respectively.

Conclusion: At least half of infants had significant CD4 depletion or advanced HIV disease at HAART initiation. A single integrated system for early HIV diagnosis and treatment is more efficient than a decentralized program. New emphasis on early diagnosis
and rapid initiation of HAART in the first weeks of life is essential.

No conflict of interest

**Abstract: P_31**

**Treatment of pediatric HIV infection**

**Characteristics and prognosis of B-Cell lymphoma in VIH-infected children since HAART**

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**Background:** Chronic HIV-infection leads to increased risk of malignancy, particularly non-Hodgkin B-cell lymphoma. However, only few recent data are available about the current management and prognosis of B-cell lymphoma in HIV-infected children since HAART era.

**Materials & Methods:** This multicentric retrospective study reports all cases of B-cell non-Hodgkin's lymphoma that occurred in HIV-infected children in France between 1996 and 2009. Data collection included markers of HIV infection and lymphoma characteristics, treatment and outcomes.

**Results:** Twelve children (9 males, 3 females) developed B-cell non-Hodgkin's lymphoma during the study period with a median age of 11 years. Vertical transmission was the predominant source of HIV infection. Most of them had presented severe immunosuppression in their lifetime (8 AIDS). At lymphoma diagnosis, all had CD4 counts less than 25% and a high viral load (median 4.8 log). Six patients had received antiretroviral treatment, only two had received HAART for more than 2 years. Discriminating between lymphoma and opportunistic infection was difficult for 2 high risk patients. Nine children had extra-cerebral primary sites and three a central nervous system tumor. Eight lymphomas were Burkitt lymphoma and four were diffuse large B-cell lymphoma. Concomitantly with HAART, all children with extra-cerebral lymphoma were treated with LMB protocol-adapted intensive chemotherapy, those with cerebral lymphoma received intravenous high-dose methotrexate. No toxicity-related death was reported. Ten patients achieved complete remission, two died of tumoral progression despite a second line therapy. After remission, no relapse was described with a median follow-up of 72 months. One child developed a second malignancy 18 months after remission and died, another died of HIV-disease 7 years after lymphoma diagnosis. Regarding HIV infection, after 6 months on HAART, 3 children maintained a high viral load: 2 due to poor adherence to HAART, 1 because of multiple resistance genotype.

**Conclusion:** B-cell lymphomas have been rare in France among HIV-infected children since HAART era. Patients without severe comorbidity can tolerate intensive chemotherapy regimens in association with a mandatory HAART treatment, taking into account drug interactions. Prognosis of patients unresponsive to first line treatment remains poor, but relapse seems rare when complete remission is achieved. The subsequent evolution still depends on adherence to antiretroviral treatment.

No conflict of interest

**Abstract: P_32**

**Treatment of pediatric HIV infection**

**HIV-1 drug resistance profile in children and adolescents using 1st HAART regimen and response rate to the new antiretroviral regimen.**

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**Background:** Antiretroviral resistance is a problem that can limit HIV treatment success...
and genotyping test is not available worldwide. Our aim was to describe the resistance mutation profile to HAART in children and adolescents that presented a first therapeutic failure and the effectiveness of the new antiretroviral regimen guided or not by genotyping test.

**Methods:** We conducted a cross-section study and included children and adolescents perinatally HIV infected with a first therapeutic failure detected > 6 months of 1st HAART followed at IMIP Hospital. The data were collected by patient’s medical records. All patients were followed by two physicians with > 20 years of HIV treatment experience.

**Results:** Sixty patients were included in the study. The mean age was 11 years, 33 (55.0%) were female, and 44 (73.3%) non-white. The mean age of starting HAART was 2.2 years and 48 weeks to the 1st HAART failure and switching antiretroviral regimen. Forty (66.7%) used as 1st line therapy the combination of 2 NRTIs + 1 NNRTI. Among the patients, 32 (53.3%) had new antiretroviral regimen guided by genotyping test and 28 (46.7%) participants had the rescue treatment guided by specialist’s experience. Mutations and associated resistance to NRTI was found in genotyping guided patients (184V> 215 F > 214F). Mutations and associated resistance do NNRTI was found in 30 (93.8%) patients (103N > 181 C > 190A). Mutations and associated resistance to PI was found in fewer patients with different profiles, with sensibility range from 88.3% (LPV/r) to 100% (ATV/r, DRV/r or FPV/r). The response rate to the new antiretroviral regimen was 20 (62,5%) on the genotyping test guided group and 15 (53,6%) on the physician experience guided group with not statistical significance.

**Conclusion:** It was not found difference in the response rate of treatment guided by genotyping test or physician’s experience.

No conflict of interest

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**Abstract: P_33**

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**Treatment of pediatric HIV infection**

**Predictors of Treatment Outcomes among Children Initiating Antiretroviral Therapy in Côte d’Ivoire during 2004-2008**


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**Introduction:** During 2004-2008, 2,821 children (<15 years old) initiated antiretroviral therapy (ART) in Côte d’Ivoire. Investigating predictors of ART outcomes can identify opportunities for program improvement.

**Materials & Methods:** In a retrospective cohort study among all children initiating ART during 2004-2008 at 29 of 30 ART facilities with >10 pediatric ART enrollees, we investigated retention (the proportion alive on ART) and determinants of retention using multivariable logistic regression.

**Results:** Of the 2,821 children enrolled on ART in Côte d’Ivoire during 2004-2008, 2,110 (75%) had been enrolled at the selected 29 facilities. Among these 2,110 enrollees 46% were female, 7% were infants, 26% aged 1-3 years, 15% aged 3-5 years, and 51% aged 5-14 years. ART start year was 2004, 2005, 2006, 2007, and 2008 for 9%, 17%, 26%, 24% and 24% of children, respectively. Median baseline CD4% was 10.8%. Completion of age-appropriate yellow fever, measles, and combination diphtheria-tetanus-pertussis-polio-hepatitis B (DTPPH) vaccination was documented for 9% of patients. Stavudine or zidovudine, lamivudine, and efavirenz or nevirapine comprised 79% of first-line regimens. Retention at 6, 12, 24, and 36 months was 84%, 79%, 77%, and 73%, respectively. Compared with infants, odds of 6-month retention were higher for children aged 1-3 years [adjusted odds ratio (AOR) 1.91; 95% confidence interval (CI) 1.35-2.70], 3-5 years (AOR=2.57; 95% CI 1.32-4.99),
abstract describes outcomes of a paediatric HIV cohort where care is provided in a decentralized, rural primary health care setting in Buhera district Zimbabwe.

**Methods:** Data were prospectively entered into an electronic patient register. Kaplan Meier survival method was used to calculate rates of mortality and loss to follow-up for age groups ≤2 yrs, 2.1-5 yrs and 5.1-9 yrs.

**Results:** This analysis included 445 patients; 70, 141 and 234 patients were in the age groups ≤2 yrs, 2.1-5 yrs and 5.1-9 yrs respectively. Sex was equally distributed in all three groups. Mortality was 7.7 (95%CI 3.5-17), 1.4 (95%CI 0.0-4.3) and 4.0 (95%CI 2.3-6.9) per 100 person years in the three age groups respectively. Rates of lost to follow up were 23 (95%CI 14.6-36.9), 2.8 (95%CI 1.3-6.3), 4.3 (95%CI 2.6-7.3), per 100 person years respectively.

**Conclusions:** Outcomes from this analysis show similar findings to other paediatric cohorts. For the older age groups acceptable outcomes were achieved through care being given in a decentralized setting. The high loss to follow up amongst children < 2 years of age (20 of whom were < 1 year) most likely includes a significant proportion of misclassified deaths. Improved early diagnosis and timely ART initiation is essential to improve care in this age group.

No conflict of interest

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**Abstract: P_34**

Treatment of pediatric HIV infection

**Antiretroviral treatment outcomes from a decentralized paediatric ART program in rural Zimbabwe**

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**Background:** Zimbabwe has an estimated 150,000 children living with HIV and a prevalence of 3.1% in children aged between 0-14 years. Paediatric HIV care is still perceived as requiring centralized, specialist care in most settings. Improving access to paediatric HIV care whilst maintaining acceptable outcomes is a challenge in many resource limited settings. The following
Abstract: P_35

Response to Antiretroviral therapy of HIV-1 Infected Ugandan children in urban and rural settings


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Background: HIV infected children in Africa reside in different settings which may affect their response to antiretroviral therapy (ART). We set out to ascertain and compare the response to ART in urban and rural settings of Uganda.

Methods: From 2006 to 2010 we conducted a cohort study involving 913 children aged <18years, obtaining ART from 8 centres under the President's Emergency Plan For AIDS Relief (PEPFAR) supported TREAT programme run by the Joint Clinical Research Centre in Uganda. Clinical, immunological and virological parameters were ascertained at baseline, weeks 12, 24, 36, 48, 96 and 144 after ART initiation. Eligibility criteria at enrolment were: ART-naive for at least 3months, joining the TREAT programme as ART naive and consent for study participation. Adherence to ART was assessed at enrolment by Self report (SR) and clinic based pill counts (PC). Two age strata (<5years and ≥5years) were created while investigating immunological changes. Differences between urban and rural children among categorical and continuous variables were analysed using chi-square and t-tests respectively.

Results: Overall, 489/913 (54%) children were female; 53% (480/908) started ART on stavudine and 46% (412/908) on zidovudine in combination with lamivudine and nevirapine or efavirenz; median follow-up time was 139.0weeks (IQR 75.4,144.0). 46.2% (422/913) were resident in towns or cities (urban children) and 53.8% (491/913) were resident in rural settings (rural children). Among urban versus rural children, the mean age at ART initiation was 11.8±4.4 versus 11.4±4.1years (p=0.2148); the median distance from home to the clinic was 3 versus 10km (p<0.0001). At ART initiation, 58.3 % (246/422) urban children and 61.3% (301/491) rural children were in WHO clinical stages 3 and 4 (p=0.355). The mean weight (kg) among urban versus rural children increased throughout follow-up from 21.1versus 19.5 (p=0.0266) at baseline to 31.2 versus 28.1 (p=0.0139) at week 144 respectively. Similarly height (cm) among urban versus rural children increased from 115.2 versus 112.4 (p= 0.2645) at baseline to 131.3 versus 123.4 (p= 0.0176) at week 144 respectively. During follow-up on ART, 108/421 (25.7%) urban versus 88/487 (18.1%) rural children developed new WHO stage 3/4 events (p=0.006). Also 33/421 (7.8%) urban versus 12/487 (2.5%) rural children switched to second line ART (p<0.0001). The mean CD4% in the urban versus rural children aged <5yrs increased throughout follow-up from 18.8% versus 24.3% at baseline (p=0.5496) to 34.3% versus 40.7% at week 144 (p=0.2167), whereas the mean CD4 count (cells/µl) in the urban versus rural children aged ≥5years increased from 325 versus 477 at baseline (p=0.0861) to 800 versus 821 at week 144 (p=0.6055). At week 144, mean reductions in viral load (log copies per ml) in the urban versus rural children were 6.108 versus 5.8306 (p=1.000). Adherence of ≥95% was observed in 87.9% of urban versus 91.1% of rural children by SR (p=0.123), and in 79.2% of urban versus 88.8% of rural children by PC (p<0.0001).

Conclusions: Children resident in urban and rural settings of Uganda responded favorably to ART clinically, immunologically and virologically. However the rural children did better clinically and were more likely to adhere perfectly to ART.

No conflict of interest
Abstract: P_36

Treatment of pediatric HIV infection

Incidence of elevated ALT pre-HAART initiation, and the effect of HAART on ALT levels, amongst HIV-infected infants in Soweto, South Africa.

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Background: Routine hepatic function monitoring is no longer recommended by the World Health Organisation in the management of HIV-infected children. This study observes the incidence of pre-HAART transaminitis (elevated ALT) and the effects of HAART on ALT in HIV-infected infants.

Methods: A retrospective analysis was performed of an observational cohort of HIV-infected infants enrolled in a treatment care programme in Soweto, South Africa. Included infants were born between 1 January and 31 December 2009 and initiated HAART before one year of age. All infants received lopinavir/ritonavir plus 2 NRTIs as treatment. 84 (58%) were receiving cotrimoxazole prophylaxis at entry. PMTCT regimens, maternal CD4 count during pregnancy or within 3 months of delivery, infant pre-HAART CD4 count, CD4 percentage, viral load and ALT level, as well as ALT from weeks 4 and 12 were screened for hepatitis B - all were negative for hepatitis B infection. No association existed between Grade 3/4 ALT and maternal PMTCT regimen (OR:1.2, CI:0.25-5.84), maternal CD4 count (OR:1.001, CI:0.999-1.003), infant PMTCT regimen (OR:0.84, CI:0.17-4.30), cotrimoxazole prophylaxis (OR:1.5, CI:0.60-3.64), or baseline CD4% (OR:0.98, CI:0.95-1.02). Fourteen of 15 infants with Grade 3/4 elevations had week 4 and 12 data. By week 4, 12/14 (86%) Grade 3/4 elevations had resolved to ≤ Grade 1 and 14/14 (100%) by week 12. 27/42 (64%) Grade 1/2 ALTs resolved to Grade 0 by week 12.

Conclusion: Elevated ALT occurs commonly in HIV-infected infants but resolves quickly on HAART. We support the recommendation not to monitor transaminase levels and recommend not delaying HAART on the basis of raised ALT. Further research is required to ascertain the cause of infant Grade 3/4 transaminitis.

No conflict of interest

Abstract: P_37

Treatment of pediatric HIV infection

Immunologic and virologic failure after first-line highly active antiretroviral therapy in HIV-infected children

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Objectives: There is limited data describing treatment outcomes in HIV-infected children from Asia. Here, we report the long treatment outcomes in Thai children.

Methods: Antiretroviral (ART)-naïve HIV infected children treated with non-nucleoside
reverse transcriptase inhibitor (NNRTI)-based highly active antiretroviral therapy (HAART) during 2001-2008 were included. The CD4 counts were performed every 12 weeks and plasma HIV-RNA every 24 weeks. Virological failure (VF) defined as HIV-RNA > 1000 copies/ml after at least 24 weeks of HAART.

Results: 107 ART-naive HIV infected children, 52% female, 6% CDC clinical classification N:A:B:C 4:44:30:22% were included. Baseline data were median (IQR) age 6.2 (4.2-8.9) years, CD4% 7 (3-15)%, HIV-RNA 5 (4.9-5.5) log_{10} copies/ml. Nevirapine (NVP)-based and efavirenz (EFV)-based HAART was started in 70% and 30%, respectively. At 96 weeks, none had progressed CDC clinical classification to AIDS and one died from pneumonia. Significant improvement of weight, height, hemoglobin, CD4, HIV-RNA were seen (all p<0.001). The median (IQR) CD4% and HIV-RNA at 96 week were 25 (18-30)% and 1.7 (1.7-1.7) log_{10} copies/ml. Only 1% of children experienced immunologic failure (IF; defined as persistent decline of ≥ 5% in CD4% in children with CD4% < 15% at baseline OR decrease CD4 count ≥ 30% from baseline). Thirty one (88.6%0 of 35 children who developed VF occurred in the first 48 weeks. The sensitivity (95% CI) of IF to VF was 4 (0.1-20.4)% and specificity was 100 (93.9-100)%.

Conclusion: At 96 weeks of NNRTI-based, 75% of children had virological control and 89% had immune recovery. Almost of VF occurred in the first year after HAART commencement. HIV-RNA should be performed at least once in the first year to detect early treatment failure. Immunologic failure had low sensitivity and should not be recommended.

No conflict of interest

Abstract: P_38

Treatment of pediatric HIV infection

Clinical outcomes and factors contributing to loss to follow-up of paediatric patients on ART in rural Zambia: retrospective cohort study 2004-2010

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Introduction: Children comprise less than 8% of the total population accessing Antiretroviral Therapy (ART) in Zambia. This proportion is less in rural areas with limited data available on paediatric patient outcomes. The Ministry of Health in Zambia, analysed paediatric data from a rural hospital to determine treatment outcomes in order to better inform policy and strategy for programme improvement

Methods: A retrospective cohort study of 163 HIV-positive children <15 years old who initiated ART at a rural district hospital between October 2004 to July 2010 was conducted. The probability of remaining in care and factors associated with loss to follow-up were examined

Results: A total of 163 children (81 boys and 82 girls) initiated ART during this period. Seventeen (10.4%) children initiated ART before the age of one, 43 (26.4%) before the age of three, 22 (13.5%) before the age of five, and 76 (46.6%) after the age of five, with the median age of 58 months (range 2 -179). Among them 15 (9.2%) were with World Health Organization clinical stage I, 26 (16.0%) with stage II, 103 (63.2%) with stage III and 8 (4.9%) with stage IV. By the end of July 2010, 5 children (1 boy and 4 girl; 3.1%) had died and 25 children (12 boy and 13 girl; 15.3%) had been lost to follow-up. Probabilities of remaining in care after 6, 12, 24, and 48 months of ART were 0.90, 0.89, 0.83, 0.81, and 0.68 respectively. There was a significant correlation between the age at the ART initiation and treatment outcomes, in which younger children were less likely to remain in
care (correlation coefficient - .245, p < .001). Further analysis on the cases of lost to follow-up found that among 25 children, 18 (72%) were under 5 years old. Among them 12 (48%) were lost within 6 months of treatment, of those 92% were less than 3 years of age. Interestingly, 60% of the children were already lost to follow-up by their second clinical visit.

Conclusions: Outcomes of paediatric ART in rural Zambia was comparable to that of urban setting. However, higher risk of loss to follow-up among young children, especially of those under 3 years old was identified, which might indicate late initiation of treatment for those children. Urgent effort is needed for early initiation of ART in infants and strengthening of the initial visits’ clinical assessment and treatment adherence preparation. Active tracking mechanism, such as use of community health workers should be part of the support that caregivers of paediatric patients receive in order to reduce the early attrition rates in this population. The Ministry has developed an action plan based on these findings.

No conflict of interest

Abstract: P_39

Treatment of pediatric HIV infection

The effect of highly active antiretroviral therapy on the survival of HIV-infected children in a resource-deprived setting: a cohort study

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Introduction: The effect of highly active antiretroviral therapy (HAART) on the survival of HIV-infected children has not been well quantified. Because most pediatric HIV occurs in low- and middle-income countries, our objective was to provide a first estimate of this effect among children living in a resource-deprived setting.

Material & Methods: Observational data from HAART-naive children enrolled into an HIV care and treatment program in Kinshasa, Democratic Republic of Congo between December 2004 and May 2010 were analyzed. We used marginal structural models to estimate the effect of HAART on survival while accounting for time-dependent confounders affected by exposure.

Results: At the start of follow-up, the median age of the 790 children was 5.9 years, 528 (66.8%) had advanced or severe immunodeficiency, and 405 (51.3%) were in HIV clinical stage 3 or 4. The children were observed for a median of 31.2 months and contributed a total of 2089.8 person-years. Eighty children (10.1%) died, 619 (78.4%) initiated HAART, six (0.8%) transferred care, and 76 (9.6%) were lost to follow-up. The mortality rate was 3.2 deaths per 100 person-years (95% CI 2.4–4.2) during HAART and 6.0 deaths per 100 person-years (95% CI 4.1–8.6) during receipt of primary HIV care only. The mortality hazard ratio comparing HAART to no therapy from a marginal structural model was 0.25 (95% CI 0.06–0.95).

Conclusions: HAART reduced the hazard of mortality in HIV-infected children in Kinshasa by 75%, an estimate that is similar in magnitude but with lower precision than the effect of HAART on survival that has been reported among children in the United States.

No conflict of interest

Abstract: P_40

Treatment of pediatric HIV infection

Characteristics at initiation and outcomes after 52 weeks of ART in a pediatric cohort in Gaborone, Botswana initiated prior to 24 months of age

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Introduction: Without effective antiretroviral therapy (ART), approximately one-third of HIV-infected infants will die by age one year, and half will die by age two. Yet with the scale-up of ART programs for HIV-infected children, mortality rates have declined considerably. In 2008 the World Health Organization (WHO) recommended that all HIV-infected infants be initiated on ART regardless of their clinical/immunologic status. In 2010 WHO conditionally expanded this recommendation to children aged 12-to-24mos. Current Botswana National Guidelines on infant ART initiation are consistent with WHO’s 2008 recommendation. The Botswana-Baylor Children’s Clinical Centre of Excellence (COE) is Botswana’s largest pediatric ART site, with >2,000 HIV-infected children in care. This study describes a cohort of HIV-infected children < 24 months of age - at baseline and after 52 weeks of ART initiation.


Results: 34/38 (90%) < age12 months (range:2-11months; mean=3.8 months); 60% females (23/38). WHO clinical stage: baseline:I-13/38(34%); II-3/38(8%); III-12/38(32%); IV-10/38(26%) Immunological status: baseline: 20/38 (52%) severe per WHO criteria; including all 4 > age 12 months. Virological status at 52wks: 33/38 (87%) VL< 400 copies/mL. One lost-to-follow up (LFTU). Of those 4 with detectable VL; 3 on Lopinavir/ritonavir (LPV/r)-based ART, 1 on Nevirapine (NVP)-based ART, all with documented adherence problems. ART Adherence (most recent visit)-31/37 (84%) with poor adherence; 28/37 (76%) >105%, 3/37 (8%) < 95%.ART regimen - LPV/r-based regimen- 27/37 (73%); NVP-based regimen-10/37 (27%).No deaths registered 52wks post-ART initiation. LTFU: 1/38 (2.5%), alive at 52weeks.

Conclusions: This cohort experienced no mortality in the first year on ART. Early age-of-initiation (mean < 4mos) is a likely contributor to this. Most patients were virologically-suppressed at 52 weeks, regardless of regimen. The overall poor adherence in the cohort is mostly due to apparent overusage; ART syrups can prove difficult to use for caregivers. Although a small sample, all children ages 12-24mos had severe immunosuppression, supporting 2010 WHO recommendations to initiate ART in children < 24mos on the basis of age alone.

No conflict of interest

Abstract: P_41

Treatment of pediatric HIV infection

Protease genotypes in children and adolescents failing protease inhibitor (PI) - based antiretroviral therapy (ART) in Gaborone, Botswana

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Introduction: In Botswana, second-line antiretroviral therapy (ART) for children and adolescents includes a protease inhibitor (PI), as do most salvage regimens. There is limited protease genotype data from southern African children and adolescents who have failed PI-based ART, despite such information being critical in predicting success of subsequent ART regimens.

This study’s objective was to describe protease genotypes obtained after failure of PI-based ART by children and adolescents at the Botswana-Baylor Children’s Clinical Centre of Excellence (COE), allowing commentary on their implications for current and future HIV care and treatment options.

Materials & Methods: Retrospective chart review of protease genotypes (n=42) from 28 children and adolescents (ages: 3-17) obtained during virologic failure on second-line or salvage PI-based regimens. Adherence was determined by pill count.

Results: PI at time of virologic failure was nevirapine (NFV; n=5) or lopinavir/ritonavir (LPV/r; n=37). 11 patients with exposure to both NFV and LPV/r; 1/11 also with saquinavir-exposure. Patients with protease mutation = 7(25.0%). 7/7 with major mutation; 5/7 (17.9%) with >1 major mutation; 5/7 also with minor mutation; 4/7 with history of NFV followed by
LPV/r; 2/7 with history of LPV/r-only; 1/7 with history of NFV only. No patients with only minor mutations. Specific major mutation frequency: IS4V-4, V82A-3, L90M-3, D30N-2, N88D-2, M46I-1, L33F-1. Specific minor mutation frequency: A71V-2, L10F-2, A71T-1, L10I-1. Patients with polymorphisms only = 17 (60.7%). Genotype without protease mutations = 4(14.3%). Of 23 patients with documented pill counts, 56.5% (13/23) had poor adherence (< 95% or >105%) on minimum two-of-last-three visits prior to genotyping.

Conclusion: Patients with major mutations tended to have received unboosted NFV prior to LPV/r and subsequent virologic failure; NFV was the only PI available in Botswana until LPV/r was introduced in 2005. All patients in our cohort with major protease mutations would be predicted to have full susceptibility to ritonavir-boosted darunavir (DRV/r) - important, given DRV's availability now for salvage ART for children and adolescents in Botswana. Most (6/7) would be predicted to have full susceptibility to ritonavir-boosted tipranavir (TPV/r), which is yet to be introduced for pediatric use in Botswana. Non-adherence to ART underpins virologic failure, including for those with major protease mutations, half of whom would be predicted to have retained most or all susceptibility to LPV/r despite virologic failure on LPV/r.

No conflict of interest

Abstract: P_42

Treatment of pediatric HIV infection

Hospitalization rates, risk factors and costs in HIV infected children receiving antiretroviral therapy in Thailand


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Background: There are scarce data on hospitalization rates, risk factors and costs in children after initiation of antiretroviral therapy (ART), particularly in lower-middle income countries. Costs of paediatric hospitalizations from a health care provider's perspective are important to inform decision analyses models and national programmes.

Methods: Hospitalization data were extracted from Serious Adverse Event reports in a prospective observational cohort of children who initiated ART in Thailand between 1999 to 2009. Inclusion criteria for analysis were antiretroviral naive and age<18 years at initiation of ART. Hospitalization rates per 100 person-years (PY) were calculated from start of ART to death or last follow up, allowing for multiple hospitalizations per child. Zero inflated Poisson models were used to examine factors associated with early (<12 months since start of ART) and late hospitalization (≥12 months) and frequency of hospital admissions. Hospitalization costs were calculated based on WHO inpatient unit cost estimates (International US$ 2000) per hospital level in Thailand multiplied by the duration of inpatient care and expressed as cost per person month on follow up.

Results: 578 children were included in the analyses. At start of ART (baseline) the median (IQR) age was 7 years (2-10), CD4 7% (2-16), 52% were in CDC disease stage B/C. Initial regimen was dual nucleoside in 11%, protease inhibitor based triple combinations in 6% and non-nucleoside based combinations in 83% of children. Median duration of follow up was 64 months (IQR, 43-82). Overall, 202 (35%) children were hospitalized at least once, with a total of 429 admissions, 50% of which occurred <12-months of ART initiation. Seventy percent of primary diagnosed causes were infectious disease related: pneumonia was the leading cause accounting for 30% of all admissions. Eighty-nine percent of hospitalizations were resolved, 3% discharged, 5% (n=22) died during hospitalization, and 2% (n=10) were resolved/discharged and died <3-months of hospitalization. The hospitalization rate was highest at 57 per 100PY <6 months of ART and declined to ~10 per 100PY after 2 years. The cost of hospitalization peaked at

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$31 per patient-month <6 months and declined to under $5 after 2 years.

In the multivariable analyses, CDC disease stage B/C and low height for age z-score at baseline were associated with higher risk of early hospitalization. Among those hospitalized higher frequency of admissions was associated with low weight-for-height z-score (WHZ), initiation on dual therapy, late calendar year of initiation and female sex (all p<0.05). There were no predictors for risk of late hospitalization, although among those hospitalized, higher frequency of admissions was associated with low WHZ, CDC stage B/C, age<2 years or >7 years at baseline and hospitalization <12-months on ART (p<0.01).

Conclusions: The risks and costs of hospitalization were highest during the first year of ART and rapidly declined thereafter. Factors associated with high frequency of early and late hospitalization include severe wasting and CDC stage B/C at start of ART. Early initiation of ART, before advanced disease progression, is likely to reduce short and long-term hospitalization and costs to the health care system.

No conflict of interest

Abstract: P_43

Treatment of pediatric HIV infection

Adherence and viral suppression among infants and young children initiating Protease Inhibitor-based antiretroviral therapy

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Background: High levels of adherence to antiretroviral therapy (ART) are considered necessary to achieve viral suppression. We analyzed data from a cohort of HIV-infected children under 2 years initiating ritonavir-boosted lopinavir (LPV/R)-based ART to identify optimal adherence levels and methods to ascertain adherence.

Materials & Methods: 269 children enrolled in a clinical trial in Johannesburg, South Africa were initiated on LPV/R-based ART. At scheduled visits, a pharmacist measured the quantity of each antiretroviral drug returned (medication return – MR) and asked questions about missed doses and adherence barriers. The primary endpoint was viral suppression (<400 copies/mL) at 24 weeks. GEE models were used to define the relationships between adherence and suppression.

Results: ART was initiated at a mean age of 10 months. 197 children (73%) achieved viral suppression <400 copies/mL by 24 weeks. Missed doses were reported at 94/1206 (8%) visits; there was no difference in report of missed doses between suppressors and non-suppressors. Various MR cutoffs to define adherence were examined to estimate the optimal threshold for each of the three antiretroviral drugs separately. Based on MR, adherence >80% to LPV/R most strongly predicted suppression (OR 3.01 [95% CI: 1.43-6.67], p=.004). Adherence defined by MR to D4T was weakly associated with adherence. Adherence to 3TC, at any cut-off, was unrelated to suppression. Adherence <80% to any of the three drugs with MR occurred at 84/1089 (8%) visits; at these visits only 6 caregivers reported a missed dose. There was no significant association between acknowledged adherence barriers, such as forgetting or fear of side effects, and suppression.

Conclusions: Caregiver reports of missed doses are a poor predictor of viral response. Medication return is a better measure of adherence and is strongly related to virologic response. For children on a LPV/R-based regimen, >80% adherence with LPV/R specifically was the strongest predictor of virologic suppression.

No conflict of interest
Abstract: P_44

Treatment of pediatric HIV infection

Antiretroviral treatment response of HIV-infected children after prevention of mother to child transmission (PMTCT) in West Africa

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Background: The antiretroviral treatment (ART) response of children infected with HIV despite a PMTCT exposure has not been described so far in West Africa, where virological follow-up is not usually available. We aimed to assess the clinical and immunological response of HIV-infected children after 12 months on ART in the Pediatric IeDEA West Africa Collaboration (pWADA) according to their history of perinatal PMTCT exposure.

Methods: We conducted a retrospective cohort study in children <5 years after ART initiation and included between January 2004 and June 2009 in the pWADA clinical centres, in Bamako-Mali and Abidjan-Côte d’Ivoire. Information available in pWADA database was updated through a direct review of medical records. The survival without clinical and immunological failure was estimated according to PMTCT exposure. Clinical failure was defined as any clinical disease progression with a change of WHO staging or recurrence of opportunistic infections despite ART, or any death occurring after treatment initiation. Immunological failure was defined as stability or decrease of CD4% compared to CD4% at initiation or a decline by ≥25% compared to the CD4% peak achieved after ART initiation.

Results: Among the 1035 children eligible children, 503 were Malians (48.6%), 56% were male, 7% were previously exposed to PMTCT, 280 (27%) were not exposed and 682 (66%) had an unknown exposure status. The main PMTCT regimen received by those exposed was AZT + 3TC + NVP (60%). At ART initiation, the median age was 11 months (interquartile range IQR [8.0 – 23.0]) for PMTCT-exposed children, 27 months [18.0 – 39.5] for unexposed children and 29 months [19.0 – 44.0] for the others. About 88% of children presented AIDS clinical manifestations and their median CD4% was 13.5% [9.0 – 18.2]. After 12 months on ART, 89 children died with 77.5% of deaths occurring <6 months. The overall probability of death or loss to follow-up (last visit >6 months) was 19.5% [17.2%-22.1%]. The survival without clinical failure was 87.3% [76.2%-93.4%] for PMTCT-exposed children, 80.4% [74.3%-85.2%] for unexposed children and 71.0% [66.7%-74.8%] for the others (logrank test <0.0001). The survival without immunological failure was 88.9% [76.9%-94.8%] for PMTCT-exposed children, 91.3% [85.7%-94.7%] for unexposed children and 87.4% [83.6%-90.3%] for others (logrank test 0.03). Adjusted on age, a PMTCT exposure was not significantly associated with survival without clinical failure (Wald test: p=0.1). This event was correlated with immunosuppression (OR: 1.5 [1.1-1.9]) and weight-for-age z-score > -3 (OR: 0.8 [0.6-0.9]) at ART initiation.

Discussion: Virological monitoring of ART-treated children is not available under field conditions in West Africa. We failed to show different clinical and immunological outcomes according to PMTCT exposure. However, children who had received PMTCT prophylaxis tended to have a better survival than the others. Immunosuppression and severe malnutrition appeared as the main risk factors of HIV mortality in this operational context. Virological follow-up of children according to WHO guidelines should be strengthened in resources-limited setting.

No conflict of interest
Abstract: P_45

Treatment of pediatric HIV infection

Efficacy of PI vs. NNRTI-based first-line antiretroviral therapy in HIV-infected children - a prospective cohort study in China

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Background: The current first-line antiretroviral treatment (ART) regimen in China is two NRTIs plus a NNRTI. Some studies indicate that a lopinavir/ritonavir (LPV/r)-based regimen has better outcomes than a NNRTI-based regimen. To evaluate this, a prospective cohort study was conducted within the Chinese Network of Pediatric Antiretroviral Therapy (CN-PART). The aim of this study is to assess the efficacy and tolerability of protease inhibitor (PI) vs. non-nucleoside reverse transcriptase inhibitors (NNRTIs)-based regimens as first-line therapy in HIV-infected children in China.

Material and Methods: It is an open, prospective, multicentre, compared clinical study. The proposal was approved by IRB and children and their guardians were required to sign the informed consent. From January 2008 to October 2010, a total of 258 children who met eligibility criteria were enrolled. 125 children received efavirenz (EFV) compared with 133 children taking LPV/r, together with lamivudine (3TC) and zidovudine (AZT). As the primary measure indicator, CD4 count, HIV RNA level, were measured every 3 months from initiation of HAART. Clinical and laboratory results accounting for drug efficacy and tolerability were measured concurrently.

Results: The median age at ART initiation was 6.0 (IQR 4.0-9.0) years. Gender distribution was 58% male. 133 (51.6%) children were on AZT or D4T+3TC+LPV/r regimen, while 125(48.4)% were on AZT or D4T+3TC+EFV. At baseline, Median CD4 percentage of LPV/r and EFV were 8.0(1.3-14.0)% and 10.0(3.0-14.0)%, and plasma HIV RNA level was 5.03 lgcopies/ml and 4.83 lgcopies/ml. There was no significant difference in LPV/r and EFV group at baseline. At 12 months, Median CD4 percentage of LPV/r and EFV were 21% and 24% (P=0.75). 83.3% and 84.4% had HIV RNA level of <400 copies/ml respectively (P=0.75) depending on the intent-to-treat analysis. Comparing toxicity and withdrawal rates in LPV/r and EFV group, the gastrointestinal(GI) symptom like nausea(P=0.006), anorexia(P=0.069) and diarrhea(P=0.06) appeared more in LPV/r, CNS disturbances like dizziness was observed more in EFV(P=0.004). Triglyceride increased from baseline more in LPV/r than in EFV (P<0.05). Four children died from AIDS-related disease, 3 death occurred in LPV/r group and 1 in EFV group. Five (3.1%) withdrew, 1 withdrew because of abnormal liver function, 4 lost follow up.

Conclusion: Both LPV/r group and EFV group indicated comparative virologic and immunologic efficacy and each regimen developed the category specific side effect within one year observation. Using which one as the primary recommendation needs to weight efficacy, tolerance, price and conveniences.

Supported by Important National Science and Technology Specific Projects in China (2008ZX10001-007)

Abstract: P_46

Treatment of pediatric HIV infection

A 60 month retrospective review of the outcomes of HIV positive children on antiretroviral treatment at public sector hospital in South Africa

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Background: National programs in the developing world are making strides to provide...
access to HAART for children. Such resource poor areas pose the additional burdens of poor nutrition, socio-economic deprivation and high rates of concomitant tuberculosis. This study reviewed children who were started on HAART in a public health program from 2004. It aimed to determine the laboratory outcomes of children during the first 60 months after initiation of as well as the rate of virological failure and need for drug regimen changes.

Methods: A retrospective chart analysis was attempted on the first 250 found files in a public sector clinic. Attempts were then made to track the following markers from initiation through 60 months of follow-up: hemoglobin, albumin, globulin levels CD4 counts, and viral loads as well as HAART regimen changes. This data was captured in a standardized questionnaire and entered into an access data base. This data was then analyzed with standard statistical methods.

Preliminary results: Challenges were found in tracing records of all children started on HAART from 2004. 249 active files reviewed (45, 4% female, 54, 6% male) There was an 18, 8% lost to follow up. Majority of the patients (62, 9%) were > 5 years at initiation with only 2, 4% initiated below 1 year. Majority of patients used an NNRTI based regimen (82, 4% (11, 5% used a PI based regimen). CD4 count changes showed significant improvements from a mean of 9% at baseline to reach a normal levels by 30 months on treatment. There were no significant changes in the CD4 counts from 30 months onwards. Changes in Hemoglobin, albumin and globulin levels all showed a significant change from initiation to normal levels by 18 months. Virological suppression took longer in patients > 5 years compared with patients < 5 years. Only 18, 3% of patients needed drug changes in the 60 month follow-up (n=1) with 44, 3% needing these changes due to adverse drug reactions and 36, 5% needing drug changes due to virological failure. The virological failure rate was only 5, 8%.

Conclusion: Despite significant gaps in missing data, evaluation of the first 250 children started on HAART indicate medium to long-term sustainability of public sector pediatric ARV programs in resource poor settings. Furthermore, this study provides evidence that first line regimens, including NNRTI-based regimens are sustainable for 2-5 years. Hemoglobin, albumin and globulin levels mimic CD4 count recovery and indicate an 18 month improvement period till a plateau phase is reached. There was a low level of Virological failure noted. Public sector pediatric HAART programs are sustainable with the possibility of changes in albumin, globulin and Hemoglobin being used as markers to improvement. There is a need for improved data gathering systems to ensure the validity of information on a continuous basis.

No conflict of interest

Abstract: P_47

Treatment of pediatric HIV infection

Long term immune response at 5-years of highly active antiretroviral therapy (HAART) in HIV-infected children in Thailand.


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Background: Immune restoration is a key goal of antiretroviral therapy. There are scarce data on long-term immune response in children in resource-limited settings, many of whom initiate therapy when severely immunocompromised. We assessed the probability and determinants of immune restoration at 5 years after HAART initiation in children in Thailand.

Methods: Between 1999-2009, children initiating HAART were enrolled in an observational cohort (Clinicaltrials.gov NCT00433030). CD4 and HIV plasma RNA (VL) assessments were done at HAART.
initiation (baseline) and 6-monthly thereafter. Inclusion criteria for analysis were: age ≤18 years, antiretroviral naïve at initiation of HAART and follow-up for ≥12-months. Immune reconstitution was defined as two consecutive CD4≥25% after 6 months of HAART, and analyses were restricted to children with baseline CD4<25%. Kaplan-Meier probability of immune reconstitution was estimated. Cox proportional hazard models were used to assess the role of potential factors: baseline characteristics, early immune and virologic response at 6-months and long-term viral suppression<400 copies/mL (allowing for 1 blip <1000 copies/mL).

**Results:** 515 children initiated HAART, at 12-months of therapy 27 (5.2%) died, 12 (2.3%) were lost to follow up, 19 (3.7%) voluntarily withdrew, the remaining 457 (88.7%) children alive and on follow-up were eligible for analyses. At baseline, median (IQR): age was 7.3 years (4.2-10.0), CD4 7% (2-14), viral load 5.1 log10 copies/mL (4.6-5.5), 52% CDC stage B/C. Initial therapy was nevirapine-based in 54%, efavirenz-based in 39% and protease-inhibitor based in 7%. Median follow-up time was 66 months (49-82), median number of CD4 measurements was 10 (8-12). At 6-months of therapy, 160 (36.8%) children had CD4% increase of ≥10 from baseline and 358 (81.2%) had viral suppression<400 copies/mL. Furthermore, 294 (64.3%) children had continuous viral suppression throughout their follow-up time. Among the 439 children (96%) of children with baseline CD4<25%, 291 (65%) achieved immune restoration. Probability (95% CI) of reaching CD4≥25% was 22.6% (18.9-26.8) at 1 year, 56.9% (52.2-61.6) at 3 years and 68.5% (63.8-73.1) at 5 years. Median time to event was 7.3 months in children with baseline CD4 15-24% as compared to 23.7 months in baseline CD4<5% (log rank test p<0.0001). Immune restoration was independently associated with: young baseline age; aHR 1.9 (95% CI, 1.2-3.0) in <2 years, aHR 1.5 (95% CI, 1.1-1.9) in 2-7 years as compared to ≥8 years (p=0.003); high baseline CD4%; aHR 1.9 (95% CI, 1.4-2.5) in CD4 5-14%, aHR 5.8 (95% CI, 4.0-8.3) in CD4 15-24% as compared to CD4<5% (p<0.0001); CD4% increase of ≥10 from baseline at 6-months; aHR 2.6 (95% CI, 1.9-3.3, p<0.0001); and continuous VL suppression<400 copies; aHR 1.9 (95% CI, 1.4-2.4, p<0.0001).

**Conclusions:** Two-thirds of children achieved immune restoration despite initiating therapy at very low CD4 levels, although the most immunocompromised children took up to 3 times longer to reach the safe threshold. Young age, high CD4% at HAART initiation, early immune response at 6-months and sustained viral suppression were independent predictors of immune restoration. These findings support efforts for earlier therapy initiation at higher CD4 thresholds and emphasize the importance of early immune response and long-term viral suppression.

**No conflict of interest**

**Abstract: P_48**

**Treatment of pediatric HIV infection**

**Association between Hyperlipidemia and High Plasma Efavirenz Levels in Children in the PHPT Observational Cohort, Thailand**


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**Background:** Antiretroviral therapy (ART) has been associated with metabolic abnormalities including lipid abnormalities. The long term consequences of such abnormalities in children are not well known but may be detrimental. Can antiretroviral dose reductions be envisioned?

**Methods:** We selected children who initiated, between 2002 and 2009, in the prospective PHPT pediatric cohort in Thailand (41 sites), efavirenz-lamivudine-zidovudine or stavudine as first line regimen and had lipid and plasma efavirenz levels measured. Children received EFV daily doses on the basis of body weight. Total cholesterol was defined as high if ≥200 mg/dL and triglycerides if ≥150 mg/dL (ATP-III classification). Baseline variables were...
categorized according to median and tested for association with outcome using logistic regression models after univariate analysis (Fisher test). Between 12 to 16 hours after efavirenz intake, a blood sample was drawn to measure efavirenz plasma concentration using HPLC.

**Results:** 82 children (46% male) had a median (IQR) age 7.9 years (5.4 to 10.2), Thai norms based height for age z-score (HAZ) -2.2 (-3.1 to -1.4), weight for age (WAZ) -1.2 (-1.6 to -0.8), weight for height -0.6 (-1.1 to 0), CD4 4.5% (1.1% to 11%), HIV RNA 5.1 log_{10} copies/mL (4.7 to 5.5), hemoglobin 11.1 g/dL (9.9 to 11.9), ALT 34 IU/L (20 to 51), random glucose 78 mg/dL (71 to 85), cholesterol 141 mg/dL (116 to 162) and triglycerides 123 mg/dL (69 to 190). At time of plasma efavirenz concentration measurement, 12 months (6 to 24) after ART initiation, efavirenz concentration was 1,628 ng/mL (709 to 2,218), cholesterol 162.5 mg/dL (142.5 to 187.0), and triglycerides 100 mg/dL (79 to 141). However, 73% of children with higher efavirenz concentration had a viral load <400 copies/mL, versus only 44% with lower efavirenz concentration (p=0.01). In the multivariate analysis, factors associated with high cholesterol were high efavirenz concentration (P=0.03) and abnormal ALT levels at baseline (≥1.25 xULN) (P=0.03), while high triglycerides were associated with older age (p=0.01) and HIV RNA above median at baseline (P=0.03).

**Conclusions:** Children with high efavirenz concentrations were more likely to have high cholesterol but more likely to suppress viral replication. Before any dose reduction, the risk of viral breakthrough should be carefully considered.

*No conflict of interest*

**Abstract:** P _49_

**Treatment of pediatric HIV infection**

**Evaluation of adherence to antiretroviral therapy among perinatally HIV-1 infected children and caregivers.**

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**Background:** The Department of STD-AIDS and Viral Hepatitis of Brazilian Ministry of Health delivers antiretroviral medications to all HIV-infected citizens free of charge and drugs are dispensed by authorized pharmacies in monthly or bimonthly visits. Nevertheless, adherence is still a challenge particularly among children and adolescents.

**Methods:** We conducted a multicenter national study among HIV vertically infected children, adolescents and their caregivers. The main objective was to investigate how parental adherence to treatment correlates with children’s and adolescents’ adherence. Quantitative component of this study was composed by data from children/adolescents and caregivers: recent viral load, response to adherence questionnaire (missed ART doses in the past three days) and instruments to detect alcohol and other substances use. Adolescents responded their own questionnaires while children’s data were collect with caregivers.

**Results:** From 571 HIV+ children and adolescents followed at five sites, 256 vertically infected subjects in use of ART for at least 8 weeks and their caregivers were included in this analysis. Eighty percent (n=205) were children and 19.9% (n=51) adolescents. Forty-four percent (112/256) of caregivers were HIV+ and 69.6% (78/112) were in use of ART. Fifty-three percent of adolescents and 62% of children had undetectable viral load (<50 copies/mL) in blood samples collected at a median time of 25.8 months in use of a stable ART regimen [IQR: 9.8-37.5]. No difference was found on viral load control among children and adolescents cared by HIV+ or HIV- adults. Ninety percent of the caregivers reported children’s complete adherence to treatment: 88.3% of biologic mothers, 90% of biologic fathers, 92.9% of unrelated caregivers and 100% of health workers from foster care units. Eighty-three percent of adolescents reported...
no ART missed dose in the last three days. Among HIV positive care givers on treatment only 53% had undetectable viral load (41/78) and 81% of them reported complete adherence. Sixty-three percent of HIV+ caregiver under ART with virologic control had children with undetectable viral load, whereas 60% from the caregivers without virologic control had children with viral load <50 copies/mL. No significant association was found between viral load control among children, adolescents and caregivers and alcohol or other substances use.

Conclusions: Response to adherence questionnaire was not sufficiently sensitive to predict control of viral load among adolescents, children and caregivers. Adherence to ART is a complex phenomenon that needs complementary approaches for broader evaluation. The lack of maximal virologic suppression among caregivers of perinatally HIV-infected children signalizes for the urgent need of strategies to promote adherence within the family living with HIV.

No conflict of interest

Abstract: P_50

Treatment of pediatric HIV infection

Antiretroviral use among children and adolescents in Brazil

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Background: The Department of STD-AIDS and Viral Hepatitis of Brazilian Ministry of Health launched in 2009 a call for research to evaluate social, clinical and behavior aspects of children and adolescents living with HIV in our country. We report here some of our initial findings for the study conducted with this support, aiming to provide an updated overview of antiretroviral use among children and adolescents in Brazil, where access to specialized care and potent antiretroviral regimens are broadly available.

Methods: Five Pediatric HIV services from different geographic regions were involved. Procedures included chart review to capture clinical, laboratory (CD4 and viral load), and ART use. Inclusion criteria were perinatal infection and use of ART for at least eight weeks with available recent viral load.

Results: Enrollment occurred from May to October of 2010. During this period a total of 571 HIV infected children and adolescents were seen at the five centers (53% female). Perinatal infection responded for 95.3% (544 patients), 20 adolescents had been sexually infected (3.5%), 6 unknown source of infection (1.1%) and 1 through blood transfusion. Fifty-seven percent had biological mother or father as primary caregiver (325/571); 133 (23.3%) were cared by another relative, 42 (7.4%) were at foster care institutions and 35 (6.1%) had been adopted. Ninety percent were in use of ART (514/571) and 265 (46.4%) had undetectable viral load at the last available evaluation (<50 copies/mL). These children had been admitted to care at median age of 2.6y [IQR: 0.6-6.4]. Median age from May to October 2010 was 9.6y [IQR: 5.9-13.3] and median duration of ART use was 5.4y [IQR: 2.2-8.4]. Median age when first ART have been prescribed was 2.9y [IQR: 1.15-6.13]. Forty-five percent of patients were enrolled in the study (256/571). Among them, 110 (43%) had HIV diagnosis because of symptomatic conditions, 72 (28%) were followed since early age as born to HIV+ mothers and 71 (27.7%) were tested because someone in the family was found to be HIV+. At admission into care, 104/256 (40.6%) of these children had clinical and/or laboratory criteria for AIDS. From these 32/146 (21.9%) have been tested before symptoms and were detected as result of family screening, and 67/110 (60.1%) had test performed because of symptomatic conditions (p<0.01). At study enrollment 126 patients were classified as AIDS (22 progressed while on specialized care). As to ART use, at enrollment 156 (61.2%) were in use of HAART with PI and 100 (38.8%) were receiving HAART with NNRTI; 160 (62%) were on their first or second ART regimen and 96 (38.3%) on third regimen or beyond. We found no correlation between type of HAART or number of previous regimens and virologic control.
Conclusions: Although availability of specialized care, HAART and programs to avoid mother-to-child-transmission, new cases among children and adolescents are still being diagnosed with significant clinical delay. Once children are diagnosed, treatment is promptly started but even under treatment, this population has sub-optimal virologic control.

No conflict of interest

Abstract: P_51

Treatment of pediatric HIV infection

Safety and efficacy of maraviroc (MVC) in CCR5-tropic HIV-1-infected children aged 2 to <18 years

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Background: MVC is a CCR5 antagonist, approved for treatment of CCR5-tropic HIV-1 in adults, but not yet approved for pediatric use.

Materials & Methods: This is an open-label, two-stage (stage 1: dose finding; stage 2: safety/efficacy evaluation), age-stratified, non-comparative, multi-center study to evaluate safety, tolerability, and pharmacokinetics of MVC plus optimized background therapy (OBT) in treatment-experienced children. Subjects infected with CCR5-tropic HIV-1 are enrolled into one of four age and formulation cohorts: cohort 1: ≥2 - <6 years (liquid); cohort 2: ≥6 - <12 years (tablet); cohort 3: ≥6 - <12 years (liquid); and cohort 4: ≥12 - <18 years (tablet). No formal statistical analyses are performed. All data are summarized descriptively in each cohort and include subjects' duration of treatment, baseline plasma HIV-1 RNA concentration, and median baseline CD4⁺ counts.

Results: Thirty-one subjects were enrolled by 08/27/2010 (n=2, 12, 5, and 12 in cohort 1, 2, 3, and 4, respectively), 45% of them were male. Five subjects were of Asian, 18 of Black, and 8 of Caucasian race. The median duration of treatment was 200, 341, 322, and 166 days: median baseline plasma HIV-1 RNA concentration 5.7, 4.3, 4.9, and 4.7 log₁₀ copies/mL and median baseline CD4⁺ counts 151, 478, 192, and 312 μ/L in cohorts 1, 2, 3, and 4, respectively. Subjects were initially dosed twice-daily (BID) according to body surface area and OBT interactions with MVC. Dose adjustment occurred if MVC average concentrations <100 ng/mL at Week 2. Maintenance MVC doses ranged from 50-450 mg BID. Six treatment-emergent, non-treatment-related serious adverse events (AEs) were experienced by five subjects: uncontrolled behavior, gastrocutaneous fistula, H1N1 infection, pulmonary tuberculosis, and one subject experienced two AEs of prurigo and pneumonia. Five subjects experienced 11 treatment-related AEs (all ≤Grade 2): vomiting, elevated liver enzymes, nightmares, cardiac murmur, prurigo, abdominal pain, skin rash, decreased appetite, dizziness (2), and depression. Eight subjects had nine Grade-3 abnormal laboratory results: hyponatremia (4), neutropenia (4), and hypercholesterolemia (1). No deaths or discontinuations due to AEs occurred.

Plasma HIV-1 RNA <48 copies/mL was achieved in 13/20 (65%) and 6/9 (67%) patients at Weeks 24 and 48, respectively. Eight subjects discontinued; four with virologic failure without tropism change or MVC resistance at failure time, but with pharmacokinetic evidence of poor adherence.

Conclusions: Preliminary data suggest that MVC plus OBT in treatment-experienced children was safe, well tolerated, and effective. Enrollment is continuing.

Presenting author is an Employee of Pfizer Inc. and has commercial ties with ViiV Healthcare.
Abstract: P_52

Treatment of pediatric HIV infection

Treatment failure in resource limited settings: the experience from two paediatric cohorts in Beira (Mozambique) and Kampala (Uganda).

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Background: Scaling up paediatric combination antiretroviral treatment (cART) in low and middle-income countries has been proved to be safe and effective for almost 5 years. However provision of cART is now facing the challenge of first line treatment failure: delays in detecting treatment failure and switching to second line therapy lead to the development of drug-resistance, compromising subsequent regimens. Data on the occurrence of treatment failure and its related predictors in resource-limited settings is still limited.

Methods: HIV-infected infected children attending the Beira Central Hospital (Mozambique) and the St. Raphael of St. Francis Nsambya Hospital NHC Department (Kampala-Uganda), who started cART from January 2005 to December 2009, were studied. Treatment failure was defined according to WHO clinical and immunological criteria as recommended by 2006 guidelines. Incidence rate of treatment failure was examined. The probability of failing treatment over time post-initiation was estimated using Kaplan Meier method. Potential baseline predictors for treatment failure at cART initiation (age, sex, country, WHO clinical stage, type of cART, tuberculosis co-infection, BMI, immunodeficiency status and level of adherence) were explored in unadjusted and adjusted Cox proportional hazard models.

Results: 740 children (median age at treatment initiation 5.0 years, IQR 2.2-9.2) were included in this analysis for a total of 1088.5 years of follow-up. At treatment initiation immunosuppression was mild in 35 children (5%), advanced in 66 (9%) and severe in 581 (79%). Children were also significantly symptomatic with 73% (n=541) being in WHO clinical stage 3 or 4 at treatment initiation. The cART regimen most commonly used in first line therapy was a non-nucleoside-reverse-transcriptase-inhibitors (NNRTI) based regimen with 523 (71%) patients starting NVP and 120 (16%) starting EFV. The remaining children were started on a LPV/r-based regimen (24,3%) or on a 3NRTIs based regimen (73, 10%) if TB co-treatment was needed. A total of 218 events of treatment failure (29%, 95%CI 26-33) were identified during the follow up period, with a crude incidence rate of 20 events per 100 person years (95%CI 17.5-22.9). Treatment failure after adjusting for other factors was lower in the group of patients aged 36-59 months (HR 0.64, 95%CI 0.41-1, p 0.05) as compared to those aged ≥5 years, and higher in children with TB co-infection (HR 2.27, 95%CI 1.5-3.4, p<0.001), and in those starting treatment with WHO clinical stage 4 (HR 1.57, 95%CI 1.02-2.4, p 0.04) as compared to children with WHO clinical stage 3 without TB. The type of cART regimen was not significantly associated with the risk of treatment failure.

Conclusions: Over a one quarter of patients in this cohort experienced treatment failure over a five years period. TB is confirmed to be a significant predictor of treatment failure. TB as well as patients presenting with stage 4 disease are at higher risk of treatment failure meaning that. Early initiation of cART is highly recommend.

No conflict of interest
Abstract: P_53

Treatment of pediatric HIV infection

Prevalence and Cofactors of Viral Suppression Among Infants Receiving Early Antiretroviral Therapy (ART) in Kenya

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Background: There are limited data on virological outcomes among HIV-1 infected infants receiving early empiric ART, as is currently recommended by WHO guidelines. Among asymptomatic infants diagnosed early (<3 months of age) and initiating ART prior to disease progression, previous studies have noted a high proportion may have viral suppression during the first year of ART (>70% by 48 weeks). Here we report on incidence and correlates of viral suppression among infants <5 months of age initiating ART in the context of symptomatic HIV-1 disease at presentation to care.

Materials & Methods: HIV infected children aged <5 months were identified at clinics and in hospital wards and enrolled into an ongoing randomized clinical trial with a 2 year pre-randomization phase. First-line ART regimens included a backbone of 2 nucleoside reverse transcriptase inhibitors and either nevirapine (NVP) or lopinavir-boosed-ritonavir (LPV/r) (in infants with NVP exposure). Viral suppression was defined as a plasma HIV-1 RNA level <500 copies/mL. Univariate linear regression was used to evaluate correlates of baseline viral load (VL). Kaplan-Meier analysis and univariate and multivariate Cox proportional hazards regression were used to evaluate incidence and correlates of viral suppression.

Results: Among 88 infants with an available pre-ART viral load, the median age was 3.6 months, CD4% was 19%, weight-for-age z-score (WAZ) was -2.57, and height-for-age z-score (HAZ) was -1.90. The median plasma HIV-1 RNA level was 6.4 log10 copies/mL. At baseline, WHO stage III/IV (0.53 log; P=0.001), lower WAZ (0.13 log; P=0.006), lower CD4% (0.02 log; P=0.035), lower CD4 count (0.02 log per 100 cells; P=0.016), and previous hospitalization (0.36 log; P = 0.03) were significantly associated with a higher baseline viral load. Receipt of PMTCT with combined zidovudine/nevirapine was associated with a lower baseline viral load compared with no PMTCT (-0.48; P=0.05), whereas SD-NVP alone was not. The 3, 6, and 12 month probabilities of ever having viral suppression were 16.2%, 43.2%, and 67.6%. In univariate Cox proportional hazards analyses of time to first suppression, pre-ART infant CD4% ≥25% (HR=2.62; P=0.01) was associated with faster viral suppression. Never having been breastfed was also associated with faster viral suppression (HR=2.64; P=0.02); however, this association was a trend (P=0.1) when adjusted for CD4%. Age >3 months (HR=1.96; P=0.09) at ART was associated with a trend towards faster viral suppression. Some infants had evidence of viral failure following early suppression; the prevalence of viral suppression at 12 months was 40.4% (n=47); 12 of 28 infants who were not suppressed at 12 months had previous viral suppression.

Conclusion: Among infants initiating ART at <5 months of age, baseline VL was associated with clinical disease and was lower among infants who received combined PMTCT. Following ART early viral suppression was associated with higher CD4% at baseline and was not sustained in some infants. It will be important to define cofactors of viral failure during longer follow-up in these infants.

No conflict of interest

Abstract: P_54

Treatment of pediatric HIV infection

Similar Outcomes in HIV-1-infected Infants Receiving Nevirapine- vs Lopinavir-Boosted-Ritonavir-Based Antiretroviral Therapy (ART)

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Background: The WHO recommends that all HIV-1 infected infants receive early ART, regardless of clinical disease status or CD4%. The choice of ART regimen for these infants, who will likely receive lifelong ART, is generally limited to either a NVP- or LPV/r-based regimen. We compared virologic, immune, and growth responses to Nevirapine (NVP)- vs lopinavir-boosted-ritonavir (LPV/r)-based ART in HIV-1 infected infants initiating ART at age <5 months.

Materials & Methods: HIV-1 infected infants were identified through screening of mother-infant pairs attending PMTCT and in hospital. Infants were enrolled into a randomized clinical trial with a two-year pre-randomization period, and received empiric ART. First-line regimens included 2 nucleoside reverse transcriptase inhibitors (NRTIs) and either NVP or LPV/r (if NVP exposed for PMTCT). Infants with NVP exposure, or baseline non-nucleoside reverse transcriptase inhibitor (NNRTI) resistance, and treated with NVP-ART were excluded from this analysis. Wilcoxon rank sum tests were used to compare plasma HIV-1 RNA, CD4%, weight-for-age Z-scores (WAZ), weight-for-height Z-scores (WHZ) and height-for-age Z-scores (HAZ) between infants receiving NVP- vs LPV/r-based regimens. Wilcoxon sign-rank tests were used to compare baseline and follow-up measures.

Results: Among 99 infants, 80 initiated NVP-ART (with no NNRTI exposure or resistance), and 31 initiated LPV/r-ART. At entry, infants receiving NVP or LPV/r were similar: median age was 3.6 (NVP) and 3.6 (LPV/r) months, plasma HIV-1 RNA level was 6.8 log_{10} copies/mL (NVP) and 6.6 log_{10} copies/mL (LPV/r), CD4% was 21.3% (NVP) and 19.4% (LPV/r), WAZ was -3.24 (NVP) and -2.09 (LPV/r), WHZ was -0.83 (NVP) and -0.58 (LPV/r) and HAZ was -1.87 (NVP) and -2.10 (LPV/r). Infants who received LPV/r-based ART had a trend towards higher baseline WHZ (P=0.1); all other differences were not significant. Compared to baseline, the 1-month post-ART median decrease in log_{10} plasma viral load was -2.54 (P<0.001) and -2.32 copies/mL (P=0.001) in the NVP and LPV/r groups; these declines were similar between groups (P=0.3). 3-12-month viral loads were 3.39, 2.96, and 4.60 (NVP) and 3.41, 3.08, and 3.34 (LPV/r), with no significant differences between groups (P=0.8; P=1.0; P=0.4). Compared to baseline, the 12-month post-ART median increase in CD4% was 7.0% (P=0.08) and 7.5% (P=0.002) in the NVP and LPV/r groups; these increases were similar between groups (P=1.0). After 6 and 12 months post-ART, CD4% were 28.0% and 26.1% (NVP) and 27.7 and 26.6% (LPV/r). At 12 months post-ART, the median WAZ, WHZ, and HAZ were -1.62, -0.95, and -2.02 (NVP) and -1.20, -0.34, and -2.03 (LPV/r) (P=0.8; P=0.2; P=0.4) and did not differ between groups. The increase from baseline to 12-month WAZ (P=0.01) was significant but was not for WHZ (P=0.4) and HAZ (P=0.5). The rate of change in growth parameters did not differ between groups.

Conclusion: Among infants initiating ART at age <5 months, there were not significant differences in virologic, immune or growth trajectories between infants receiving NVP- and LPV/r-based ART. Although infants had significant declines in virus levels and significant increases in CD4% and WAZ, there was no significant change in HAZ or WHZ.

No conflict of interest

Abstract: P_55

Treatment of pediatric HIV infection

Correlates of Neurological Development in Kenyan HIV Infected Infants Who Initiated Early Empiric Antiretroviral Therapy


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Background: Although it is well documented that untreated HIV-infected infants have a high prevalence of developmental delay, less is known about the correlates of developmental delay in HIV-infected infants in sub-Saharan
treatment of HIV-infected infants may be important to prevent developmental delay. Defining early correlates of delayed development may enable early identification of at-risk infants and contribute to development of interventions to reduce developmental delay.

No conflict of interest

Abstract: P_56

Treatment of pediatric HIV infection

Long-term efficacy of combination antiretroviral therapy and antiretroviral drug resistance mutations in Rwandan HIV-infected children


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Background: There are increasing numbers of children receiving combination antiretroviral therapy (cART) in Rwanda, but data on long-term success, durability of efficacy and emergence of HIV drug resistance (HIVDR) is limited. The aim of this study was to evaluate the clinical, immunological and virological outcome of cART and to evaluate HIVDR in children on cART for more than one year.

Methods: Retrospective cohort study from two majors HIV clinics in Kigali, Rwanda. Baseline data were extracted from patient and hospital electronic files. Clinical parameters by questionnaire and physical exam, CD4, and viral load (VL) were collected during the study visit. HIVDR was analyzed in children randomly selected who had HIV-RNA >1,000 copies/ml.

Results: 424 children were recruited, 219 (52%) were female. The median age was

Africa particularly among infants receiving early empiric ART.

Materials and Methods: Infants <5 months old, identified through PMTCT clinics and hospital wards, were enrolled and followed in an ongoing study in Nairobi, Kenya. All infants initiated empiric ART shortly after enrollment, consistent with WHO guidelines. Analyses were restricted to infants >3 months old at enrollment with a baseline neurological assessment. Age of achievement of neck control, unsupported walking and monosyllable speech were used as a measurement of neurologic development using the Denver developmental screen. Correlates were evaluated using Wilcoxon rank sum test and Spearman rank correlation test.

Results: At enrollment, 56 infants with HIV-1 were >3 months of age and had developmental assessment prior to ART; the median age was 3.8 months, CD4% was 18%, viral load was 6.4 log_{10} copies/ml, weight-for-age z-score (WAZ) was -2.1, height-for-age z-score (HAZ) was -1.9 and weight-for-height z-score (WHZ) was -6. Fifty-six infants achieved neck control during follow-up, 71% by 5 months of age and 93% by 6. Older age at enrollment (P=.01), lower WAZ (P=.001) and lower HAZ (P=.01) at enrollment prior to ART were associated with later established neck control. Following >7 months of ART, 54 infants demonstrated ability to walk unsupported during follow-up; 9% walked by 12 months and 80% were able to walk by 18 months. Baseline clinical progression prior to ART as measured by WHO HIV stage III/IV (P=.02), lower baseline infant CD4 count (P=.001), and lower baseline WAZ (P=.0002), HAZ (P=.01) and WHZ (P=.03) scores were associated with significantly older age of first walking. 6% of the 53 infants, who acquired monosyllabic speech during follow-up, acquired it by 12 months of age and 72% by 18 months. Baseline WHO HIV stage III/IV (P=.01), lower baseline infant and maternal CD4 count (P=.0003, .02) and lower baseline WAZ (P=.0001) and HAZ (P=.001) scores were associated with later milestone achievement.

Conclusions: Older age at enrollment and malnutrition were associated with older age of achieving neck control in untreated HIV infected infants. After >7 months of sustained ART, poor baseline immunologic status, reduced maternal health status and malnutrition at enrollment was associated with later attainment of unsupported walking and monosyllabic speech. Earlier detection and

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10.7 years (range: 1.7 to 18.8) and the median period on cART was 3.4 years (IQR: 1.9 to 4.8). cART consisted of a NRTI backbone (AZT or d4T plus 3TC in 95%) plus either nevirapine (64%), efavirenz (31%) or a protease inhibitor (5%). At study visit, all children were in a good clinical condition (absence of moderate or severe illness). The mean weight-for-age z-score (WAZ) increased from -1.6 (95% CI: -1.8 to -1.4), at cART initiation to -1.1 (95% CI: -1.2 to -0.9, p<0.001). Eighty-two percent (95% CI: 78-86) of children had an increase of the CD4 count, with a median of +330 cells/mL (IQR: 97 to 614). cART initiation CD4 count was a significant predictor of the CD4 cell response (ß=0.2, 95% CI: 0.2 to 0.3), and an inverse relationship was found between age and CD4 cell count (ß=0.7, 95% CI: -0.9 to -0.6, p<0.001). In univariate analysis, children with CD4 cells ≥350 mL at study visit were 13 (CI: 6.0 to 28.9) times more likely to suppress VL. For age z-score (HAZ), WAZ and CD4 cells ≥350 mL at cART initiation were not found to predict VL. Of the 424 children 124 (29%) had HIV RNA >1000 copies/mL; Genotypic resistance was analyzed in 57 children. K101AEKT were found in 1/52 (2%) of 2/52 (4%). V108IV, V179D, V106IV, V109I and 3/52 (6%), V179IT 2/52 (4%) and G190A/S 8/52 (15%), A98G 5/52 (10%), E138A/E 21/52 (40%), Y181C/I/V 17/52 (33%), K101P/E 8/52 (15%), A98G 5/52 (10%), E138A/E 3/52 (6%), V179IT 2/52 (4%) and G190A/S 2/52 (4%), V108IV, V179D, V106IV, V109I and K101AEKT were found in 1/52 (2%) of children.

Conclusion: A discouraging proportion of children were found with virological failure (VF), of which the majority had major NRTI and NNRTI mutations and >10% showed reduced susceptibility to both classes. Clinical condition and CD4 count at cART initiation were not good indicators of VF; nor did children who developed VF show clinical indicators at study visit. Affordable routine VL testing is needed for the early detection of VF, and to prevent ongoing accumulation of HIV-DR mutations which may jeopardize treatment options.

No conflict of interest

Abstract: P_57

Prevention of Mother-to-Child transmission

Genetic features of HIV-1 envelope gp120 (V3-V5) derived from plasma and breast milk viruses from breastfeeding mothers in Burkina Faso

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Introduction: Human immunodeficiency virus type 1 (HIV-1) primarily infects vital cells in the human immune system such as T-helper cells (CD4+ T cells), dendritic cells and macrophages. In addition to the presence of cell associated viruses within infected cells, free viral particles are found in several liquid compartments such as blood, semen, vaginal fluid, pre-ejaculate, spinal fluid, sputum, bronchoalveolar lavage and breast milk.

Material and Methods: In order to characterize the V3-V5 region of the HIV-1 glycoprotein (gp)120, paired plasma and breast milk or breast milk cells – derived viruses were obtained from 12 HIV-1 positive breast-feeding mothers from Burkina Faso.

Results: These subjects were infected either by CRF02_AG (8/12) or CRF06_cpx (4/12) HIV strains. Phylogenetic analysis showed three distinct clustering patterns of viral sequences between plasma and breast milk compartments: a compartmentalized pattern in 8/12 subjects (75%), partially compartmentalized and non-compartmentalized patterns in two subjects respectively. Plasma derived HIV-1 sequences were more diversified than those from the
breast milk. Prediction of the potential co-receptor usage on the basis of the critical amino acids within V3 loop (positively charged at the position 11/25), the V3 loop net charge and the Geno2pheno web tool disclosed very few potential CXCR4-tropic viruses in both plasma and breast milk. The GPGQ motif at the crown of the V3 loop was the most frequent motif (75%) followed by GPGR (24%) and GPGP (0.7%), none of which were subtype specific. The number and the position of potential N-glycosylation (PNLG) sites in paired samples were relatively conserved in both compartments. Overall, the viral populations in these compartments were distinct in almost all patients but there was no relationship between compartmentalization, predicted phenotype and PNLG.

Conclusion: These findings suggest that infants infected through breastfeeding may harbor viruses different from those in the mother’s plasma.

No conflict of interest

Abstract: P_58

Prevention of Mother-to-Child transmission

Adverse events in kenyan infants born to HIV-infected mothers receiving triple antiretroviral regimens for prevention of Mother-to-Child transmission

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Introduction: In many developing countries, nevirapine-based antiretroviral regimens are administered during pregnancy and breastfeeding to prevent mother-to-child HIV transmission (MTCT). Nevirapine is associated with life-threatening hepatic and cutaneous toxicities. It is unknown whether exposure to nevirapine in utero or during breastfeeding places infants at risk for toxicity. We evaluated toxicity rates among infants exposed to maternal nevirapine versus infants exposed to neilnavir, which has not been associated with these toxicities.

Materials & Methods: During 2003–2006, we enrolled 522 HIV-infected pregnant women, initiating 3-drug antiretroviral regimens at 34 weeks’ gestation and continuing through 6 months postpartum. Infants received a single-dose of nevirapine at birth as standard of care. We assessed the association between age-specific hyperbilirubinemia, elevated alanine aminotransferase (ALT) level, and grade 2 (severe) rash and maternal exposure to nevirapine versus neilnavir among term (≥36 weeks) infants. We also assessed the association between these toxicities and other clinical factors.

Results: Hyperbilirubinemia developed in 17 (6.3%) of 270 nevirapine-exposed and 16 (7.8%) of 206 neilnavir-exposed infants (odds ratio [OR]: 0.8; 95% confidence interval [CI]: 0.4-1.6) and in 8 (22%) of 36 low-birth-weight infants (OR: 4.7; CI: 2.0-11.4). ALT levels were elevated in 1 (0.4%) nevirapine-exposed infant and 4 (1.9%) neilnavir-exposed infants (OR: 0.2; CI: 0.02-1.7). Severe rash developed in 7 (2.6%) nevirapine-exposed infants and 1 (0.5%) neilnavir-exposed infant (OR: 5.5; CI: 0.7-44.9). All outcomes were transient and resolved without change in the mother’s antiretroviral regimen or cessation of nursing. Neither elevated levels of ALT nor severe rash was associated with any factor evaluated.

Conclusions: Infants exposed to nevirapine in utero and through breastfeeding were not at increased risk of hyperbilirubinemia, elevated ALT, or severe rash. Our data indicate that nevirapine-based antiretroviral regimens during pregnancy and breastfeeding to prevent MTCT are as safe for infants as neilnavir-based regimens.

No conflict of interest
Abstract: P_59

Prevention of Mother-to-Child transmission

HIV exposed uninfected (HEU) infants: evidence of severe infectious morbidity in South Africa

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Background: 300 000 HEU infants are born annually in South Africa. HEU infants may have higher morbidity and mortality from infectious diseases than HIV-unexposed (UE) infants. We present the first prospective clinical outcome data for South African HEU infants.

Methods: A prospective cohort study commenced in Cape Town, South Africa in 2009. Primary clinical outcomes included the number and severity of infectious events in the first year of life, severity defined as need for hospitalisation. Growth and nutrition was measured as weight- and height-for-age CDC Z-scores at 1 year.

Results: Fifty nine infants, 31 HIV-exposed and 28 UE were enrolled. Four HIV exposed infants were HIV-infected and excluded. The mean follow-up (9.64 and 10.89 months in UE and HEU respectively), mean birth weight (2966 +/-413g) and gestational age (37.78 +/-2.45 weeks) were not significantly different between the two groups. All but one HEU infant were exclusively formula fed; all UE were breastfed to a median of 12 weeks. UE infants had lower weight- (0.01<p<0.02) and height-for-age (0.02<p<0.05) Z-scores at 1 year. There were 181 infectious events with no difference in the total number of infections between the 2 groups. HEU had significantly more severe infections: 16 in 10 HEU compared to 4 in 4 UE, with a relative risk of 3.6. Severe lower respiratory tract infections dominated, accounting for 9 of 16 severe infections in HEU and 2 of 4 in UE. The remainder of the severe infections included gastroenteritis, viral exanthems, urinary tract infections and neonatal sepsis. There were no deaths in the HEU and one UE death secondary to adenovirus pneumonia.

Conclusion: HEU and UE experienced a similar frequency of infection but HEU were 3.6 times more likely to experience severe infections than UE infants. Further investigations are needed to determine the mechanism(s) of susceptibility to severe disease.

No conflict of interest

Abstract: P_60

Prevention of Mother-to-Child transmission

Successful integration of PMTCT services into maternal and child health services in Nigeria

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Background: Jhpiego is implementing a CDC-funded Prevention of Mother to Child Transmission and HIV Counseling and Testing Project (PMTCT/HCT) in 12 hospitals in Nigeria. In these same hospitals, Jhpiego is also implementing a USAID supported Maternal and Child Health Integrated Program (MCHIP). MCHIP services include: Focused Antenatal Care, Maternal and Child follow-up services, and Family Planning services while the PMTCT/HCT services include PMTCT interventions, Community Mobilization and outreach. Because of client demand for access to PMTCT services at the same point as ANC-MCHIP services, these two separate projects were successfully integrated in the 12 supported sites.

Methodology: Data for specific service indicators in the 12 supported facilities were captured one-year before (January to December 2008) and one-year after the integration of the PMTCT programs into the
other existing maternal and child health programs (January to December 2009) in the 12 facilities.

**Results:** One-year before PMTCT integration, 36% of ANC clients had 4 or more ANC visits during their pregnancy in the 12 facilities but after integration the percentage increased to 86% (p<.001). In addition, before the integration, only 15% of clients were counseled and tested for HIV during their pregnancy but after the intervention, 73% were counseled and tested (p<.001). The percentage of children that were delivered in the hospitals and brought back to complete the four courses of immunization before the intervention was 10%, this percentage increased to 91% after the integration. Finally, 17% of clients accessed family planning services prior to integration but after integration, 63% of clients accessed family planning services (p<.001).

**Conclusion:** The results of the analysis before and after the integration of PMTCT services into existing maternal and child health services resulted in improved ANC attendance, an increase in counseling and testing for HIV during pregnancy; an increase in immunization service uptake; and increased uptake in family planning services among clients in 12 Nigerian hospitals. Integration also allowed the clients to seek more services at one point of care rather than having to access specific services (PMTCT) at other sites/facilities, this in itself encourages and improved service uptake.

**No conflict of interest**

**Abstract: P_61**

**Prevention of Mother-to-Child transmission**

**Pediatric HIV Vaccine Design in the Context of Immune System Development**

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**Background:** A pediatric vaccine to prevent breast milk transmission of HIV needs to be effective early after birth when the infant immune system is still immature. A detailed understanding of age-related differences in immune responses between infants and adults will therefore be essential for the development of a successful pediatric HIV vaccine. Optimal priming by myeloid dendritic cells is a prerequisite for the induction of potent CD4 T helper 1 responses that can then induce CD8 T cell and B cell responses. Our studies define distinct steps in mDC and CD4 T cell activation that differ between infants and adults. Results were applied to a more rationale pediatric HIV vaccine design.

The only pediatric vaccine that induces T helper 1 responses that are comparable to adults is the BCG vaccine. Thus, we hypothesized that a recombinant attenuated *Mycobacterium tuberculosis* vaccine with better safety than BCG, but similar immunogenicity would be a suitable vaccine candidate, and could potentially protect against HIV and *Tb* infection.

**Methods:** Phospflow analysis was used to define differences in cytokine and TLR signaling in CD4 T cells and mDC, respectively, of human cord and adult blood. Longitudinally collected rhesus macaque blood samples from birth to 1 year of age were analyzed by flow cytometry for differentiation markers and functional responsiveness. Plasma and salivary IgG and IgA antibodies were determined by ELISA. Next, infant rhesus macaques were immunized orally at birth with rAMtb-SIV and received a systemic boost at 3 weeks. SIV and Mtb-specific T and B cell responses, and mDC function were measured in blood and tissues using multiple immunological and molecular techniques.

**Results:** We identified several differences in infant and adult signaling pathways: In response to TLR stimulation, infant mDC showed reduced NF-kB phosphorylation compared to adults. Infant CD4 T cells showed reduced IFN-g responses due to significantly lower phosphorylation of STAT1, a transcription factor critically important in IFN-g signaling. In contrast, IL4 signaling and activation of STAT6 were comparable between infant and adult CD4 T cells. A replication-attenuated rAMtb-SIV with deletions in immune evasion genes was able to overcome inherent immune deficiencies in infants: (i) The rAMtb-SIV vaccine promoted in vivo mDC activation indicated by stronger IL-12 and TNF-a production by mDC after in vitro stimulation in vaccinated compared to mock-immunized...
animals. (ii) CD4 and CD8 T cell responses to both SIV and Mtb antigens were induced in vaccinated infant macaques. (iii) Vaccinated animals developed SIV- and Mtb-specific antibodies. Importantly, while IgA is generally not detectable until 8-12 weeks of age, SIV-specific IgA was detectable in saliva of vaccinated macaques. Finally, it should be noted that the rAMtb-SIV vaccine did not result in any dissemination of rAMtb even if tested in immunocompromised infant macaques.

Conclusions: Immunological studies elucidating differences in pathways leading to mDC and T cell activation in infants compared to adults will be essential for the design of successful pediatric vaccines. Towards this goal, we provide evidence that a novel pediatric combination rAMtb-SIV vaccine is safe and highly immunogenic in infant macaques.

No conflict of interest

Abstract: P_62

Prevention of Mother-to-Child transmission

Feasibility Study of HIV-1 Voluntary Counseling and Testing of Sexual Partners of Pregnant Women Receiving Prenatal Care in Porto Alegre, Brazil

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Background: Pregnant women are at a significantly higher risk of HIV acquisition during gestation and while breastfeeding than non-pregnant counterparts due to behavioral and biological factors. Acute seroconversion during pregnancy or breastfeeding results in increased HIV mother-to-child transmission rates and therefore, has been identified as a major public health challenge to the prevention of mother-to-child transmission efforts in the south of Brazil.

Methods: We conducted a prospective cohort study evaluating the feasibility of offering HIV-1 voluntary counseling and testing (VCT) to sexual partners of HIV-negative pregnant women receiving antenatal care at a large metropolitan hospital in Porto Alegre, Brazil. From 9/10 to 2/11, 798 HIV-negative women who met study criteria were approached to participate in study during prenatal care visits. Seven hundred fifty three (94%) women agreed to participate in the study and were encouraged to bring their stable sexual partner (>3mos relationship) for HIV VCT via rapid testing. Women were interviewed during prenatal care and re-interviewed following delivery to measure uptake of the intervention.

Results: Of 753 HIV-negative pregnant women enrolled during prenatal care, 361 (48%) male sexual partners received HIV testing and 3 (0.8%) were diagnosed with HIV infection. Thirty three (4%) HIV positive women were excluded from this analysis. Two hundred eight (27%) pregnant women have delivered to date, with 201 (98%) confirming HIV testing was suggested to their partner. Despite prompting during interviews, no adverse outcomes were reported. The most common reason provided by women for partners not being tested was work (78%) and inconvenience (7%). Logistical regression analysis demonstrated that women who self-identified as white (n=288), were unemployed (n=208), denied condom use during pregnancy (n=318), and knew their own HIV status (n=306) were more likely to have partners tested (p<0.05). Interviewed male partners displayed a wide range of high risk behaviors including IVDU (2%), extra-relationship affairs (9%), bisexuality (3%) and >10 lifetime sexual partners (33%).

Conclusion: HIV partner testing during prenatal care is feasible, however, for high acceptance rates greater than 50%, programs likely need to expand services beyond regular work hours. Increased feasibility of the partner-testing approach renders this intervention attractive to public health programs targeting prevention of HIV, syphilis, and other STDs. Partner testing has the potential to be highly effective in the prevention of perinatal transmission of these infections.

No conflict of interest
Abstract: P_63

Prevention of Mother-to-Child transmission

Exclusive breast feeding 6 Months among HIV positive mothers delivering & attending post natal clinics at Mulago in Kampala, Uganda (Jan2006-Jun2010)

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Background: Before Jan 2009, the MOH infant feeding guidelines recommended all identified as HIV positive for counseling to Exclusively Breastfeed (EBF) until 6 months of age if replacement feeding is not Acceptable, Feasible, Affordable, Safe, and Sustainable (AFASS). In Jan 2009, the MOH Uganda further strengthened the infant feeding guidelines for HIV infected mothers to strongly recommend exclusive breastfeeding for infants of HIV infected women for the first 6 months of the infant’s life, irrespective of the infant’s HIV status, unless replacement feeding is acceptable, feasible, affordable, sustainable and safe (AFASS) for them and their infants before that time.

Objectives:
1. To compare proportion of women practicing EBF in the first six months of life following the MOH messages during these two time periods
2. To describe the effect of the updated infant feeding guidelines compared to the earlier 2006 guidelines

Methods: Women identified as HIV-positive were counseled to EBF for the first six months of life. We compared the proportion of women who chose to exclusively breast feeding at birth and continue to exclusively breast feed at six weeks and six months, during the periods Jan 2006-Dec 2008 and Jan 2009 to Dec 2010 before and after infant feeding policy change in Jan 2009.

Results: A total of 9,072 HIV positive women delivered between Jan 2006 - Dec 2008; and 7,136 delivered between Jan 2009 and Dec 2010. At delivery 7,345 [(81%) 95% CI (80-82%)] and 6,010 [(84 %) 95% CI (83-85%)] decided to practice EBF for 6 months during Jan 2006 - Dec 2008 and Jan 2009 - Dec 2010 respectively. Among those who returned at six weeks 852/1,155[(73%) 95% CI (70-76%)] and 973/1,267[(77%) 95% CI (75-79%)] were still EBF during the respective time periods. However only a small proportion of women were still EBF at six months: 74/495 [(15%) 95% CI (12-18%)] and 130/565(23%) 95% CI (20-26%), respectively during the two time periods.

Conclusion: From a program perspective, HIV-positive women who decide to breastfeed continue to EBF until six weeks but only a few women sustained EBF up to six months. Stronger emphasis on EBF to 6 months in the 2009 MOH infant feeding guidelines did not have much impact with only a quarter of mothers still EBF at the 6 month visit. These results suggest more innovative strategies are needed to roll out WHO/MOH guidelines and to increase rates of EBF among HIV infected women.

No conflict of interest

Abstract: P_64

Prevention of Mother-to-Child transmission

Trends in male partners HIV testing in antenatal clinics and Labour/Delivery units at Mulago Hospital, Kampala Uganda, 2007-2010

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Introduction: Male involvement in Prevention of Mother to Child HIV transmission (PMTCT) remains low in Uganda with less than 10% of the men fully participating in Antenatal and <5% at labor and Delivery.
**Abstracts**

**Materials & Methods:** Mulago National referral Hospital offers routine HIV counseling and testing (RCT) to women and their partners during antenatal and at labor/delivery. Since 2006, Mulago Hospital put several strategies to improve male partner involvement in reproductive health and PMTCT, including an evening Men's access clinic to attract men who cannot make it during normal working hours, health education messages by counselors and peer volunteers and invitation letters for men. In March 2010 a special waiting area for men was opened at the labor/delivery to offer RCT, health education, educational and entertainment videos. We analyzed the trends in proportion of women whose male partners were HIV tested in antenatal clinic (ANC), men’s access clinic and labor/delivery, from 2007-2010.

**Results:** Over 33,000 pregnant women at Mulago Hospital access RCT annually. Between 2007 and 2010, the proportion of pregnant women whose male partners were HIV tested increased from 5.9% to 14.6% in the antenatal clinics (p-value for trends<0.0001) and from 3.6% to 8.8% (p-value for trends <0.0001) in the labor/ with highest increase in 2010. There was no significant increase in the proportion of men tested in the men's access clinic, (1.7%-2.0% p-value for trends=0.13).

**Conclusion:** There has been a gradual increase in male partner HIV testing in the Antenatal clinics, labour/ delivery units. However, testing in the men's access clinic has remained stable over time. Further male friendly strategies are needed to attract men into Reproductive Health and PMTCT programs in Uganda.

No conflict of interest

**Abstract: P_65**

Prevention of Mother-to-Child transmission

SMS technology of TRACnet system saving lives of Rwandan HIV infected infants

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**Introduction:** Without treatment, 50% of HIV infected infants born from HIV infected mothers die before their first birthday anniversary. Testing and Treatment initiated early are the only ways of saving lives of these infants. However, delays to obtain PCR results were a big challenge for the clinicians to initiate treatment since years ago. Health facilities could wait for PCR results for more than 3 months. We are here reporting an SMS based technology as a solution to the result delays. This TRACnet technology was developed by Voxiva, in collaboration with the Rwanda Ministry of Health and the U.S. Centers for Disease Control and Prevention (CDC), with PEPFAR funding.

**Methods:** The solution consisted of creating a new module for PCR Lab tests within TRACnet system. As soon as the results are ready at National Reference Laboratory and entered into PCR module, Short Text Messages (SMS) and emails of PCR results are sent to two recipients at Health facility where samples originate. All the information entered into the module is stored in a database and produces automatic reports and charts to show the basic statistics and indicator performance.

**Results:** This module has been designed and is in use from March 2010. Today, 10547 results have been sent to all 404 heath facilities performing DBS/PCR in Rwanda of which 395 tested HIV positive (3, 1%). An average of 8 days is registered from sample collection to sample reception at NRL versus 33 days in baseline assessment. Moreover, this average is 6 days from results availability at NRL to result reception to Health Facility versus 90 days in baseline assessment one year ago

**Conclusion:** The module has helped to shorten the PCR results turnaround time from 4 months to 2 weeks. The sooner the result was received, the earlier Antiretroviral treatment was initiated and this saved lives of many HIV positive infants.

No conflict of interest
Abstract: P_66

Prevention of Mother-to-Child transmission

Etravirine Penetration in Cervicovaginal Compartment exceed the Median Inhibitory Concentration in HIV-1 infected Women (DIVA-02 study)

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Introduction: The penetration of antiretroviral drugs into the female genital tract may impact sexual and vertical transmission as well as resistance to antiretrovirals (ART). We studied the penetration of etravirine (ETR), a second generation NNRTI.

Methods: HIV-1 infected women over 18 years old receiving an ETR-containing ART with plasma HIV-RNA (VL) < 40c/mL for at least 3 months were enrolled after informed consent. Paired samples of blood plasma (BP) and cervicovaginal fluids (CVF) were collected. Intervals between last drug intake and sampling were recorded. CVF sampling was performed using blotting paper, in absence of menstruation, sexual intercourse or intravaginal treatment within the last 2 days. Screening for genital tract infections was performed with Gram and culture. VL was determined (Roche Taqman) in BP and CVF with LOD < 40c/mL and < 200c/mL, respectively. ETR BP and CVF concentrations were measured at steady-state using UPLC-MS/MS method (Acquity UPLC-Acquity TQD) after sample pretreatment (LOQ-5ng/ml). Results are presented as median (IQR25%-75%).

Results: 12 non-pregnant women were enrolled. Median age was 39 years (36-45) and CD4=480/mm³ (260-639). ETR treatment duration was 142 days (121-235) in association with a median of 3 other ARV (1-4), including darunavir/ritr in 5, raltegravir in 6, maraviroc in 1 and NRTI in 6. At time of sampling, all patients had undetectable VL in CVF and BP despite evidence of gardnerella vaginallis genital infection in 2 cases. CVF and BP ETR concentrations were 857 ng/mL (385-1682) and 592 ng/mL (391-839), determined 13.25 (9.5-14) and 12.4 (9-14) hours respectively after the last drug intake. CVF/BP ratio of ETR concentrations was approximately 1.19 (0.4-4.80).

Conclusion: ETR had good penetration into the genital tract. Median ETR CVF exposure was approximately 350 fold higher than the EC50 for wild type HIV-1 (0.3-2.3ng/ml), possibly contributing to virological control in the compartment.

No conflict of interest

Abstract: P_67

Prevention of Mother-to-Child transmission

Effect of single dose carbamazepine on pharmacokinetics of and resistance to nevirapine in perinatal HIV prevention: a quasi-randomized trial


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Background: Single-dose nevirapine (sdNVP) is a highly cost-effective strategy to reduce perinatal HIV-1 transmission. Its major disadvantage is the selection of NVP resistance in at least 35-40% of the women, a fact that is probably attributed to the long elimination half-life of NVP. A pilot study in HIV-negative healthy women showed that the NVP elimination half-life was significantly decreased by the addition of a single dose of an enzyme inducer, carbamazepine (CBZ), to sdNVP. We aimed to confirm that sdCBZ decreases NVP half-life and further, to investigate the effect of sdCBZ on the development of NVP resistance in pregnant
HIV-infected women and their newborns in Moshi, Tanzania.

Methods: This was an open label, parallel-group and superiority trial. Antiretroviral-naive, HIV-infected, pregnant women aged 18-40 years, with CD4 >200 cells/mm³, willing and able to regularly attend the antenatal clinics in Moshi, Tanzania were enrolled 1:1 by alternate allocation to receive 200 mg sdNVP alone, or in combination with 400 mg single-dose carbamazepine (sdNVP/CBZ) at delivery. Infants received 2mg/kg oral dose of NVP within 72 hours of birth. The co-primary outcomes were nevirapine plasma concentrations one week and nevirapine resistance mutations six weeks post-partum. Analyses were based on those still eligible at delivery.

Results: Ninety-seven women were assigned to sdNVP and 95 to sdNVP/CBZ during pregnancy, of which 75 sdNVP and 83 sdNVP/CBZ were still eligible at delivery at study sites. The median (interquartile range) NVP plasma concentration was 1.55 (0.88-1.84) mg/L in sdNVP (n=61) and 1.40 (0.93-1.97) mg/L in sdNVP/CBZ (n=72) at delivery (p=0.91), but 1 week later was significantly lower in sdNVP/CBZ (n=63; 0.09 (0.05-0.20) mg/L) than in sdNVP (n=52; 0.20 (0.09-0.31) mg/L) (GMR: 0.642, 95%CI 0.428-0.965; p=0.03; and rank-sum p=0.004). Six weeks postpartum, NVP mutations were observed in 11/52 (21%) in sdNVP and 6/55 (11%) in sdNVP/CBZ (odds ratio=0.46 (95% CI 0.16-1.34), p=0.15). K103N was the most frequently observed mutation in both the control and the intervention arms.

Conclusion: Addition of single-dose carbamazepine to single-dose nevirapine at labour onset in HIV-infected, pregnant women did not affect nevirapine plasma concentration at delivery, but significantly reduced it one week postpartum, with a trend towards fewer nevirapine resistance mutations.

No conflict of interest

Abstract: P_68
 Prevention of Mother-to-Child transmission
 Quantification of HIV drug resistance in women and infants exposed to maternal ZDV and sdNVP by pyrosequencing and oligonucleotide ligation assay


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Introduction: Single-dose-nevirapine (sdNVP) to prevent mother-to-child-transmission (pMTCT) selects mutants that either decay to clinically insignificant concentrations, or persist and diminish the efficacy of later NVP-containing-ART. Thus, in 2010 WHO recommended mothers receive ART or zidovudine (ZDV)-monotherapy to pMTCT. We examined the dynamics of drug-resistant-HIV-1 in women and infants, and compared mutant detection by the oligonucleotide-ligation-assay (OLA), an inexpensive quantitative test sensitive to 2%, to pyrosequencing.

Methods: Serial specimens (n=148) from 14 infants and 15 women collected over 4-12 months following maternal ZDV (median of 63 days) and sdNVP had the concentrations of NVP-resistance-mutants quantified by OLA at RT codons 103, 106, 181 and 190. Detection of resistance was compared by pyrosequencing analysis of 300-1000+ amplifiable copies/specimen in 45 specimens, with thymidine-analog-mutations also tallied at codons 41, 67, 70, 210, 215 and 219.

Results: NVP-resistance in infants followed two patterns; infants initially had wild-type viral populations and accumulated NVP-mutants that peaked at a median concentration of 63% at 6-8 weeks of age and subsequently decayed to a median of 7% by 4-12 months. Alternatively, infants’ viral populations were ~100% NVP-mutant soon after infection and persisted at concentrations >95% mutant over 4-12 months. In women, NVP-resistance
concentrations peaked at <30%, then decayed. The only ZDV-resistance detected was K70R at a concentration of <1% in 3/15 women. The concentrations of NVP-resistance-mutants by pyrosequencing and OLA were similar (n=33; r= 0.93). Pyrosequencing detected NVP-mutants in 13/57 codons that tested wild-type by OLA (n=3 at concentrations 2-5%; n=10 at <2%, below OLA limit-of-detection).

Conclusions: Following sdNVP, NVP-resistant mutants decay to low concentrations in women and some infants, but persist as the dominant population in other infants. Short-course ZDV selected K70R in a minority of mothers. OLA quantification of mutants correlates highly to pyrosequencing, and could serve as an economical tool to monitor HIV-1 drug resistance.

No conflict of interest

Abstract: P_69

Prevention of Mother-to-Child transmission

Prenatal care differences between HIV infected and HIV non-infected women – Is premature labor a matter of quality of care?

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Background: Although several interventions are known to decrease the HIV mother to child transmission, the pregnancy outcomes are still a concern. Studies contradict each other in assessing the influence of the status of women infected with HIV on the outcome of pregnancy, and several factors, such as access to prenatal care were not studied. The aim of this study is to evaluate intervening variables in the occurrence of prematurity in pregnant women infected or not with HIV.

Methods: It is a cross-sectional study. We compared data from HIV infected pregnant women (HIPW), derived from a prospective cohort study of all HIV-infected pregnant women followed from 1995 to 2005, at the Instituto de Puericultura e Pediatria Martagão Gesteira – Rio de Janeiro, and data from HIV non-infected pregnant women (HNIWP), derived from a random sample of all pregnant women who gave birth at Rio de Janeiro Municipality between 1999 and 2001.

In order to evaluate differences between HIPW and HNIWP prenatal care, all relevant socio-demographic, nosological, and pregnancy outcomes data are retrieved from both studies. The Kotelchuck modified index was calculated for all the population. It measures the concentration of prenatal visits during the care period, and it is based on months of initiation of prenatal care and the proportion of visits observed on the number of queries expected, according to gestational age at birth. Comparisons were performed using Student-t and Chi-square tests. Variables with p-value<0.25 were included in an unconditional logistic regression model.

Results: 713 HIV-infected women and 2145 HIV non-infected women were evaluated. Prematurity was present in 15% of the HIPW group and 10.9% HNIWP group (p-value<0.01). The main differences between HIPW and HNIWP in the multivariate analysis were: Age OR=1.05, per year (95%CI=1.03 – 1.08); does not live with a partner OR=3.31 (95%CI=2.44 – 4.48); less than eight years of formal education OR=1.32 (95%CI=1.01 – 1.73); family income – less than 3 Brazilian minimum wage OR= 5.36 (95%CI=4.03 – 7.14); tobacco use OR=2.31 (95%CI=1.70 – 3.14); hypertension during pregnancy OR=1.42 (95%CI=0.93 – 2.15); syphilis during pregnancy OR=9.63 (95%CI=4.98 – 18.63); cesarean-section OR=3.12 (95%CI=2.38 – 4.07); prematurity OR=1.31 (95%CI=0.92 – 1.87), inadequate Kotelchuck index OR=2.88 (95%CI=2.09 – 3.95).

Conclusion: Prematurity was not associated with HIV infection, when adjusting to socioeconomic status, and the quality of prenatal care. Probably HIPW have lower access to health care, due to social inequities. Although in Brazil, the HIV care is free of charge, pregnant women are still having difficulties to reach the specialized care, with consequently higher rates of prematurity. Better access to care must be offered to this population, and studies of prematurity in the
HIV infected women must evaluate how late these women reach their care.

No conflict of interest

Abstract: P_70

Prevention of Mother-to-Child transmission

Malformations among HIV vertically exposed newborns – Results from a Brazilian Cohort Study

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Background: Although antiretroviral (ARV) treatment should not be delayed or stopped due to pregnancy, there are some evidence of teratogenesis while using some ARVs, mainly in the first trimester. The aim of this study is to describe the malformations from the concepts whose HIV infected mothers participated in a Brazilian cohort study.

Methods: Description from a cohort study of HIV infected pregnant women. 45 days after birth, all puerperal women from this study were evaluated by an obstetrician, who collected all data about labor and delivery, as well as the children's health (data were also collected from children's immunization card, where all the problems of the child health must be recorded).

Results: 1228 pregnancies were studied, with 1240 concepts (12 cases of twins) and 7 stillbirths. 25 children with malformations were described: 4 genetic syndromes (one with Down's Syndrome), 5 with congenital cardiopathy, 3 with neurological syndromes (2 with epilepsy and one hydrocephaly), 2 with gastrointestinal malformation (esophageous atresia and congenital megacolon), two with cleft lip, 3 with extremities malformations, 4 with genitorurinary malformations (2 with kidney stones, two undescendent testicle >36 weeks), 2 abdominal mass, and one accessory nipple (two children presented more than one malformation). Eight patients started ARV in the first trimester, 15 in the second trimester, and three in the third trimester of gestational age. 13 patients used PI-based ARV regimen, 6 used a NNTRI-based ARV regimen and 6 a NRTI-based ARV regimen.

Conclusion: In conclusion, the incidence of malformation was 2.03%, and an specific ARV was not associated with malformations.

No conflict of interest

Abstract: P_71

Prevention of Mother-to-Child transmission

Integration of ART in MCH Settings: The Way Forward for Increasing Access to ART for Eligible HIV-Positive Pregnant Women in Zimbabwe

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Introduction: The Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) has provided support to the national prevention of mother-to-child transmission (PMTCT) of HIV program in Zimbabwe since 2001. By June 2010, over 818,000 pregnant women had received PMTCT services at 724 EGPAF-supported health facilities. Of those identified as HIV-positive, 91% received antiretroviral drug (ARV) prophylaxis for PMTCT. Antiretroviral therapy (ART) -eligible pregnant women who have the highest risk of transmitting HIV to their infants do not receive appropriate prophylaxis measures, due to vertical service delivery and weak linkages between the PMTCT and ART programs. Of the ART-eligible pregnant women attending ANC identified in this program between June and September 2009, only 3% of ART-eligible HIV-
positive pregnant women were initiated on antiretroviral therapy during their pregnancy.

**Material & Methods:** To increase HIV-positive pregnant women's access to and uptake of ART, EGPAF supported the Ministry of Health and Child Welfare (MOHCW) to integrate ART in maternal and child health (MCH) clinics at 20 learning sites. Stakeholder meetings were held to advocate for integration of services, sensitize stakeholders and facility managers, and develop implementation plans. Standard operating procedures (SOPs) for implementing ART in the MCH setting were developed, nurse-midwives were trained on opportunistic infections (OIs) and ART management, and resources were mobilized to provide point-of-care CD4 machines within MCH clinics.

**Results:** Fifty nurses were trained in adult OI/ART management; 22 were placed at health facilities to gain practical experience in ART initiation, OI/ART management. The percentage of ART-eligible women who received ART during pregnancy increased from 3% (June-Sept 2009) to 26% (June-Sept 2010).

**Conclusion:** Integration of ART into MCH services improved access to and uptake of ART by treatment-eligible pregnant women. This experience revealed that advocacy with stakeholders, clear SOPs, and access to CD4 testing are cornerstones for successful integration of ART into MCH. With proper training and mentorship, nurse-midwives are able to initiate ART for pregnant women and manage their care; nurse-led ART initiation should be scaled-up to expand access to ART for eligible pregnant women nationwide.

No conflict of interest

**Abstract: P_72**

**Prevention of Mother-to-Child transmission**

**Pharmacokinetics of Darunavir Once or Twice Daily During and After Pregnancy**


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**Background:** Protease inhibitor concentrations are often decreased during pregnancy; darunavir (DRV) exposure during pregnancy is not well described.

**Methods:** IMPAACT P1026s is an on-going, prospective, non-blinded study of antiretroviral (ARV) pharmacokinetics (PK) in HIV-infected pregnant women. Two cohorts include women receiving ritonavir-boosted DRV either as 600/100mg, twice daily (QD), or 800/100 mg, once daily (QD), as part of a combination ARV regimen during pregnancy and 6-12 weeks postpartum (PP). Intensive steady-state 12 or 24-hour PK profiles were performed during 3rd trimesters (3rd trim) and PP. Maternal and umbilical cord blood samples were obtained at delivery. DRV concentrations were measured by HPLC (detection limit, 0.09 mcg/mL). Minimum PK targets were DRV AUC_{0-12} or 24 of 43.6 or 56.5 mcg*hr/mL, for QD or QD, respectively which represent 70% of the expected mean DRV AUCs in non-pregnant adults (62.3 or 87.9 mcg*hr/mL).

**Results:** DRV PK data were available for 31 women (19 on BID, 12 on QD). Two PP PK evaluations (1 BID and 1 QD) were excluded for non-adherence with no detectable DRV concentrations. Geometric mean 3rd trim / PP ratios (and 90% CI) were 0.71 (0.54-0.92) and 0.76 (0.64-0.91) for AUC and 1.42 (1.09-1.84) and 1.31 (1.10-1.55) for CL/Fs with BID and QD administration. PK parameters are presented below for 3rd trim and PP as median (range) and the number who met the AUC targets. Values with "*" indicate p<0.05 compared to PP.

For the women who received DRV/r 600/100mg BID (3rd trim and PP):

AUC_{0-12} was 50.7 (23.8-102)* and 70.0 (40.3-175.5) mcg*hr/mL; and 13/19 and 11/13 met the AUC_{0-12} target. CL/F was 11.83 (5.89-25.21)* and 8.57 (3.42-14.89) L/hr. C_{12h} was 3.13 (0.78-8.85) and 2.81 (1.61-5.50) mcg/mL.

For the women who received DRV 800/100mg QD (3rd trim and PP):

AUC_{0-24} was 67.7 (30.3-105.5) and 87.9 (77.5-150.2) mcg*hr/mL; and 8/12 and 7/7 met the AUC_{0-24} target. CL/F was 11.82 (7.58-26.4) and 9.10 (5.33-10.32) L/hr. C_{12h} was 1.37 (0.15-3.49) and 2.59 (<0.09-3.96) mcg/mL.

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Median cord blood DRV concentrations were 0.2 (<0.09-1.1) mcg/mL and median ratio of cord blood/maternal delivery DRV concentrations were 0.23 (0.06-0.58).

Conclusions: Compared to PP and nonpregnant adults, DRV CL/F is increased and AUC is decreased during the 3rd trim with twice daily dosing. Troughs levels are low during 3rd trim with once daily dosing. Twice daily dosing should be used during pregnancy, and higher doses during pregnancy may be needed.

No conflict of interest

Abstract: P_73

Prevention of Mother-to-Child transmission


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Introduction: In most rural communities in Nigeria, eligibility for antiretroviral therapy (ART) for the over 360,000 children and 1.6 million women living with HIV/AIDS is based on absolute CD4 count. This investigation is only available once a week on clinic days making it difficult for the vast majority of children and pregnant women who test positive on non clinic days to have access to baseline CD4 estimation. In addition, the burden of travelling long distances to and fro clinics for initial blood draw and receipt of test results has led to attrition in the number of children and pregnant women who test positive to HIV versus the number who eventually commence ART. This paper aims to describe the impact of daily CD4 estimation on uptake of pediatric and prevention of mother to child transmission (PMTCT) services in rural clinics.

Material and Methods: In a bid to improve uptake of PMTCT and pediatric services at three HIV care and treatment rural clinics located in Northern Nigeria, the USAID funded PrO-ACT project of Management Sciences for Health held a stakeholders forum with community leaders, women groups and health workers on the need to increase uptake of HIV counseling and testing (HCT), PMTCT and pediatric services for pregnant women and children. HCT outreaches were conducted at selected points in the community where distance to clinics poses a challenge. Interventions introduced at the health facility level include reducing long waiting time for pregnant women and children by employing the use of data clerks to fill laboratory request forms for CD4 investigations instead of the few available doctors. Blood sample collection points were established close to the pediatric and maternity units in order to improve accessibility. Clinic days for HIV positive women and exposed children were harmonized to ensure adherence to clinic appointments. The capacities of laboratory technicians were built on the use of automated CD4 equipments in order to make up for the dearth in human resources for health. Daily CD4 estimation was established (Mondays to Fridays) ensuring that women and exposed children who test positive to HIV on non clinic days have access to baseline CD4 monitoring. In addition, clients attending clinics from long distances and difficult terrains can also access laboratory services on any day of the week. Test results are released within 24 hours in order to ensure timely initiation on antiretroviral therapy for eligible clients.

Results: Over a period of 12 months, 7,005 women and 3,178 children received HCT. Number of HIV positive children and pregnant women who accessed CD4 investigations increased from 52.4% to 90% and 53.8% to 90% respectively. In addition, the number of pregnant women receiving ART increased from 50% to 83%. Laboratory turnaround time for CD4 result reduced from 7 days to 24 hours. Average client waiting time on clinic days reduced from 4 hours to 1 hour 30 minutes.

Conclusions: Effective interventions to improve uptake of pediatric and PMTCT services in resource constrained settings should include laboratory systems strengthening; task shifting, community mobilization and improved referral linkages.

No conflict of interest
Abstract: P_74

Prevention of Mother-to-Child transmission

Period Characteristics of HIV positive children in China

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Background: Mother-to-child transmission (MTCT) is the primary route of infection for Chinese pediatric patients. The PMTCT program of China began in 2004 in a few pilot areas and was scaled up in 2005. Certain factors, including maternal delivery mode, the type of breastfeeding, and antiretroviral drug intervention, are known to affect the rate of MTCT of HIV. This information, however, was not collected consistently through the PMTCT program. We performed a retrospective survey to collect maternal delivery and breastfeeding data among HIV positive children infected via MTCT.

Materials and Methods: From July 2005 to July 2009, all HIV-infected children from one HIV/AIDS clinic in each of four provinces (Henan, Guangxi, Yunnan and Xinjiang) known to be high HIV epidemic areas of China were surveyed. After informed consent, a questionnaire was administered to the parent or guardian of the child for demographics, method of HIV diagnosis, delivery and breastfeeding history, and whether prevention of mother-to-child transmission (PMTCT) interventions were used. Children infected by MTCT were included in this analysis.

Results: Among 483 HIV-infected children surveyed in the four clinics, 394 were infected through MTCT and were included. 58.4% were male, average age at HIV diagnosis was 4.9 years and at time of survey was 9.5 years. 93.5% of births were delivered vaginally with the remaining by Caesarian section. 92% of mothers breastfed their infants for an average of 17.3 months with the length of breastfeeding trending down over time, from 32 months in 2000 to 12 months in 2009. No mothers received PMTCT services and only two infants received antiretroviral prophylaxis. 98% of children were diagnosed through HIV antibody tests. Only 8 children were identified through RNA testing at <18 months of age.

Conclusion: In this retrospective survey of known HIV-infected mother-infant pairs, the vast majority were delivered vaginally and breastfed for >1 year. HIV diagnosis was primarily based on HIV antibody testing and children were diagnosed late (median 4.9 years old). These data suggest that the mothers did not realize their HIV status, did not understand the HIV risk to their child, or did not understand the benefits of PMTCT interventions. Although the PMTCT program in theory covers the entire country, these data underscore the importance of continued efforts to scale up education and intervention in this population to decrease the rate of MTCT of HIV.

No conflict of interest

Abstract: P_75

Utilising DHIS data to improve PMTCT program access and outcomes in Metsweding district, Gauteng Province in South Africa.

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Background: Metsweding District has an antenatal HIV prevalence rate of 33.3%. District Health Information System (DHIS) data for 2009 reported that 5,532 pregnant women accessed antenatal services, but only 54% were tested for HIV, 14% had a CD4 count
assessed, 14% accessed antiretroviral (ART) prophylaxis, 27% of eligible pregnant women were initiated on ART, and the HIV infection rate by polymerase chain reaction (PCR) in exposed infants ranged from 11% to 14%. Based on these indicators, and an evaluation of the deprivation index, the Department of Health (DOH) selected the Metsweding District as one of 18 districts to initiate improvements to PMTCT services. EGPAF worked with the DOH to ensure improvements in PMTCT services through several quality improvement approaches. One of which was to use DHIS data as it allows changes to be made in DHIS within six weeks if data could be verified by sites by getting a copy of their monthly DHIS data, cross checking it with the data that was sent and report any identified errors to DHIS team for correction.

**Materials and methods:** Quality improvement (QI) strategies to improve PMTCT services were initiated in July 2009 by EGPAF in partnership with the DOH. These included process mapping to identify gaps in the DHIS data, facility reporting system and all processes in the PMTCT cascade; EGPAF conducted training of 36 DOH health care workers (HCW) on data management and QI methods mostly nurses, data captures and counsellors and each facility was represented. Additionally, each facility formed a QI team, initiated improvement cycles on their identified gaps and implemented two-way data flow processes (where data was sent back to sites for verification every month). EGPAF mentored and coached HCW at facility level and quarterly QI learning sessions were organized where all sites met to share their improvement cycles, and EGPAF provided technical assistance to help facilities address encountered challenges. Monthly joint supportive supervision visits between EGPAF technical team and the district health team were made to encourage QI skills improvement and sustainability of QI strategies.

**Results:** Between July 2009 and July 2010 improvements were noted in the PMTCT cascade in the district: HIV counselling was offered to all pregnant women, HIV testing of pregnant women improved from 54% to 92%, all women who had tested positive for HIV received CD4 testing and results. ART prophylaxis improved from 14% to 96%, initiation of eligible pregnant women on ART improved from 27% to 66%, and the PCR positivity rate decreased from 11-14% to 5%. Additionally, it was noted that the practice of sharing improvement cycles was beneficial as it helped create effective communications and adaptation of promising practices around QI approaches.

**Conclusions:** Data management initiatives should be complemented with QI interventions to ensure improved outcomes. Two-way data flow processes should be encouraged to verify data within the six-week DHIS timeframe. A collaboration effort within facilities with guidance and support from district health management is recommended and QI methods should be integrated into existing PMTCT services for better outcomes.

No conflict of interest

**Abstract: P_76**

**Prevention of Mother-to-Child transmission**

**Chlamydia prevalence and risk factors among HIV-infected childbearing women in Ukraine**

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**Background:** Chlamydia is the most common bacterial sexually transmitted infection (STI) worldwide, associated with adverse reproductive sequelae including pelvic inflammatory disease, and neonatal complications in up to 20% of infants of infected mothers. Ukraine has the highest HIV prevalence in Europe at 1.6%, against a backdrop of increasing STI prevalence since the break-up of the USSR. We aimed to describe the prevalence of and risk factors for chlamydia in a postnatal cohort of HIV-positive women in Ukraine.

**Methods:** Data on 1407 women enrolled in the Ukrainian Cohort Study of HIV-infected Childbearing Women between December 2007 and March 2011 were analysed. Women (diagnosed as HIV-positive before delivery) typically enrol in the cohort 6 to 12 months postpartum. Poisson regression models were used to investigate factors associated with
diagnosis of chlamydia infection during last pregnancy or postnatally.

Results: Median age at enrolment was 27.6 years, 49% (683/1399) of women were married, 34% (481/1399) cohabiting and 17% (235/1399) single; 68% (766/1127) of women were diagnosed with HIV antenatally. A quarter (298/1220) had a history of injecting drug use (IDU). Of those tested for each infection, 25.8% (209/811) were positive for chlamydia, 2.4% (28/1168) for syphilis, 0.4% (4/939) for gonorrhoea, 57.7% (614/1064) for genital HSV and 10.8% (65/600) for T. vaginalis. Of 209 HIV-infected women with chlamydia, 76% (n=158) had at least one other infection. Bacterial vaginosis was found in 13.6% (138/1016) (33% with vs. 12% without chlamydia (χ²=32.51 p<0.01)) and vulvovaginal candidiasis in 51.5% (529/1027) (66% with vs. 48% of those without chlamydia (χ²=14.79 p<0.01)). Consistent antenatal condom use, reported by 19%, was not associated with chlamydia infection (p=0.5). Of the 982 women sexually active at postnatal cohort enrolment, the 77% (754/981) using condoms as their only contraception had a lower prevalence of chlamydia than those using condoms plus other contraceptive methods (23% vs. 37%, χ²=8.75 p=0.03). In univariable analyses, a chlamydia diagnosis was significantly (p<0.01) associated with unmarried cohabitation (vs. being married), current smoking, current alcohol use, IDU history, having an IDU partner, unintended pregnancy, not knowing partner’s HIV status, >1 previous pregnancy terminations (vs. none), HIV diagnosis during 1st/2nd trimesters (vs. pre-conception) and postnatal ART, but not associated with age, education, or antenatal ART receipt. In multivariable analyses adjusting for centre and all variables significant univariably, characteristics associated with an increased risk of chlamydia diagnosis were unmarried cohabitation (vs. being married), AIRR 1.52, 95% CI 1.12-2.07, p<0.01), IDU history (AIRR 1.69, 95% CI 1.21-2.37, p<0.01), not knowing partner’s HIV status (AIRR 1.64, 95% CI 1.18-2.28, p<0.01) and having had >1 pregnancy terminations (vs. none, AIRR 1.41, 95% CI 1.01-1.96, p=0.04).

Conclusions: A quarter of women tested had chlamydia, reflecting behavioural risk factors common with HIV acquisition and underlining the importance of STI screening and treatment among HIV positive pregnant women. Unmarried cohabiting women, those with a history of IDU, a history of pregnancy terminations and/or without knowledge of their partner’s HIV status were at an increased risk of a chlamydia diagnosis.

No conflict of interest

Abstract: P_77

Prevention of Mother-to-Child transmission

Women’s experience of PMTCT services in Johannesburg, South Africa

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Introduction: Prevention of HIV-infection in children in resource-limited settings has been suboptimal despite availability of effective treatment options for this purpose. In order to prevent HIV infection in children and to diagnose infants at an early age, pregnant women should be offered HIV testing in pregnancy and if diagnosed HIV-positive should receive counseling, education as well as pharmacotherapy in order to optimize prevention of HIV transmission to their infants (PMTCT) and ensure that infants are tested as early as possible. We aimed to establish how HIV-infected women experience the care provided for PMTCT at these services, and their understanding of how to care for themselves and prevent infection to their babies.

Methods: HIV-infected women were interviewed after delivery when they brought their infants to clinics for immunization August-October 2010. Women attending 6 week immunization visit at 5 different clinics in 2 districts of Johannesburg, South Africa were interviewed and asked about their experience of the services at ante-natal and delivery sites.

Results: 79 HIV-infected women were interviewed. Their recollection of information from antenatal sites; 63(90%) were aware that medication should be used for PMTCT, 43(61%) remembered being told that they should use condoms. Mostly lay-counselors 47/68(69%) provided this information with 26/68(38%) and 3/68(4%) being given
information by a nurse and doctor respectively. Of 57 women who responded about what they were told to do when they went into labour, 24(42%) remembered being told to request nevirapine and 18(32%) to disclose their HIV status, 10(18%) to disclose existing treatment. 70 women responded to a question about feeding options, 34(49%) knew that either exclusive formula or breastfeeding was best, 42(60%) felt they had a choice of feeding method whereas 24(34%) felt they had no choice, 4(6%) remembered being advised to exclusively breastfeed. Of 64 responders, 60(93%) were told that their baby should be tested at 6 weeks. At delivery sites 34 women responded about the feeding information they were given and 18 felt they had no choice with 19 being advised to formula feed. 9 women (10%) felt that they received inadequate care at delivery services, with 11/75(14%) women experiencing rude and/or unprofessional behavior by nurses at the sites. In some cases women reported that NVP failed to be administered even on request and some experienced xenophobic and discriminatory remarks by nursing staff.

Conclusion: Despite the fact that these women received HIV counseling/education during their pregnancy, there are gaps in women’s understanding of what they should do or expect from the health services to help prevent HIV infection in their children. Included were misconceptions about how best to prevent HIV, feeding options and transfer of information to staff at delivery sites. Patient recall limits the findings in this study. Nevertheless, review of the messages that patients receive at different healthcare sites is warranted. Fragmentation of the health services results in interrupted continuity of care to the detriment of women and the PMTCT programme. The abuse by staff of these vulnerable women further undermines efforts to improve PMTCT.

No conflict of interest

Abstract: P_78
Prevention of Mother-to-Child transmission
Clinical and economic impact of scaling-up World Health Organization (WHO) 2010 PMTCT guidelines in Zimbabwe

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Introduction: Zimbabwe plans to implement the 2010 WHO PMTCT guidelines with "Option A," (combination ART for women with CD4≤350/µL or Stage 3-4 disease; antenatal zidovudine and extended infant nevirapine in breastfeeding for less advanced maternal disease). This will replace a program based primarily on single-dose nevirapine (sdNVP). We projected the impact of "uptake" of PMTCT services (the proportion of mother-infant pairs completing a PMTCT regimen by the time of delivery) on the clinical outcomes and costs of these new PMTCT regimens.

Methods: Zimbabwean clinical, programmatic, and cost data were used in a validated computer model of HIV to simulate the cohort of 392,460 women becoming pregnant each year in Zimbabwe, through the period of pregnancy and breastfeeding. At conception, mean maternal age was 24 years, HIV prevalence was 16% (mean CD4 451/µL), and HIV incidence was 1%/year; breastfeeding duration was 18 months. Four PMTCT regimens were modeled: 1) no antenatal antiretroviral drugs (ARVs; for comparison only, assuming women could link to HIV-related care and ART when eligible after delivery), 2) sdNVP, 3) Option A, and 4) Option B (combination ART for all identified HIV-
infected women through pregnancy and breastfeeding, regardless of CD4 or disease stage). Each PMTCT regimen was evaluated at three levels of PTMCT uptake: 1) the Zimbabwean 2009 estimate (56%), 2) the WHO target of 80%, and 3) an “optimal” uptake of 95%. Clinical outcomes at 18 months post-delivery included number of infant infections. Cost outcomes at 18 months included pediatric healthcare costs, maternal healthcare costs, PMTCT program costs, and total (pediatric + maternal + PMTCT) costs (2008 USD, healthcare system perspective, discounted at 3%/year, excluding scale-up costs).

**Results:** At 56% uptake, if no antenatal ARVs had been provided for PMTCT, 17,420 infant infections would have occurred by 18 months of age among infants of all Zimbabwean women becoming pregnant in 2009, with a healthcare cost of $51.90 million (M). The sdNVP-based program is projected to have averted 4,020 infections in 2009 (resulting in 13,400 infections). At a cost of $51.75M, the sdNVP-based program also saved money compared to no antenatal PMTCT. If the sdNVP-based program were replaced by an Option A-based program at 56% uptake, costs would be projected to increase by 6% (to $54.71M), but infections would be projected to decrease by 17% (to 11,130). In scenarios simulating improved PMTCT uptake, Option A at 80% uptake (8,420 infections, $55.82M) or 95% uptake (6,640 infections, $57.12M) would result in fewer infections than Option B at 56% uptake (10,450 infections, $58.51M), but slightly more than Option B at 95% uptake (5,540 infections, $62.03M).

**Conclusions:** Replacing sdNVP with Option A in Zimbabwe will reduce pediatric HIV infections by a greater proportion than it will increase costs. Improving uptake of Option A to target levels will prevent more infections than implementing Option B at the current uptake level. The cost-effectiveness of this PMTCT transition will depend on scale-up costs and long-term survival and treatment costs for HIV-infected children.

No conflict of interest

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**Abstract: P_79**

**Prevention of Mother-to-Child transmission**

**Low mother-to-child transmission of HIV at a routine antenatal facility in a high HIV-prevalence, low income setting in South Africa: A cohort study.**

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**Introduction:** The 2009 antenatal clinic survey in South Africa estimated the national HIV prevalence among antenatal women aged 15-49 years to be 29.4%. KwaZulu-Natal had the highest provincial HIV prevalence of 39.5% with certain of its districts demonstrating even higher HIV prevalence. In order to improve outcomes of mother-to-child transmission of HIV (MTCT) prevention programs, the South African department of health recently changed its guidelines to initiate antiretroviral therapy (ART) prophylaxis at 14 weeks of gestation and lifelong ART for mothers with a CD4 cell count below 350cells/µl. Nevertheless, high HIV transmission rates continue to be reported. Furthermore, the post-natal follow-up of mother-infant pairs is poor. The government’s district health information system is poorly implemented and collects aggregated data that is cross-sectional in nature. Little data on accurate HIV transmission rates and cohort outcomes therefore exists in routine settings. This study describes the baseline characteristics of HIV-positive pregnant women and mother-infant pair MTCT outcomes at a routine antenatal facility in a high HIV-prevalence, low income setting.

**Materials and Methods:** A cohort study was conducted with data obtained at a public antenatal facility in Umungundlovu district, Kwa-Zulu Natal. This district has an estimated HIV antenatal prevalence of 40.1%. Clinical information of HIV-positive mothers was collected prospectively by nurses from the time of booking until 18 months post-partum. Data capturers entered data from clinical records into an electronic data collection tool. Cohort data of all mother-infant pairs for the period...
January 2005 until March 2011 were included in analyses.

Results: A total number of 453 mother-infant pairs were analysed. At the time of booking, mothers had a median age of 26 years (IQR: 22.1–32.7 years), a median gestational age of 23 weeks (IQR: 19–28 weeks), a median CD4 cell count of 377.5 cells/µl (IQR: 238–537), with 43.0% having a CD4 cell count below 350 cells/µl. 445 (98.2%) infants received nevirapine within 72 hours after birth. 421 (92.9%) infants received an HIV DNA polymerase chain reaction (PCR) test at 6 weeks, however only 376 (83.0%) results were returned. Amongst infants with available PCR results, seven (1.8% [95% CI: 0.8%–3.8%]) were positive. Amongst 34 infants with available post-weaning PCR results who had negative or unavailable 6 week PCR results, two (5.9%) were HIV positive. Amongst 51 children born at least 18 months prior to site database closure, 25 (49.0%) had an available 18 month HIV ELISA test result, with all 25 being negative. Of the nine infants testing HIV positive in the cohort, only three were referred to an HIV treatment facility and two were initiated on ART.

Conclusions: In routine antenatal settings with high HIV prevalence, low MTCT transmission rates are possible. Improved early infant HIV testing with retrieval of results, as well as improved follow-up of mother-infant pairs until 18 months is needed to better evaluate the impact of routine PMTCT programs. All infants testing HIV positive during the follow-up period need to be tracked and referred for appropriate care.

No conflict of interest

Abstract: P_80

Prevention of Mother-to-Child transmission

Safety of Prolonged Maternal Valacyclovir Administration in Infants Receiving Antiretroviral HIV-1 Prophylaxis

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Background: Maternal administration of the acyclovir prodrug valacyclovir is compatible with pregnancy and breastfeeding. However, the safety profile of prolonged infant exposure to acyclovir in the context of antiretrovirals (ARVs) for prevention of mother-to-child HIV-1 transmission (PMTCT) has not been described.

Material & Methods: Between April 2008 and July 2009, 148 pregnant Kenyan women co-infected with HIV-1/HSV-2 were enrolled in a double blind, placebo-controlled, randomized clinical trial of twice daily 500 mg valacyclovir in women ineligible for antiretroviral therapy (WHO 1 or 2, CD4 counts > 250 cells/mm3). Women were randomized to receive valacyclovir or placebo in a 1:1 allocation scheme beginning at 34 weeks gestation and for 12 months postpartum. All women received zidovudine from 28 weeks gestation and single dose nevirapine was offered to women and infants at the time of delivery for PMTCT according to Kenyan guidelines. Infant blood was collected at 6 weeks for creatinine and ALT. Breast milk specimens were collected at 2 weeks postpartum from 71 women in the valacyclovir arm; acyclovir levels were determined for a random sample of 44 (62%) specimens. Chi-square and Wilcoxon rank-sum tests were used for analysis. This trial is registered at http://clinicaltrials.gov (NCT00530777).

Results: A total of 146 mother-infant pairs were followed postpartum; 2 women were lost to follow-up after enrollment. PMTCT ARVs were administered to 98% of infants and all mothers. Valacyclovir was not associated with infant or maternal toxicities or adverse events, and no congenital malformations were observed. Infant creatinine levels were all normal (< 0.83 mg/dl) and median creatinine (median 0.50 mg/dl) and infant growth did not differ between study arms. Acyclovir was detected in 35 (80%) of breast milk samples collected at 2 weeks postpartum and median and maximum acyclovir levels were 2.62 and 10.15 mg/ml, respectively (interquartile range 0.6 – 4.19). HIV-1 was detected in 7 (16%) of these specimens; there was no association between the quantity, or detection, of HIV-1 and acyclovir in breast milk.

Conclusions: Valacyclovir and PMTCT ARVs did not put infants at risk of toxicity or growth failures and can be safely administered
Abstract: P_81

Prevention of Mother-to-Child transmission

Prevalence, correlates and outcomes of low birth weight and prematurity in Kenyan HIV-exposed uninfected infants


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Introduction: The rapid scale-up of interventions for prevention of mother-to-child transmission (PMTCT) has decreased the number of infants with HIV-1. However, HIV-exposed uninfected infants in these programs may continue to have risk for other adverse outcomes. We determined prevalence, correlates and outcomes of low birth weight (LBW) and prematurity in HIV-1 exposed uninfected infants in a perinatal HIV-1 cohort.

Materials & Methods: Pregnant HIV-1 seropositive women in Nairobi were enrolled in a study of perinatal HIV transmission from 1999-2004. Women received zidovudine prophylaxis for PMTCT and mother-infant pairs were followed from birth through the first year of life. Maternal CD4 values, HIV-1 viral load, disease history and sociodemographic data were collected at 32 weeks gestation. Gestational age at delivery was assessed by study pediatricians using last menstrual period (LMP) and fundal height.

Results: A total of 416 HIV-1 exposed infants were HIV-1 PCR negative within 48 hours of birth. Of 352 infants with birth weight recorded, 22 (6.3%) infants were LBW. Of 386 infants with a recorded gestational age, 29 (7.5%) were premature. LBW was strongly correlated with prematurity; 67% (20/30) of infants with LBW were also premature (p<0.001).

Factors associated with LBW in a univariate model included number of rooms in the home (OR 1.7, 95%CI 1.1-2.5), maternal weight (OR 0.95, 95%CI 0.90-1.0), female sex (OR 2.5, 95%CI 1.0-6.4), and maternal CD4% at 32 weeks gestation (OR 0.94, 95%CI 0.89-1.0). Advancing maternal HIV disease was also associated with LBW. Each 1-log10 increase in maternal HIV-1 viral load at delivery was associated with a 2.3-fold (95%CI 1.3-4.0) increased risk of LBW. Women with CD4 counts <350 cells/mm3 at 32 weeks gestation were more than twice as likely to deliver a LBW infant (OR 2.5, 95%CI 1.0-6.3). Maternal delivery viral load remained predictive of LBW after adjusting for the number of rooms in the home, female sex, and maternal weight (OR 2.3, 95%CI 1.3-4.0), and the association with CD4 count <350 was reduced to a trend (OR 1.9, 95%CI 0.75-5.0).

Univariate correlates of prematurity included preeclampsia (OR=6.5, 95%CI 1.1-37), number of rooms in the home (OR 1.8, 95%CI 1.3-2.5), and number of people in the home (OR 1.3, 95%CI 1.1-1.7). Maternal CD4% at 32 weeks gestation (OR 0.96, 95%CI 0.91-1.0) was associated with premature delivery.

LBW and premature deliveries had significant consequences for infant survival. HIV-exposed uninfected infants were 5.8 times as likely to die (95% CI 2.1-16) if they were LBW and 6.5 times as likely to die if they were premature (95% CI 2.3-18). Maternal death was also strongly correlated with infant death (OR 5.3, 95%CI 1.6-18). When adjusting for maternal death, the risk of mortality remained 7-fold higher in LBW infants (HR 6.9, 95%CI=2.5-19), and 8-fold higher in premature infants (HR 7.7, 95%CI 2.7-22).

Conclusions: As access to PMTCT services continues to expand, the population of HIV-exposed uninfected infants will grow. HIV-exposed uninfected infants are at risk for LBW, prematurity, and death during the first year of life and measures to prevent these adverse outcomes need to be incorporated into PMTCT programs.

No conflict of interest
Abstract: P_82

Prevention of Mother-to-Child transmission

Prevalence and correlates of nevirapine resistant virus in HIV-1 infected infants

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Background: Nevirapine (NVP) provided as either single-dose NVP (sd-NVP) or with zidovudine (AZT) for prevention of mother-to-child transmission (PMTCT) of HIV-1 commonly leads to development of resistance to non-nucleoside reverse transcriptase inhibitors (NNRTI), which may compromise future NNRTI based antiretroviral therapy (ARV). We determined the prevalence and correlates of NVP-R virus in infants (<12 months of age), prior to initiation of ART therapy.

Materials and Methods: HIV-1 infected infants were screened from PMTCT clinics and hospital wards in an ongoing clinical trial in Nairobi, Kenya. Previous exposure to NVP for infants was based on self-report from mothers. An ‘in-house’ genotypic population based sequencing method was used to detect the presence of drug resistance mutations in the reverse transcriptase viral genome from plasma samples. Infants <5 months old were enrolled into an ongoing trial examining empiric early ART, and demographic information was obtained; CD4 cell counts and viral loads were monitored for mother-infant pairs. A Fisher’s exact test was used to compare the prevalence of resistance in the younger versus older infants. Within the enrolled younger cohort, correlates of resistance were evaluated using Fisher’s exact and Wilcoxon rank sum statistical tests.

Results: At screening, 97 mother-infant pairs had reported exposure to NVP. 13 of 42 (31%) infants <5 months of age, and 11 of 55 (20%) infants >5 months of age, had detectable NNRTI resistance mutations (p=0.242). The common NNRTI resistant mutations detected in the younger (<5 months olds) NVP exposed infants were Y181C (N=6), K103N (N=4), G190A (N=2), and dual K103S and Y181C mutations (N=1), while in the older infants were mainly K103N ((N=9) and Y181C (N=2), that causes high level resistance to NVP and other NNRTI. Detection of NVP resistance in the younger infants was not associated with HIV-1 subtype, maternal CD4 cell count, infant viral load and CD4 percent, or infant sex or age. There was a trend for higher prevalence of NNRTI resistance in the younger infants exposed to sd-NVP (13/36, 36%) compared to infants with NVP plus AZT prophylaxis (0/6, 0%) (P=0.153).

Conclusions: Among NVP-exposed infants, prevalence of NNRTI resistance was higher in young infants and less likely among those with NVP-AZT rather than SD-NVP exposure.

No conflict of interest

Abstract: P_83

Prevention of Mother-to-Child transmission

Stunting and hospitalizations in HIV-exposed uninfected (HEU) children – are these associated with maternal psychological & socio-demographic factors?

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Background: There is increasing evidence that HIV-exposed, uninfected (HEU) infants have increased morbidity and poorer growth compared to infants born to mothers who are not HIV-infected, although, to date, the reasons for this are not fully understood. The purpose of this analysis was to determine the extent to which socio-demographic and a mother’s psychological state during pregnancy
might contribute to hospital admissions and stunting among these children in the first two years of life.

Materials & Methods: Between 2003 and 2005, 317 HIV positive women (318 babies) attending antenatal clinics in Southwest Tshwane, South Africa were enrolled in the study shortly after finding out that they were HIV-infected. Mothers and their infants were followed for 24 months. The interview conducted at enrollment during pregnancy included socio-demographic data and measures of depression (CES-D), active and avoidant coping (Brief COPE) and measures of support and self-efficacy. At each follow-up interview mothers were asked about hospital admissions and the children were measured.

Results: Thirty eight (12%) children were shown by PCR testing to be HIV-infected, the HIV status could not be definitively determined for 70 (22%) and 210 (66%) were confirmed to be uninfected. Of the latter, 85% completed follow-up at 18 months. In this uninfected group, 29% of the families had incomes below the poverty line, 65% lived in houses made of bricks or cement, and 35 % had running water inside the house. 57% of the uninfected children were male and the mean gestational age was 39.5 weeks. During follow-up, 18.7% of HEU children were categorized as stunted (WHO standards: height Z score < -2), 18.1% had been hospitalized and six children (3.3%) died. In unadjusted analyses stunting was significantly associated (P<0.05) with male gender, prematurity, a low family income and the mother’s report of lower self-efficacy when pregnant. These variables in a logistic regression analysis showed only male gender and prematurity as significantly associated with stunting (P<0.05). Hospitalization of the children was associated with living in housing that was not made of brick or cement (P=0.07) and had no running water (P<0.05). The mothers of hospitalized children had reported increased levels of unwanted support from others (P=0.01). When entered into a logistic regression analysis, none of the variables remained statistically associated with hospitalization, although prematurity was of borderline significance (P=0.066).

Conclusions: A number of studies conducted in developing countries have demonstrated that maternal psychological characteristics during pregnancy – particularly depression – can have adverse effects on the growth and health of their children. The results of this study suggest that maternal psychological characteristics in pregnancy, including depression, are not an explanation of poor growth and poor health of HEU infants and that prematurity is the main factor contributing to stunting among these children.

No conflict of interest

Abstract: P_84  
Prevention of Mother-to-Child transmission

Preliminary Results of HIV Transmission Rates Using a Lopinavir/ritonavir based regimen and the New WHO Breast Feeding Guidelines for PMTCT of HIV

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Introduction: The WHO recommendations for infant feeding by HIV positive mothers in developing countries have recently been changed to encourage exclusive breast feeding until 6 months of age and then supplemental feeding until 1 year when full weaning occurs. Previous studies have demonstrated that Maternal HAART can reduce the rate of HIV transmission during the period of exclusive breastfeeding, but whether supplemented breast feeding can be made safe using this approach is unknown.

Methods: The Aluvia study enrolled a cohort of 279 HIV positive Zambian women who received AZT+3TC+LPV/r 400/100 tablets BID antepartum and for 12 months postpartum while breast feeding according to the new WHO recommended regimen. Infant HIV PCR results were assessed using dried blood spots. Initial data on HIV MTCT at 12 months is presented here.

Results: 279 women have delivered 230 liveborn infants. 4/194 (2.1%) infants tested...
had a positive PCR result by 6 weeks postpartum, suggesting in-utero or peripartum or early breast feeding transmission. 93/230 have 12 months of age postpartum PCR results. 1/93 (1.1%) infants acquired HIV between 6 weeks and 12 months, and 1/49 infants acquired HIV after 12 months (2.0%). Self reported adherence was suboptimal in the one patient who transmitted between 6 weeks and 12 months. There were 2 infant deaths between 6-12 months postpartum.

Conclusions: Maternal LPV/r based HAART appears to be effective in PMTCT both during periods of exclusive and then supplemented breast feeding. This is the first study to demonstrate this finding, and thus support the new WHO guidelines. Updated results will be presented.

Partial Funding Support for project from ABBOTT Laboratories

Abstract: P_85

Co-infections in HIV-infected children

Low prevalence of Hepatitis B co-infection and Hepatitis B seroprotective antibody among perinatally HIV-infected Thai adolescents

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Background: HIV and Hepatitis B(HBV) co-infection is associated with high risk of progression to chronic liver diseases. Universal HBV immunization for Thai infant was implemented since 1992, the 20-year seroprotective rate in healthy Thai population was 60.5%. Data among HIV-infected individuals remain unknown. This study aims to determine both seroprevalence of HBV co-infection and seroprotective antibody in perinatally HIV-infected adolescents.

Methods: A cross sectional study of HIV infected adolescents aged between 12-25 years was performed. Hepatitis B surface antigen(HBsAg), surface antibody (anti-HBs) and core antibody(anti-HBc) were measured. Co-infection was defined as having HBsAg positive, natural infection was defined as having antiHBc positive, and seroprotective antibody was defined as having anti-HBs ≥ 10 mIU/mL. Viral suppression was defined as having HIV RNA level < 400 copies/mL within the past 12 months.

Results: From Nov 2010 to Feb 2011, 408 patients were enrolled;182 (45%) were male. Their current age was 14.9 years (SD2.3). Their mean current CD4 lymphocyte count was 689(SD320); 87% are viral suppressed. 273(66%) cases have either reported or documented childhood HBV vaccination, 75 of 273 (27%) were those who received HBV revaccination after immune recovery as a result of antiretroviral treatment. Fifteen children were HBV/HIV co-infected [3.7%; 95% CI: 2% to 6%]. Natural infection was evidenced in 18 cases (4.4%; 95%CI: 2% to 6%). Twenty-five percent of those children had protective antibody against HBV with significantly higher proportion among adolescents who received HBV revaccination (93% vs. 10%, p<0.01). No gender difference was observed.

Conclusions: The prevalence of HBV co-infection in HIV-infected Thai adolescents slightly exceeds that of general population. The prevalence of HBV seroprotection rate is low despite of childhood vaccination; three-fourth of cases are at risk for HBV infection. Revaccination of HBV vaccine is encouraged.

No conflict of interest
Abstract: P_86

Co-infections in HIV-infected children

Bacteriology of ear discharge in HIV-infected children on ART in the ARROW trial in Uganda and Zimbabwe.


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Introduction: Otitis media is common in HIV-infected children. There are few data on the common causative agents, their antimicrobial sensitivity patterns and the variation with age among HIV-1 infected African children on antiretroviral therapy (ART).

Methods: ARROW is a randomised trial investigating first-line treatment and monitoring strategies in 1207 previously untreated HIV-1 infected children initiating ART. Children who presented with an ear discharge during follow-up had ear swabs taken to determine the causative organisms and sensitivity patterns using standard microbiological techniques.

Results: 266 samples were collected from 153 patients (median age 2.5 years, IQR 2.3-2.9; 52% males) over a 3 year period. 209 (79%) cultures were positive. The overall rate in 3040 child-years of follow up was 6.8 events / 100 child-years. Rates per year of follow up were: 13.8 / 100 child-years (1st year), 3.0 / 100 child-years (2nd year) and 2.0 / 100 child-years (3rd year). Rates per age group were 9.7 / 100 child-years (0-6 years), 4.8 / 100 child-years (7-13 years) and 0.6 / 100 child-years (>13 years). The isolated organisms were: *Pseudomonas aeruginosa* 51 (24.4%), *Staphylococcus aureus* 35 (17.7%), *Proteus mirabilis* 35 (16.8%), other *Proteus* species 16 (7.7%), *Klebsiella* species 9 (4.4%), other *Staphylococcus* species 9 (4.3%), *Escherichia coli* 9 (4.3%), *Streptococcus pneumoniae* 7 (3.4%), *Moraxella* species 4 (1.9%), *Haemophilus influenzae* 1 (0.5%) and other bacteria 31 (14.8%). *Pseudomonas aeruginosa* was mostly susceptible to ciprofloxacin, gentamicin, polymyxin B and carbapenem but resistant to ceftriaxone. Other isolates were susceptible to ceftriaxone and amoxicillin/clavulanic acid but the majority (96%) were resistant to cotrimoxazole.

Conclusion: Ear infection rates in HIV-infected children decreased with age and increasing time on ART. *Pseudomonas aeruginosa* and *Staphylococcus aureus* were the most commonly isolated organisms. Most isolated organisms were resistant to cotrimoxazole.

No conflict of interest

Abstract: P_87

Co-infections in HIV-infected children

Impact and Incidence of sputum positive Tuberculosis on children in the ART era attending Kanombe Military Hospital between January 2009-June 2010

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Introduction: Tuberculosis (TB) infection has markedly increased in the HIV era and TB is the most common opportunistic infection in HIV patients. However with ART the impact of TB is expected to be reduced.

Methods: We conducted a retrospective cohort study utilizing chart review of all patients on TB treatment at Kanombe Military Hospital in Kigali, Rwanda from January 2009 to June 2010 were reviewed. We abstracted demographic data, sputum acid fast bacilli (AFB) stain, and HIV serostatus. Data were analysed using STATA version 10.
**Results:** A total of 452 TB cases on treatment were reviewed. The male: female ratio was 2:1 with a median age 29 years (age range: 0.125 to 99 years). Pediatric TB (aged ≤18 years) accounted for 19.5% (88/452) with a median age of 5.25 years (IQR: 1.2-12.5 years). Pediatric HIV/TB coinfection was found to be 13/88 (14.8%) and 4.6% (4/88) pediatric patients had sputum positive TB and were adolescents.

The incidence of smear-positive PTB was 138/452 (30.5%) with HIV coinfection 30.9% (44/138). The overall median age for the sputum positive TB was 29 years (IQR: 24-37.5 years) and for HIV coinfected patients was 34 years (IQR: range 27 to 42 years). The burden of smear positive PTB was 108/266 (40.6%) and 30/186 (16.1%) in 2009 and 2010 respectively with an odds ratio (OR) of 0.28 (CI: 0.5-1.1) and a p-value of 0.22.

On bivariate and multiple logistic regression, risk factors for sputum smear positive TB were: being 15-18 years, >18-25 years and >25-35 years OR: 0.125 (CI: 0.04-0.36), OR: 2.3 (CI: 1.32-4.0) and OR: 1.7 (CI 1.0-2.9) respectively with a p-values of <0.001, 0.003 and 0.035 respectively.

**Conclusion:** In resource limited areas pediatric TB continues to be high against a background of high burden of smear positive PTB/HIV coinfected adolescents and young adults. However there is evidence from this data indicating that with excellent national ART programs TB can be prevented and reduced over time. Therefore there is need for strengthening ART programs as a strategy of TB prevention with a need as well for prospective studies to assess the impact of ART on TB/HIV coinfection in the resource limited settings.

*No conflict of interest*
was 95.9% and the kappa was 0.7 (95% CI: 0.55 – 0.85, p-value < 0.05) indicating substantial or good agreement. Testing positive on the TST was associated with older age and higher weight for age z-scores but not with the T-SPOT®.TB. Both tests were associated with a history of taking anti-retroviral therapy (ART).

**Conclusion:** Before promoting use of IGRAs in children living in HIV/TB endemic countries, more research on their clinical role in TB diagnosis and cost-benefit analysis needs to be done.

No conflict of interest

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**Abstract: P_89**

**Co-infections in HIV-infected children**

**HIV and HBV transmission from mother to child in Constanta County in the past 6 years**

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**Introduction:** Constanta is one of the most affected counties by HIV from Romania and many of our HIV infected patients are coinfected with HBV. Over the last years we have noticed an increasing number of children exposed to HIV and HBV through mother-to-child transmission (MTCT).

**Objective:** To assess the mother-to-child transmission rate of HIV and HBV infections over a period of 6 years (January 2005 - December 2010).

**Material and method:** To evaluate HIV transmission we checked some parameters in children: duration and type of antiretroviral treatment given as PMTCT medication, viral load (VL) at birth; and some parameters in mothers: type of delivery, ARVT received previously delivery, VL in the last trimester of pregnancy. To evaluate HBV transmission we evaluate presence of AgHBs and VL in mothers, and in children anti HBs at 1 year of age.

**Results:** 104 children and 100 HIV+ mothers have been monitored. Out of the 104 children, 5 were HIV+, and 99 were HIV-. Out of the 104 children studied, only 3 died in their first month of age (VL undetectable in 2 cases, and VL=130 copies/ml in one case). 2 children (one HIV+ and other HIV- didn't received ARVT after birth. 97 children received ARVT in first 24 hours of their life for 6 weeks, 4 children (2 HIV+) received ARVT after first week of their life and 3 didn't received ARVT. Only 5 infants were breast feed (3/5 of HIV+ and 2/99 HIV-). Among all deliveries 23 were vaginal (4/5 of HIV+, 19/99 HIV-). Out of all 100 HIV+ mothers, 90 received ARVT during pregnancy. In third semester of pregnancy VL for HIV was undetectable in 71 cases. From all mothers HIV positive just 24 were Ag HBs positive. Only 5 mothers had viral load detectable for HBV during their pregnancy; their new born received immunoglobulin specific for HVB after birth. All children received vaccination for HBV. All children borne from mothers with HIV and HBV coinfection present anti HBs after one year of age.

**Conclusions:** The overall MTCT rate was 4.8%. The lack of HIV diagnosis in pregnant women was the major risk of MTCT. We do not register any HBV transmission from mothers to children.

No conflict of interest
Abstract: P_90

Co-infections in HIV-infected children

The challenges of implementation of Isoniazid Preventive Therapy (IPT) and Intensive Case Finding (ICF) in the paediatric HIV care package.

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Background: Intensified measures to identify and prevent tuberculosis (TB) in HIV infected individuals are now essential part of standard HIV cares in countries with high TB prevalence. Following 2011 WHO recommendations the use of an intensive-case-finding (ICF) algorithm and the provision of isoniazid-preventive-therapy (IPT) have to be integrated in any HIV paediatric programme. However, little is known about the feasibility and acceptability of this intervention outside trial settings and potential challenges for implementation still to be evaluated.

Methods: According to the new WHO recommendations, the implementation of ICF/IPT was started in Nsambya Home Care of S. Raphael of S. Francis Nsambya Hospital (Kampala, Uganda). Children attending the HIV clinic were evaluated using a specific “IPT card”, with a 3 steps collection of information such as: 1) TB contact history, past TB episodes, BCG vaccination; 2) clinical signs (current cough, fever, failure to thrive); 3) IPT initiation and lab monitoring (clinical follow-up, adherence). In children with positive screening TB was suspected unless clear alternative causes were identified. TB was ruled out according national guidelines and children older than 1 year of age for which TB was unlikely were started on 6 months of IPT. In addition to the monthly clinical follow up and 6-monthly lab monitoring (including CD4 count), LFTs were performed at IPT initiation and at weeks 4-8 in order to assess contraindication and safety of isoniazid.

Results: Among 949 (median age 5.3 years, IQR 1.2– 9.5) HIV-infected children followed by the Nsambya Home Care of S. Raphael of S. Francis Hospital, Kampala (Uganda), 184 (median age 10.1, IQR 6.1 -14.1) were screened for TB in the first 3 months of ICF and IPT implementation (20th January- 21st April), applying the WHO 2011 ICF/IPT algorithm. Of these, 52 had positive TB contact history, and presented “current cough” (103) and/or “failure to thrive” (54) and/or “fever” (78).

Only 9 children (already on cART) were diagnosed with TB; 20 out of the remaining 175 children started IPT, within a period time of 50 days from the beginning of implementation. The majority 124/175 (71%) were further investigated due to current cough and failure to thrive. Additional delay in IPT initiation was reported in 26/175 (15%) due to lab monitoring. Among children receiving IPT no signs of drug toxicity were observed.

Conclusion: TB case finding and diagnosis continues to be a great challenge for HIV-infected children in high TB prevalence settings. IPT is so far safe and tolerable. ICF/IPT algorithm has been instrumental to enhance TB case finding; even if we are not able to evaluate properly its sensitivity and specificity in our experience the high prevalence of patients with cough could jeopardize the specificity of the algorithm increasing significantly workload and delaying IPT initiation.

No conflict of interest

Abstract: P_91

Co-infections in HIV-infected children

Results from the Implementation of Occult Hepatitis Screening in the Spanish Cohort of HIV-infected Pediatric Patients (CoRISpe)

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1Hospital Universitari Vall d’Hebron, Pediatric Infectious Reviews in Antiviral Therapy & Infectious Diseases 2011_8
Introduction: Diagnosis of occult B and seronegative C hepatitis virus infection, can be missed in immunocompromised patients when using regular screening methods; leading to an increased risk of severe liver damage in case of viral reactivation. In addition, these patients are likely to be infective, including a risk of mother to child transmission. Data about these entities in HIV-infected children and adolescents is lacking. The implementation of occult HBV and seronegative HCV markers study in the regular laboratory screening in these patients may allow the detection of co-infected patients at risk of hepatic decompensation.

Patients and Methods: Cross-sectional study to assess the prevalence of occult HBV and seronegative HCV infection within CoRISpe Cohort. Demographic, clinical, immunologic and virologic data, as well as antiretroviral treatment and vaccination status were collected. Diagnosis of occult HBV infection was established in patients with positive HBV-DNA with negative HBsAg and seronegative HCV infection in patients with positive HCV-RNA and negative anti-HCV antibodies. The "anti-HBc alone" pattern was defined as as the presence of anti-HBc in the absence of HBsAg and anti-HBs. Vaccinal response to HBV was assessed by anti-HBs levels detection and considered to be protective if greater than UI/L.

Results: Overall, 254 patients were included (55.51% female, 69.2% Caucasian, median age 14 years, 94.8% of whom vertically-infected). Thirty-seven percent met AIDS criteria. At the time of assessment, 63.7% showed undetectable viral load and median CD4+ cell count was 960/mm³. Approximately, 4% and 25% mothers were HIV-HBV and HIV-HCV co-infected, respectively. Neither occult nor acute HBV infection markers were detected in children included in the study. Two patients (0.8%) showed chronic HBV infection markers (positive HbsAg and antiHBc IgG), and 6 children presented the "anti-HBc alone" pattern (2.3%).

Fifteen patients (5.9%) had chronic HCV infection markers. In addition, three patients (1.2%) had seronegative HCV infection. These 3 patients (7, 16 and 16 years of age, respectively) were vertically infected and met AIDS criteria, two were Caucasian and one came from South America. Two of them were well vaccinated and one had an incomplete HBV vaccination schedule. All three mothers had chronic HCV co-infection but one of them was diagnosed afterwards since was also seronegative and had not been studied before. Almost 50% of patients included in this study did not show protective response to a standard HBV vaccination schedule.

Conclusions: Occult HBV infection does not seem to be a serious problem in Spanish HIV-infected children and adolescents. The anti-HBc alone pattern appears to be as common as previously described but its significance remains unknown. On the other hand, vaccinal response seems to be suboptimal and routine administration of a booster dose should be considered in this population. As previously reported, HCV infection routine evaluation must include viral genome detection in order to avoid future complications in these patients as well as allowing HCV infection diagnosis in previously unrecognized mothers.

No conflict of interest
Abstract: P_92

Implementation research on PMTCT and pediatric treatment programs

The Tingathe Program: Community Health Workers Improving Case Finding, Enrollment, and Care of HIV-Exposed and Infected Children in Malawi


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Background: In 2008, we initiated an outreach program in Malawi, called Tingathe, focused on using dedicated community health workers (CHWs) to improve identification and early referral to care of HIV-exposed and infected children.

Material & Methods: CHWs conduct community and home-based HIV testing and counseling (HTC), and active case finding within health centers. CHWs are also assigned to HIV-infected pregnant women and follow mother-infant pairs until final diagnosis of the infant. Newly identified patients receive monthly visits to ensure they are receiving proper care. Exposed, pre-ART, and ART patients are followed together within the HIV clinic.

Results: Within the first 30 months, 20 CHWs conducted 49,713 HIV tests. 29,951 (60.2%) were conducted in the home and community. 4,766 (9.6%) new infected people were identified. Of these, 1,260 (26.4%) were adult males, 2,992 (62.8%) were adult females, and 514 (10.8%) were children.

CHW activities resulted in enrollment of 2425 children in participating clinics, a greater than 50-fold increase from program initiation. 1633 (67.3%) were exposed infants of HIV-infected mothers identified at antenatal clinic. 792 (32.7%) were infected at enrollment and identified by HTC and active case finding. Final status of the 1633 infants exposed at enrollment includes 540 (33.1%) definitively uninfected, 52 (3.2%) infected, and 1041 (63.7%) that remain exposed through breastfeeding. Of the 844 infected children (792 infected at enrollment plus 52 who were exposed but subsequently infected), 354 (41.9%) are on ART and 490 (58.1%) are pre-ART.

This CHW-based program has driven an over 30-fold increase in the number of children on ART, from 11 to 354. Children also comprise a greater percentage of the patients started on ART at these health centers, increasing from 0.7% to 8.8% (p< 0.0001).

Conclusion: Community based HIV testing with CHW case management is an effective strategy to improve identification, enrollment, and care of HIV-exposed and infected children.

No conflict of interest

Abstract: P_93

Implementation research on PMTCT and pediatric treatment programs

Community Health Workers as Case Managers: Creating a Complete Continuum of care between PMTCT, Early Infant Diagnosis, and Pediatric HIV Services

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Background: Loss to follow up (LTFU) is a major challenge in prevention of mother to child transmission (PMTCT) and Early Infant Diagnosis (EID) programmes in Malawi-reported LTFU >50%. Tingathe-PMTCT is a pilot intervention that specifically recruits dedicated community health workers (CHWs) to help retain mothers and infants. We describe the impact of the intervention on longitudinal care starting with diagnosis of the mother at antenatal care (ANC) through final diagnosis of the infant.
Methods: In 2009, 16 CHWs received a three week training in PMTCT, EID, and pediatric HIV care. Pregnant women identified as HIV infected at ANC were assigned a CHW. CHWs made monthly home visits until verification of the infant's final HIV status, and functioned as case managers to ensure patients received required services. Receipt of PMTCT medication was recorded only upon verification with the mother after delivery. Impact on patient retention and utilization of services was evaluated.

Results: 1027 HIV infected pregnant women were enrolled over 12 months. 159 (15.5%) women were already on ART. Among the remaining women, 846/ 868 (97.5%) received a CD4 test, with 804/846 (95%) receiving results. 289 women were eligible for ART of whom 215 (74.4%) were successfully initiated. There were 33 (3.2%) maternal/fetal/infant deaths. LTFU included 83 (8%) patients who moved, 19 (1.8%) who were lost, and 31 (3%) who refused ongoing PMTCT services. Of the 746 live births to date, 740 (99.2%) of the infants were tested for HIV by PCR and all 568 were received ARV prophylaxis. 568 (76.8%) infants were tested for HIV by PCR and all 568 were started on co-trimoxazole. 495/568 (87.1%) received results. 26/495 (5.3%) had a positive PCR with 24/26 (92.3%) successfully enrolled in ART clinic.

Conclusions: Case management and support by dedicated CHWs is an effective strategy to create a continuum of care between PMTCT, EID and Pediatric HIV services and dramatically reduces LTFU rates.

No conflict of interest

Abstract: P_94

Implementation research on PMTCT and pediatric treatment programs

The immunogenicity and safety of pneumococcal conjugate vaccine in human immunodeficiency virus-infected thai children

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Background: HIV-infected children have a higher risk of invasive pneumococcal disease (IPD) than uninfected children, despite receiving highly active antiretroviral therapy (HAART). This study was aimed to determine the immunogenicity and safety of a 7-valent pneumococcal conjugate vaccine (PCV-7) in Thai HIV-infected children compared to HIV-exposed uninfected children.

Methods: A prospective study was conducted among children 2 months to 9 years. The number of PCV-7 doses depended upon age and HIV status; 2-6 months of age: 3 doses; 7-23 months of age: 2 doses; HIV-infected child ≥24 months: 2 doses and HIV-exposed child ≥24 months: 1 dose. Serotype-specific pneumococcal IgG antibody concentrations were measured at baseline and 28 days after complete vaccination. Pneumococcal IgG antibodies of serotype 4, 6B, 9V, 14, 18C, 19F and 23F were performed by the 3rd generation enzyme-linked immunosorbent assay method. The primary end point was the proportion of children who achieved serotype-specific IgG antibody concentration at a cut off level ≥0.35 µg/mL. Secondary end points were a 4-fold increase in serotype-specific IgG antibody, rates of adverse events after vaccination and predictors for seroconversion among HIV-infected children.

Results: Fifty-nine HIV-infected and 30 HIV-exposed uninfected children were enrolled. The median (IQR) age was 97 months (67-111) and 61 months (51-73) among HIV-infected and HIV-exposed uninfected children, respectively (p<0.001). Among HIV-infected children, current and nadir CD4 counts were 1079 cell/mm³ and 461 cell/mm³, respectively. Fifty-three children were receiving antiretroviral therapy. The proportion of children who achieved pneumococcal IgG ≥0.35 µg/mL was in the range of 85%-98% in HIV-infected and 83%-100% in HIV-exposed uninfected children depending on serotype. The lowest response was on serotype 6B in both groups. The 4-fold increase in serotype-specific IgG concentrations was similar between HIV-infected and HIV-exposed uninfected groups except for serotype 9V (p=0.027). HIV-infected children who had history of AIDS had a lower antibody response in serotype 23F (p=0.025). Seven (12%) HIV-infected children had a
Abstracts

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Implementation research on PMTCT and pediatric treatment programs

Challenges of Early Infant HIV Diagnosis and Treatment in Malawi

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Introduction: The WHO recommends screening of all infants for HIV exposure, early infant diagnosis (EID) at 4-6 weeks of age, and initiation of antiretroviral treatment (ART) upon diagnosis of HIV-infection. We report EID experiences at two primary health care centers in the Blantyre region of Malawi.

Methods: Through the existing prevention of Mother To Child Transmission structure (PMTCT), pregnant women were informed about the importance and availability of EID. Dried blood spots (DBS) for free deoxyribonucleic acid polymerase chain reaction for HIV/DNA HIV PCR testing were collected at age 6 weeks and analyzed using a commercial assay at a quality controlled research laboratory in Blantyre. For all positive PCR results, DBS analysis was repeated, and a quantitative HIV viral load (VL) was performed at a research laboratory in Lilongwe, Malawi. Infants with confirmed HIV infection were referred for antiretroviral therapy (ART) on-site or at a distant outpatient ART clinic.

Results: Of the 7570 women participating in PMTCT, 16.6% (n=1257) were identified as HIV-infected. Of all HIV-exposed infants, 891 (70.9%) presented for EID. On initial DBS, 14.4% (128/891) infants tested positive. Despite active tracing, only 89% (114/128) of children were informed of their positive result. DBS re-testing and VL in 101 infants confirmed infection in 82 and indicated 19 false positive results, corresponding to a positive predictive value (PPV) of the initial DBS of 81% and an estimated HIV incidence of 11.6%. Of 67 infected infants with follow-up information available, 48 (71.6%) initiated ART at a median age of 4.7 months (range 2.3 – 18.9), 10 (14.9%) died before ART initiation, 3 refused ART and 6 were awaiting ART initiation.

Conclusions: A substantial proportion of children were lost at each step of the EID and treatment program. EID tools with higher PPV and point-of-care capacity as well as increased infrastructure for infant ART are needed to improve access of HIV infected infants to life-saving early ART.

No conflict of interest

Abstract: P_96

Implementation research on PMTCT and pediatric treatment programs

Group B streptococci colonization in a cohort of HIV-infected pregnant women: prevalence, maternal profile and neonatal outcomes

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Introduction: Group B Streptococci (GBS) remain a leading cause of morbidity in newborns, despite efforts in perinatal disease prevention. Vaginal and rectal colonization during pregnancy are implicated in the vertical
transmission of GBS to infants. Two newborn syndromes are recognized: early-onset and late-onset disease. GBS screening of pregnant women and use of intrapartum antibiotic prophylaxis have reduced the incidence of perinatal infection. Few data are known from HIV-infected pregnant women. This study focuses on the characteristics of GBS-colonized HIV-infected pregnant women and their infants outcomes at a Brazilian HIV-PMTCT clinic.

Methods: HIV-infected pregnant women with ≥3 follow-up visits had vaginal and rectal swabs collected at 35-37 weeks of gestation. Exclusion criteria were: use of antibiotics ≤4 weeks or vaginal cream ≤7 days before swab collection, bloody vaginal discharge at the time of swab collection. Socio-demographic, clinical and immunological characteristics of the women and infant outcomes (birth weight, apgar, and infectious events) were analyzed. Statistical analysis was performed using SPSS, version 13.0. Anova or T-tests were used for means comparisons. Chi-square test was used for categorical analysis.

Results: From November 2008 to December 2010, swabs were collected from 226/256 women. Overall prevalence of GBS colonization was 31.4%: vaginal 28.3%, rectal 9.7% and both 6.6%. GBS colonized and non-colonized women were compared for age, gestational age at delivery, mode of delivery, income, schooling, CD4 and viral load at entry and near delivery. GBS colonized were younger (mean: 26.06 years) than GBS non-colonized (mean 28.51 years): SD=6.36 (p=0.033). No other significant differences were found between both groups of women, and in the infant outcomes. One baby had early-onset disease.

Conclusion: Prevalence of GBS in HIV-infected pregnant women was higher than in previous studies. Data emphasize the importance of GBS screening in HIV-infected pregnant women mainly in the younger.

Abstract: P_97

Implementation research on PMTCT and pediatric treatment programs

The role of Primary Health Facilities in expanding pediatric HIV care and treatment services in Sub-Saharan Africa

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Background: In resource-limited settings, decentralization of HIV care and treatment is a cornerstone of rapid scale-up. Successful decentralization has been shown for adult programs, but little is known about pediatric services. We compared trends in pediatric ART enrollment and outcomes at primary versus secondary/tertiary health facilities (SHFs).

Methods & Materials: Using routinely reported aggregate data from 274 public facilities in Kenya, Lesotho, Mozambique, Rwanda and Tanzania from January 2008-March 2010, we examined trends in number of patients <15 years initiating ART by facility type. A GEE model was fit to compare lost to follow up (LTF) and mortality per 100 person years (PYs) on ART during the period by facility type, adjusting for years providing comprehensive HIV care, patient load, and percentage children <2 years of age.

Results: During the two year period, 17,155 children were enrolled in HIV care in 182(66%) PHFs and 92(34%) SHFs. The number of PHFs increased from 56 to 182, while increase in SHFs was modest (72 to 92 sites). Overall SHFs accounted for 71% of 8,475 children newly initiating ART during the two year period; however, the proportion of children newly initiating ART each quarter at PHFs increased from 17%(129) to 44%(463) during
the same time period. The average LTF and mortality rates were 9.8/100PYs and 5.2/100PYs, respectively at PHFs and 20.2/100PYs and 6.0/100PYs at SHFs. Adjusted models show PHFs associated with lower LTF (Adjusted Rate Ratio, ARR=0.4; 95% CI=0.3-0.7) and lower mortality (ARR=0.3; 95% CI=0.2-0.6).

**Conclusion:** The expansion of pediatric services to PHFs has resulted in increased number of children newly initiating ART. Early findings suggest lower rates of LTF and mortality at PHFs, although referral of children with advanced disease to SHFs may account for higher mortality. Successful scale up in the coming years will require further expansion of pediatric services within PHFs.

*No conflict of interest*

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**Abstract:** P_98

Implementation research on PMTCT and pediatric treatment programs

**Introduction of Rapid Syphilis Testing in PMTCT of HIV Programs in Uganda and Zambia: A field acceptability and feasibility study**

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**Introduction:** As a result of the President’s Global Health Initiative, Maternal and Child Health (MCH) and HIV integration is gaining renewed focus. In Zambia and Uganda, we tested the hypothesis that the introduction of rapid syphilis testing (RST) alongside rapid HIV testing is acceptable and feasible in facilities offering PMTCT services, and will improve identification and treatment of syphilis in pregnant women. The rate of HIV and syphilis co-infection in pregnant women was also explored.

**Methods:** A pre-post test study design was applied. Modified Ministry of Health registers collected service delivery data. Contingency tables and chi-square tests were used to summarize data and test for associations between frequencies of events. A quantitative and qualitative methods questionnaire was administered to healthcare workers who performed HIV and rapid syphilis testing.

**Results:** Urban (17.1% to 95.6%; p<0.0001) and rural sites (88.3% to 97.1%; p <0.0001) in Zambia saw significant increases in syphilis testing with the RST. In Uganda, syphilis testing was not available pre-intervention.

**Table 1.** Post-intervention data for pregnant women

<table>
<thead>
<tr>
<th>Country</th>
<th>Attended ANC</th>
<th>Syphilis Tested</th>
<th>Syphilis Positive</th>
<th>Syphilis Treatment Same day treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uganda</td>
<td>14,540</td>
<td>13,131 (90.3%)</td>
<td>690 (5.3%)</td>
<td>715 (103.6%) 708 (99.0%)</td>
</tr>
<tr>
<td>Zambia</td>
<td>11,985</td>
<td>11,460 (95.6%)</td>
<td>1050 (9.2%)</td>
<td>1000 (95.2%) 958 (95.8%)</td>
</tr>
</tbody>
</table>

*Higher than 100%, due to women being treated presumptively when their partners tested positive.

In Uganda, 14.3% of syphilis positive pregnant women were co-infected with HIV. In Zambia, 24.2% of women were co-infected with HIV. Healthcare workers found RST to be easy to perform, benefits patients by providing same day testing and treatment, and improved quality of services.

**Conclusions:** RST introduction into ANC is feasible in urban and remote rural clinics and resulted in high levels of same-day testing and treatment. The high rate of HIV-syphilis co-infections and the increased risk of MTCT further justifies the importance of syphilis testing as part of the PMTCT package.

*No conflict of interest*
Abstract: P_99

Implementation research on PMTCT and pediatric treatment programs

Programmatic and clinical management practices in the International Epidemiologic Databases to Evaluate AIDS (IeDEA) Pediatric Group

The IeDEA Pediatric Working Group

Introduction: Local program implementation depends on available operational resources and management practices at the clinic and national levels. Understanding the availability of these resources and how international pediatric HIV prevention, diagnosis, and treatment standards are applied provide a key context for observational clinical research. IeDEA is a multi-regional network facilitating assessment of large-scale, global epidemiologic analyses. An extensive site assessment was conducted across regions participating in the pediatric sub-cohort.

Materials and Methods: A standardized site survey was developed by IeDEA and distributed to participating clinical sites and central data management centers in the Asia-Pacific (AP), Central Africa (CA), East Africa (EA), Southern Africa (SA), and West Africa (WA). Data collection was implemented through use of a secure, web-based software program (Research Electronic Data Capture – REDCap, Vanderbilt University) and completed in January 2010. Southern African sites utilized a comparable paper-based site survey assessment, conducted from January-March 2009. The surveys covered site resources, clinical practices, and access to drugs and laboratory monitoring in the following distribution of questions: general-110, cancer-44, pediatric-61, and pediatric cancer-38 questions. A descriptive analysis was done on data from the general and pediatric categories.

Results: Of 68 clinical sites contributing pediatric data to the global cohort (AP, N=10; CA, N=4; EA, N=29; SA, N=10; WA, N=15), 49 (72%) were public programs and received funding from various sources, including local governments (N=55, 81%), the US PEPFAR program (N=36, 53%) and the Global Fund (N=19, 28%). Over half were mixed adult-pediatric clinics (N=38, 56%), and reported a range of dedicated half-day clinics for children per week (median sessions: AP, N=1.5; CA, N=2.5; EA, N=1; SA, N=10; WA, N=5). Outside of SA, laboratory monitoring included CD4 (baseline N=51, 88%; regular intervals N=54, 93%), and viral load (baseline N=46, 79%; regular intervals N=25, 43%). Although 47 (69%) of all sites had the ability to conduct acid-fast bacilli (AFB) smears, 27 (40%) could conduct AFB cultures and 26 (39%) gastric wash sampling on-site. Nutritional support for regions other than SA included food supplements (N=42, 72%) and multivitamins for clinical indications (N=36, 62%). Adherence was assessed by pill count at 26 (38%) sites. Loss to follow-up was defined as >3 months of lost contact for 28 (41%) sites, >6 months for 28 sites (41%), and >12 months for 6 sites (9%).

Conclusions: There was wide variation in practices across IeDEA's pediatric program but a generally high level of patient and laboratory monitoring that will facilitate detailed observational research studies. Anticipated reductions in global HIV funding will pose additional challenges to implementation of current international treatment guidelines for sites and countries that rely on external sources.

No conflict of interest

Abstract: P_100

Implementation research on PMTCT and pediatric treatment programs

Mobile text messaging for PMTCT: disclosure is an important variable

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Background: Evidence based findings are essential to improve the impact of text messages amongst HIV-positive women and their exposed infants. Expanding the PMTCT program requires individual patient care, and
an understanding of the relationship between women’s age, choice of interventions and disclosure of HIV status.

Methods: As part of an ongoing study evaluating the impact of mobile phone messages on infant follow-up, recently delivered HIV-positive women were provided with counselling and interviews conducted before discharge from a large maternity unit in Johannesburg, South Africa. Women enrolled could choose to receive or decline HIV or non-HIV specific messages serving as reminders and motivation. Women could stop messages by sending a free “please call me”, and would be phoned back to confirm the opt-out. This study evaluated age and the disclosure related to uptake and opt-out of text messages.

Results: Of 414 women with disclosure data, 297 (71.7%) had disclosed their HIV status to anyone. Women who had disclosed were more likely to request SMS messages (RR:1.5; CI:1.32-1.87) and to be over 25 years old (RR:1.9; CI 1.54; 2.48). Of 159 women who were randomised to receive SMS messages, 12 (7.6%) opted out. Women who had not disclosed were more likely to do so (RR:3.82; CI:1.32-11.07). The choice of HIV vs. non-HIV specific messages was not affected by disclosure but women receiving HIV-specific messages were more likely to opt-out if they had not disclosed (RR:5.86; CI:1.1-30.9).

Conclusion: Text messaging is gaining recognition as reminders and encouragement for HIV-positive patients; however, added support is required for HIV-positive pregnant women who had not disclosed their status as it may alter their health related behaviours. Text messages with additional strategies taking into account disclosure of HIV status to partner or family may help HIV-positive pregnant women and should form part of research considerations.

No conflict of interest
never arrived by hardcopy. Results were further broken down to compare urban versus rural facilities and facilities with good and bad network coverage.

Results: The evaluation found results in two areas; 1) improved TATs for EID results being sent from lab to facility 2) increased volume of EID results arriving by SMS as opposed to hardcopy. In the baseline vs pilot comparison done for the Southern Province there was found to be a 57% decrease in the total TAT. In the hardcopy vs SMS analysis that was done in Luapula province there was a 28% decrease in the overall TAT but when just the 9 rural facilities were looked at there was a 46% decrease in TATs. When comparing the volume of results arriving by hardcopy versus SMS it was found that 30% more arrived by SMS.

Conclusions: While utilizing SMS to send EID results may not guarantee more HIV+ infants enrolling in treatment, it does speed up the TAT of results delivery as well as the proportion of results arriving in facilities. These improvements are larger in rural areas than urban clinics and clinics with little or no network coverage can still use the system reliably if it is designed in an asynchronous fashion. It is recommended as a useful component of a larger national strategy for EID.

No conflict of interest

Abstract: P_102

Implementation research on PMTCT and pediatric treatment programs

Use of Dried Blood Spot Samples and In-house Assays to Assess HIV-Drug Resistance in HIV-Infected Children in Resource-Limited Settings

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Introduction: Monitoring HIV drug resistance is an important component of the World Health Organization's global HIV program to detect early warning indicators of emerging drug resistance. HIV drug resistance testing is optimal when performed on plasma samples tested with commercially-available test kits; however, that type of testing may not be feasible or affordable in resource-constrained settings. HIV genotyping from dried blood spots (DBS) with non-commercial (in-house) assays may facilitate capture of HIV drug resistance outcomes in resource-poor settings, but has had varying rates of success.

Material & Methods: We evaluated the performance of in-house genotyping assays for HIV reverse transcriptase using DBS samples from 105 HIV-infected children who were enrolled in two clinical trials (Six-Week Extended Nevirapine and IMPAACT P1060 trials) in sub-Saharan Africa. The median HIV viral load at the time of sample collection was 5.88-log₁₀ HIV RNA copies/ml (range 4.04-6.99).

Results: HIV genotypes were obtained for 94 (89.5%) of 105 samples tested. However, successful analysis of 15 (16.1%) of the 94 samples required a second step of testing (PCR with a different assay) to yield sufficient DNA for sequencing. Sub-optimal storage of DBS was associated with genotyping failure. For 34 samples, results obtained using DBS samples and in-house assays were compared to results obtained previously using plasma samples and a commercial assay (Viroseq® HIV-1 Genotyping System); the genotypes obtained from DBS and plasma were 100% concordant.

Conclusion: DBS genotyping using in-house assays provides an alternative for detection of antiretroviral drug resistance testing in children in resource-constrained regions.

No conflict of interest
Abstract: P_103

Implementation research on PMTCT and pediatric treatment programs

Operationalizing rapid implementation of changing WHO protocols for PMTCT: Experience of a private health sector initiative in India

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Background: Based on emerging evidence recommendations for PMTCT protocols have changed over the years. However, the National program in India has lagged behind in implementing these recommendations. The issues which need to be addressed during implementation are size of the target population, quality of infrastructure, efforts needed to re-train counsellors and health care providers (HCP), procurement and maintenance of supply chains, cost effectiveness, etc. The situation in India is further complicated by the complexity of the health system, which is divided in private (including both ‘for’ as well as not-for-profit) and public sector. Both are equally dominant in providing antenatal care to women. PRAYAS is implementing a PMTCT program in private sector since 2002; supported by Elizabeth Glaser Paediatric AIDS Foundation. We present our experience of rapid scale up of newer protocols in private sector which could provide useful information for scaling-up the National program.

Materials and Methods: PRAYAS PMTCT program currently has its presence in 10 districts of Maharashtra, India. Since 2002 we have enrolled more than 200,000 pregnant women and provided PMTCT services to 1371 HIV infected among them. We used contemporary WHO protocols which have changed twice since 2002. We planned roll out of newer protocols and executed it within 3-6 months. We responded to challenges of changed protocols by creating and modifying appropriate IEC materials, re-training counsellors and HCP, redefining drug procurement strategies, aligning drug delivery systems, modifying tools for monitoring and evaluation, and providing continuous technical support. The program data were meticulously maintained in a software application specially designed for monitoring and evaluation and the results are analyses of the same.

Results: We compared the uptake of different program indicators during the phases when changed protocols were implemented. September 2002 to January 2005 (n=351): Antenatal ARV-84%, Intrapartum ARV-84%, Infant ARV -97%, DNA PCR-83%. Exclusive formula feeding (FF) (provided by the program)-86.4 % Overall MTCT rate-4.8% February 2005 to February 2010 (n=799): Antenatal ARV-87%, Intrapartum ARV-86%, Infant ARV- 96%, DNA PCR-75%. FF-74%. Overall MTCT rate-5.6%. CD4 test (from 2008)-86% March 2010 onwards (n=221) (Option A of WHO 2010 guidelines): CD4-93%. Antenatal ARV-85%, Intrapartum ARV-87.5%. Infant ARV 97% and DNA PCR-84%. FF-48.5%. Overall MTCT rate-0%

Conclusions: We have shown that rapid implementation and scale up is possible in private sector. Acknowledging the fact that the size as well as outreach of public sector is mammoth, the system is highly regulated, is better equipped with human resources, there can be un-interrupted financial supply once the program is accepted as a national priority, central drug procuring and distribution systems are in place, etc. In spite of difficulties with private sector such as lack of regulation, perpetual resource crunch, etc., if such high performing and cost effective program can rapidly adapt to frequent changes in protocols; then it should be possible for government systems to roll out the same in public programs more rapidly.

No conflict of interest

Abstract: P_104

Implementation research on PMTCT and pediatric treatment programs

Evaluation of an intervention to promote resilience among young children (6-10 years) of HIV positive mothers in South Africa

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Reviews in Antiviral Therapy & Infectious Diseases 2011_8
Background: While there are extensive efforts in sub-Saharan Africa to address the needs of orphans, there has been less focus on promoting resilience among children living with their HIV-infected parents. As noted in the literature, rigorous demonstration of the efficacy of such interventions for children affected by HIV is lacking. The purpose of this study was to develop a family-focused skills group intervention for HIV-infected mothers and their children and to assess the efficacy of the intervention on improving psychological and behavioral outcomes.

Materials & Methods: HIV positive women attending clinics in Tshwane, South Africa and their children aged 6-10 years were enrolled and randomized to receive either the group intervention (G) or standard care (SC). The groups were led by trained peer-counselors and a social worker and consisted of 24 manual-guided weekly sessions (15 with mothers and children separately and 9 together) focused on parental support, parenting and parent-child communication. Evaluations were conducted at baseline, 6, 12 and 18 months and included measures of maternal depression (CES-D), parenting: (PSI and CCNES) and child behavior (CBCL) as well as other measures of child functioning.

Results: 424 mothers and their children were enrolled (214 in G and 210 in SC) and 76.4% completed follow-up at 18 months. The mean age of the children was 8.4 years and 42% of the mothers had experienced a recent illness. Of those enrolled in groups, 52% attended at least half and 26% attended three-quarters of the sessions. At baseline, children of ill mothers had significantly more internalizing and externalizing behaviors (both P<0.001).

An intention to treat analysis, using mixed linear modeling, demonstrated no significant benefits of the intervention (all comparisons P>0.05) for either mothers or their children. However, for those who attended most sessions (>75%), the children had decreased internalizing and externalizing behaviors at 18 months compared to those in the SC group (P<0.05). HIV-related illnesses during the 18-month period contributed significantly to maternal depression (P<0.0001), increased avoidant coping (P<0.05) and increased parenting stress (P<0.0001). Analyses conducted at baseline demonstrated the effect of parenting on child outcomes: maternal depression was associated with parent-child dysfunction (β=0.19, P<0.00001) and this in turn was associated with increased child internalizing behaviors (β=0.38, P<0.00001) and externalizing behaviors (β=0.37, P<0.00001). In addition a negative parenting style was associated with increased externalizing behaviors (β=0.17, P<0.0001).

Conclusions: Our inability to demonstrate a significant effect of the experimental condition over the control condition may be due to a number of factors, including the lack of attendance at group sessions. The results of the study emphasize the importance of quality parenting and stress the need to develop ways to help parents achieve better outcomes for their children. The results also illustrate the way in which illness affects the psychological state of an HIV-infected mother and how this in turn affects her parenting. Ensuring that mothers remain healthy will not only benefit their own psychological state, but also could substantially benefit their children’s functioning.

No conflict of interest

Abstract: P_105

Implementation research on PMTCT and pediatric treatment programs

Infant Weaning Outcomes Using the New WHO Breast Feeding Guidelines for PMTCT of HIV

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Abstracts

Introduction: Due to high rates of adverse infant outcomes when children are rapidly weaned at 6 months, the WHO recommendations for infant feeding by HIV positive mothers in developing countries have recently been changed to encourage exclusive breast feeding until 6 months of age and then supplemented breast feeding until 1 year when full weaning occurs. The Infant nutritional outcomes of this approach are unknown.

Methods: The Aluvia study enrolled a cohort of 279 HIV positive Zambian women who received AZT+3TC+Lopinavir/ritonavir tablets BID antepartum and for 12 months postpartum while breast feeding according to the new WHO recommended regimen. Infant weights were compared to WHO weight-for-age growth standards.

Results: Between 12 and 15 months of age average boys' weight increased from 8.7 to 9.1 kg, which corresponds to a drop from 24.7%ile to 19.2%ile of the WHO standard distribution for those ages. Similarly, on average the girls' weight increased from 8.4 to 8.8 kg corresponding to a drop from 36th to 27th %ile. On average the children gained 0.37kg (95% CI: 0.25, 0.499), which was significantly lower than the WHO comparison group, which showed mean gain of 0.65 kg (p<.001). The observed gain was also lower than that of WHO comparator children of weight 2SD below the mean (M=0.5kg, p<0.05).

Discussion: The period of weaning between 12-16 months is a time of nutritional vulnerability for these infants. Options for additional nutritional supplementation or even longer periods of breastfeeding, must be explored.

Partial Financial support for the study by ABBOTT Laboratories

Abstract: P_106

New technologies for diagnosis of HIV or co-infections

Earlier detection of perinatal HIV infection among Kenyan infants using a commercial reverse transcriptase activity assay

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Background: Early initiation of antiretroviral therapy (ART) in infected infants reduces mortality by 76%. However, only ~15% of HIV-exposed infants receive a diagnostic testing in the first two months of life. Cavidi ExaVir Reverse Transcriptase (RT) Assay is a low-cost commercial assay that can be conducted in a non-specialized facility, unlike DNA PCR assays. We therefore compared the RT Assay to DNA PCR for early HIV diagnosis among HIV-exposed infants being delivered in a non-governmental clinic in Kenya.

Methods: Two-hundred consecutive HIV-exposed newborns were enrolled within 48 hours of birth in the maternity ward, and were subsequently seen at 6, 12, 24, and 48 weeks when DNA PCR and RT assay were conducted. A positive RT assay was defined as >10,000 equivalent copies/ml. HIV antibody test was conducted at 48 weeks. HIV infection was defined as having either 1) a positive HIV antibody result at age 18 months; or 2) two positive PCR test results if an HIV antibody test was unavailable.

Results: Overall, 11 (5.5%) children were diagnosed with HIV-infection by DNA PCR. Three (1.5%) transmissions occurred in-utero/peripartum period and 8 (4%) occurred during the post-partum period. Two of 11 infected children did not have an antibody test conducted but had >1 positive DNA PCR tests. Among the remaining 9 children, the sensitivity and specificity of DNA PCR and RT assay were 100% when compared to the 18 month HIV antibody test. The RT assay diagnosed...
HIV infection a median of 6 weeks earlier than the DNA PCR assay in six (55%) of 11 infected infants.

**Conclusion:** Among HIV-exposed infants younger than 18 months old, the RT assay detected HIV infection 6 weeks earlier than DNA PCR. Use of this assay, with confirmation with DNA PCR may increase earlier access to life-saving pediatric ART treatment in resource-limited settings.

No conflict of interest

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**Abstract: P_107**

**New technologies for diagnosis of HIV or co-infections**

**Scaling up EID of HIV using DBS-PCR testing at PMTCT sites: Challenges and lessons learned in Cote d'Ivoire**

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**Background:** To assess the scalability of Early Infant Diagnosis (EID) in Cote d'Ivoire, the Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) conducted a demonstration at 18 PMTCT sites. From September 2007 to February 2008, 740 children were tested using DBS/PCR. Fourteen percent of the tested children (105) were HIV-positive. Not all children were initiated on antiretroviral treatment (ART). Reasons for this included lack of identification of HIV-exposed children, lack of a standard DBS sample transportation system to reference laboratories, slow results turnaround times, and reluctance to initiate treatment. In May 2008, the national HIV care and treatment program committed to scale-up EID.

**Methods:** From May 2008 to June 2010, EGPAF expanded EID services to 137 sites and provided support to two national laboratories. Because no standardized national specimen transport system exists, several transportation strategies were used to send DBS to reference laboratories: private couriers, partner organizations, or site staff. Other pediatric entry points—nutrition, immunization, and pediatric wards—were also involved in the EID pilot. The number of children screened increased from 740 to 7,006.

**Results:** Creative DBS transportation reduced travel time to reference laboratories (29 to 25 days) and back to sites (34 to 29 days). The result turnaround time was reduced by two days, and monitoring of HIV-infected children was improved. Of the 7,006 children screened, 89% received test results and 13% (935) were HIV-positive. Children from PMTCT programs were less likely to be HIV-positive, with a prevalence of 9.9%, while 26.6% of children from other entry points tested positive. Ninety percent of the HIV-positive children were enrolled into care, 91% received an ART eligibility test, and 73% initiated ART.

**Conclusion:** Standardizing and strengthening provider-initiated counseling and testing at all entry points helped to increase children enrolment into care. A well organized transportation system improves result turnaround time and, potentially, treatment initiation.

No conflict of interest
3rd International Workshop on HIV Pediatrics
15 – 16 July 2011, Rome, Italy

ABSTRACTS
Abstract book only
Abstract: A_1

HIV infection and adolescents

Twin adherence workshops for both adolescents and their caregivers an effective tool in promoting adherence: a case of Nsambya Home Care

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Introduction: Research has proved that sustained adherence to HAART plays a great role in improving the health and survival rates of HIV infected patients. Adolescents with chronic illness often have poor medication adherence. A study done at NHC in June 2008 revealed that 40% of adolescents on HAART had an adherence <95%. Adherence workshops were put in place to address the problem.

Materials and Methods (Description): Poorly adherent adolescents on HAART aged 10 to 17 years are identified during clinic visits. Those who are disclosed to are sent to counselors who book them for a workshop. Caregivers are also invited. Workshops are conducted in 2 days; 1st day for the adolescents and 2nd day for caregivers. One twin workshop is conducted every month each addressing 20 adolescents (including 5 adhering well) and 30 caregivers (including 10 caregivers of children <10 years). The adolescents share their challenges in taking ARVs, peer-peer counseling is done and testimonials given by those with good adherence. The counselors correct any myths that may have come up in the discussion and educate more on the benefits of adherence. Obstacles to adherence which can be averted by caregivers are discussed in their workshop the following day. Those who need special attention from each group are given one-to-one counseling.

Results/Lessons learnt: A friendly environment helps health workers to discover and address the real causes of poor adherence. Adolescents have solutions to their problems but cannot address their caretakers so need a third party to help them.

Adherence workshops involving both adolescents and their caregivers are effective in promoting adherence among adolescents on HAART. A 75% improvement has been noted among those who attend the workshops.

Conclusion: Peer-peer support is crucial in promoting adherence. Adolescents need constant reminders and close follow-up. Caregivers should know that adolescents need ongoing support.

No conflict of interest

Abstract: A_2

HIV infection and adolescents

High HIV-prevalence among Children Presenting for General Consultation in the North-West Province, Cameroon

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Background: HIV/AIDS is a major cause of childhood morbidity and mortality in sub-Saharan Africa. Symptom based screening might miss a relevant number of HIV infections in the children who might present with non-specific complaints. We aimed to detect HIV infection in previously untested children presenting for general consultation at a large paediatric outpatient department in the North West Region, Cameroon.

Methods: Voluntary counseling and serological testing for HIV using rapid tests was offered to all consecutive children presenting to the paediatric outpatient
Abstract: A_3

HIV infection and adolescents

Sexual behavior and free condom distribution at the National University of Rwanda

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Background: Despite all efforts, the HIV in Rwanda remains a public health problem as in many countries of sub-Saharan Africa. The last population-based survey on HIV prevalence found an HIV prevalence of 3.0% (95% confidence interval: 2.6 - 3.5) in the general population aged 15 - 49 (DHS 2005). The young people arriving at the University begin to feel free and independent they engage themselves in sexual intercourse, sometimes unprotected more than they did when they are over control of their parents. Knowledge of University students about HIV/AIDS is good, but their attitudes and their sexual practices need to be safer. The overall objective of this study is to assess sexual behavior of students.

Methods: Data were collected from a randomly represented sample of 1110 students of National University of Rwanda (NUR) from 2007 to 2008. The survey questionnaires were administered by trained interviewers during visits to the dormitories in order to respect the confidentiality. After a descriptive analysis of characteristics of students, the chi-square was used for to assess the characteristics associated with unprotected sex and logistic regression were used to control for other variables and to detect final influencing factors.

Results: The results indicate that students are aware that one can be infected with HIV by playing unprotected sex (87.5%) and believe that condoms are really effective in the prevention of HIV (80.5%). Therefore, significant associations were found between unprotected sex and factors such as gender, aware of the existence of preventing interventions, awareness of the existence of HIV and the protection offered by the condom use, and finally the awareness of the risk of unprotected sex.

Conclusion: Unprotected sex is still an important issue among NUR students. Interventions targeting students of NUR and aimed at increasing awareness of the role of condoms in preventing HIV but not excluding other prevention methods are still needed.

No conflict of interest
Abstract: A_4
HIV infection and adolescents
Psychological problems of early adolescents with HIV in South India
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**Background:** It is well documented that adolescents with chronic illnesses have more psychological disorders. HIV being a chronic illness there is high chance of having associated psychological disorders. The psychological problems increase as the children becomes adolescents. There are very few studies from India on the psychological problems of adolescents with HIV. The present study was conducted to study the psychological problems of early adolescents with HIV. The aim of the present study was to study the psychological problems of early adolescents with HIV.

**Materials and methods: Setting:** The Pediatric HIV clinic of a tertiary care hospital.

**Design:** Case control study design

**Method:** 20 children 12 boys and 8 girls were taken up for analysis. The children were evaluated using a semi-structured proforma to elicit clinical history data and socio demographic data. The childhood Psychopathology Measurement Schedule (CPMS) was used to study the psychological problems of children with HIV. The children in the study group were compared with a age and sex matched control group of children in the control group for psychological disorders. The children in the control group were selected from among those attending the hospital for minor illnesses.

**Results:** The adolescents with HIV scored high on the CPMS subscales of behaviour problems, conduct disorder and depression. The generalised anxiety scale ratings showed that adolescents with HIV had significantly more anxiety compared to the control group.

**Conclusions:** Adolescents with HIV have more psychological problems compared to normal population. The problems include anxiety, depression and behaviour disorders.

**Recommendations:** Psychological aspects of adolescents with HIV should be addressed when planning management strategies.

No conflict of interest

Abstract: A_5
HIV infection and adolescents
AIDS social performance: what children and teenagers who go to the support centers think
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**Introduction:** AIDS has changed its picture along its history, from being a mortal disease to a chronic illness. Children's and teenagers' feelings have been taken into consideration when finding out that they have been HIV infected, which is an incurable and socially unintelligible disease; how they deal with such disclosure and what represents to them. The impact between children and teenagers appears in different ways, besides the disease itself, discrimination and stigmatization are obstacles to their integration into community.

**Aim:** Understanding the meaning of seropositiveness to HIV/AIDS infected children and teenagers, evaluating their overview as a HIV carrier.

**Methods:** It is an analytical and qualitative research, primary data based, accomplished with HIV infected children and teenagers, carried out between June and December 2010. It has been studied 14 children and teenagers assisted at Lar das Crianças com AIDS (AIDS Children’s Home) in Campo Grande-MS, Brazil; comprising of 9 to 14-year-olds. On the purpose of gathering the children’s speech about living with HIV, a semi-structured interview was performed: “What is it like living with HIV?” Data were qualitatively analysed using the Method of Group Subject Speech and Software Qualiquantisof, which works skillfully on the data processing of qualitative researches.
As a fundamental theory, Social representation Theory has been used, which although, helps on the group comprehension, playing a role as a reality translator.

**Results:** After analysing the data, we could notice that children and teenagers: a) keep as a secret the seropositiveness condition as a strategy of avoiding prejudice from other people they live with socially; b) are afraid and anguished facing the future uncertainty; c) try to act normally day-by-day, even though keeping secret of the use of the medication; d) feel resentfull for going to the Support Home, because it makes them different from the other children and teens.

**Conclusion:** This research enables the comprehension of what and how HIV-infected children and teenagers think, what can subsidize the adoption of an approach strategy towards such public, and proper interventions to their reality. So, this research is relevant to the community, mainly dealing with vulnerable groups like HIV/AIDS children and teenagers.

*No conflict of interest*

**Abstract: A_6**

**HIV infection and adolescents**

**New HIV-1 CRF, isolated from child born from HIV-infected mother**

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**Methods:** EIA, Western blot, RT-PCR, PCR, “ViroSeq HIV-1 genotyping system v.2.0”, sequencing ABI Prism 3100 Avant genetic analyzer, alignment sequences spent with use of programs SeqScape, BioEdit, resistance mutations defined with use of ViroSeq HIV-1 genotyping system Software v.2.6 and HIV Drug Resistance Database Stanford University, the phylogenetic analysis of HIV-1 DNA fragments spent with use of program MEGA4.1.

**Results:** In April 2010 we are investigated for resistance definition blood sample from patient Mos, 6 years old girl, born from HIV-infected mother. The conducted researches have not revealed HIV-1 resistance. The phylogenetic analysis of the DNA fragment of patient Mos has shown that on pol gene the sample has been clustered with HIV-1 subtype A, but was differ from others analyzed samples and subtype A consensus IDU-A and reference sequences (AF004885). Average p-distances between sample Mos and reference sequences of A subtype from Russia, Ukraine and consensus IDU-A have made of 0.068, and with reference sequences of B subtype 0.094. Most close Mos isolate was to AF413987 Ukraine (A subtype), the p-distance 0.066. This data confirmed the relation this isolate to subtype A in pol gene. We have compared isolate Mos sequences with reference sequences of CRF03_AB (AF414006.1, Belarus and AF193276.1 CRF03_AB KAL153). Average p-distances between isolate Mos and reference sequences CRF03 have made 0.090. The comparison of sequences from gene gag p17/p24 region of isolate Mos with reference sequences HIV-1 A subtype show average p-distances 0.129, and with reference sequences B subtype – 0.075. Average p-distances on a gene gag isolate Mos with CRF03_AB (AF414006.1, Belarus and AF193276.1 CRF03_AB KAL153) have made 0.121. Thus, on a base of analysis of gag gene p17/p24 region the Mos isolate has been carried to HIV-1, B subtype. The analysis of isolate Mos sequences on V3 loop gp120 env gene region HIV-1 has shown that average p-distances with reference isolates subtype B have made 0.323, and with A subtype – 0.155. Average p-distances sequence of Mos isolate with reference isolates AF414006.1 and AF193276.1 (CRF-03_AB) have made 0.308. Thus, on a V3 loop gp120 region of env gene the isolate has been carried to HIV-1 subtype A.

**Conclusion:** Thus, it has been shown that Mos isolate is recombinant form, but differs on genome structure from earlier described CRF03_AB (ApolBpolBenv). The new variant of CRF having the following structure: BpolApolAenv.

Sequences of new HIV-1 variant in gag, pol and env genes were submitted to EMBL/Genbank/DDBJ under accession numbers: FR775442.1, FN959585.1, FR775442.1

*No conflict of interest*
Abstract: A_7

Complications of HIV therapy

Adverse Effects of Antiretroviral Therapy in Children from Resource-Limited Setting

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Background: Though HIV infection is a chronic manageable disease, an improved quality of life is limited by adverse effects of antiretroviral therapy (ART). There are very few published studies on adverse effects in Indian children. The aim was to study adverse effects (AEs) of ART and factors associated with it.

Methods: Retrospective cohort study at a tertiary care centre in Pune, India. ART-naïve children between 3 months to 15 years of age and who have at least one follow-up visit at 2 weeks after initiation of ART were included. Thirty-five children received ART consisting of d4T group (NVP=7, EFV=1) and 5 from AZT group (NVP=3, EFV=2) had developed AEs. Of these, 9 (69%) children had severe immunosuppression and 8 (62%) were from WHO clinical stage 3 at baseline. Fifty percent of the male children developed AEs. Four children developed diffuse maculopapular rash (moderate grade), 2 had anemia (moderate-1 and severe & potentially life-threatening-1), 2 had lactic acidosis (severe), 3 had hypercholesterolemia (mild-2, moderate-1), and 1 each had vomiting (moderate) and elevated SGPT (mild). Elevated fasting triglyceride level (not in toxicity range) was seen in 4 children. The rash was mainly attributed to NVP, anemia to AZT, and dyslipidemia to d4T and EFV. The offending drug in the regimen was substituted in 1 child with anemia.

Conclusions: Metabolic and rash are the commonest AEs. Most of the AEs are seen in late stages of HIV disease. Few AEs require substitution of offending drug. These results need to be substantiated with prospective studies with larger sample size.

No conflict of interest

Abstract: A_8

Complications of HIV therapy

Improved in iron status and anemia in HIV-infected Asian children after zidovudine-containing HAART without iron supplementation

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Background: Anemia is common in HIV-infection children and it is a significant predictor of survival. The prevalence of mild anemia in these children varied between 22%-94% which is 4.5 times higher than that of HIV non-infected children. Adult studies have shown a decline in the rate of anemia since the HAART era but little is known for children. The necessity of iron supplementation to prevent anemia in these children is still unclear. Moreover, thalassemia is common in Asia and further complicates this issue.

Methods: HIV-infected Thai and Cambodian children who initiated HAART at CD4 counts between 15-24% and who were followed for 3 years were included. Hemoglobin concentration (Hb), %CD4, HIV RNA, serum ferritin and iron studies were performed every
6 months. The prevalence of anemia, the change in serum ferritin after HAART and thalassemia status were determined. Iron supplementation was disallowed.

Results: 114 children were evaluated. 47% were male. 60% were Thai and 40% were Cambodian. The median age was 6 years. The median %CD4 and HIV-RNA were 19% and 4.9 log10 copies/ml, respectively. Clinical classification was category A for 62% and B for 37%. All received zidovudine (ZDV)-containing regimens. After 3 years of HAART, 106/114 (93%) children were still on ZDV-containing regimens. Six children changed from ZDV to abacavir; 4 due to anemia, 2 due to neutropenia, and 2 children stopped all medication due to the bad flavor. The median %CD4 increased from 19% at baseline to 32%. 90% had HIV RNA < 50 copies/ml. The prevalence of anemia significantly declined from 64% at baseline to 50.5%, 47.8%, and 53.5% at 1, 2 and 3 years after HAART respectively. The prevalence of iron deficiency anemia at baseline was 3.5% and remained stable after 3 years of HAART (3.6%-5.1%). The median baseline serum ferritin was 59.4 µg/L and no significant change was observed during the 3 years of HAART (47.9-53.7 µg/L). We found hemoglobin E trait in 24.6%, E homologous in 2.6%, a-thal1 trait in 9.7% and Hb Constant Spring trait in 3.5%. The thalassemia major was found only in 1 child with compound heterozygous for β<sup>0</sup> thalassemia and Hb E.

Conclusions: In this Asian pediatric HIV population with moderate immunosuppression, and high rates of anemia, ZDV-containing HAART was safe and effective. Anemia decreased after HAART without iron supplementation. The prevalence of thalassemia trait was high while the prevalence of iron deficiency anemia was rare both before and after HAART. This evidence suggested that routine iron supplementation in anemic HIV-infected children with moderate immunosuppression might not be warranted.

No conflict of interest

Abstract: A_9

Comprehensive Pediatric HIV care

Central Nervous System Manifestations of HIV-infection in Indian Children

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Background: In most children, neurological dysfunction seems to be a direct consequence of HIV infection of central nervous system (CNS). These manifestations are variable in children. There are very few published reports in Indian literature. The aim was to study central nervous system manifestations of HIV-infection in Indian children.

Methods: Prospective cohort study at tertiary care centre in Pune, India. A total of 60 HIV-infected children between 6 months to 15 years of age were studied. All these children were infected by perinatal route. The children were screened for neurological symptoms and signs. MRI of brain was done in all the children.

Results: A total of 14 (23%) children had neurological manifestations. Of them, 2(14%) children were below 18 months, 10 (71%) children were between 18 months - 8 year and 2 (14%) were between 8-12 years. Eleven children presented with neurological symptoms (delayed milestones-8, neuroregression-1, convulsion-1 and psychiatric disorder-1). In seven children neurological examination was normal. The neurological examination in remaining children revealed exaggerated deep tendon reflexes in 6, hypertonia in 2, extensor plantar reflex in 2, apathy in 1 and microcephaly in 1 child. The MRI of brain showed cerebral atrophy in 2, and cerebellar atrophy, PMLE and white matter hyperintensity in 1 each.

Conclusions: Central nervous system manifestations are commonly seen in HIV-infected children. Early identification by regular screening is of utmost importance to prevent the morbidity and mortality.

No conflict of interest
Abstract: A_10

Comprehensive Pediatric HIV care

Characterization of Medication Adherence and Persistence by Gender in a US Sample of Youth with HIV

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Introduction: Adherence to antiretroviral therapy and medical appointments as well as treatment persistence are of paramount importance for youth with HIV. In adults with HIV, variable adherence patterns have been described and gender differences have emerged. One possible explanation for gender effects may be differential depression rates. Patterns of medication and appointment adherence and treatment non-persistence rates in youth with HIV are unclear and were explored.

Materials & Methods: Retrospective review of appointment and medication adherence and treatment non-persistence conducted on a sample of youth with HIV treated in an urban clinic. Data were reviewed over a three-year period. Medication non-persistence was defined as any intentional medication discontinuation >2 weeks. T-test and Chi-Square analyses evaluated gender differences in rates of treatment adherence, non-persistence, and depression.

Results: Participants (n=138) with perinatally and behaviorally acquired HIV: ages 0-24; mean age 12.6 years (SD=6.93), 53% female, 88.4% African American, 9.4% Caucasian, 0.7% Hispanic. No significant differences were observed by gender for appointment no-show rate (p=.73), medication adherence by pharmacy pill count (p=.53), medication non-persistence (p=.12), length of time off medication (p=.33), or whether the participant had been on more than one regimen (regimen persistence; p =.27). Transmission route produced significant differences in regimen persistence (X²=6.03, p=.01) and medication non-persistence (X²=6.62, p=.01) by gender for those behaviorally infected.

Conclusions: Gender differences previously reported in adults with HIV were not supported in a combined sample of urban youth with HIV on multiple measures of medication and appointment adherence and regimen and medication persistence. Unlike adults, these results suggest youth with perinatally acquired HIV exhibit similar adherence and persistence behaviors regardless of gender. When taking into account transmission route, behaviorally infected young women appeared less likely to be medication and regimen persistent when compared to young men. Future research should prospectively examine possible gender differences in adherence and persistence behaviors.

No conflict of interest

Abstract: A_11

Comprehensive Pediatric HIV care

Lack of immunity in routinely vaccinated HIV infected children in Chicago

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Background: HIV-infected children are at high risk for complications from vaccine preventable infections, however, response to immunization in HIV-infected children may be impaired despite highly active antiretroviral therapy (HAART). It remains unknown as to whether those with impaired immunity should be revaccinated. We aim to determine the prevalence of immunity following routine childhood vaccines in HIV-infected children on HAART in preparation for studied revaccination.

Methods: Charts of 69 perinatally HIV-infected children were reviewed for their vaccination and HAART history. Blood samples were tested for the presence of IgG antibodies to hepatitis A virus (HAV), Measles, Mumps, Rubella, Varicella, Hepatitis B (HBV) surface and core antibodies.
Results: Patients in this cohort were mostly female, 40/69 (58%) ages 25 months to 22 years (mean 14.4 years) and are all treated with HAART except one long term non-progressor. All patients completed the HAV and HBV vaccine series except 2 known immune patients. All 69 (100%) and 65/69(94%) received one or two doses of measles, mumps, and rubella (MMR) vaccine respectively. Most (66/69, 95.7%) received one dose of varicella vaccine or had documentation of prior disease, 59/69 (85.5%) received 2 doses of vaccine or had documented disease. Serologic testing revealed nonreactive results for (16/63)25.4% of those tested for HAV IgG antibody; 57/64 (89%) for HB surface antibody, 20/58(34.5%) for measles antibody (titer<1:8 IFA), 17/37(45.9%) for mumps IgG antibody, 21/63(33.3%) for rubella antibody, 12/56(21.4%) for varicella antibody(titer <1:32 IFA). Of those with negative varicella antibodies, 6/12 had at least one varicella vaccine dose, 5 had two, and 3 had documented disease.

Conclusion: HIV-infected children on HAART frequently lack protective antibodies against vaccine preventable illnesses despite appropriate immunization. Further studies are ongoing to determine factors associated with lack of immunity and if booster vaccination is beneficial.

No conflict of interest

Abstract: A_12

Comprehensive Pediatric HIV care

Where are the Girls? How Female OVC can count in the face of vulnerability: The CUBS approach in two states of Southern Nigeria

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Background: As Orphans and Vulnerable Children (OVC) phenomenon increases globally, so are programmatic interventions developed to address its impending consequences. OVC in Nigeria was estimated at 17.5m in 2008 (FMWASD) and with the escalating impact of HIV/AIDS the Girl-child seems worst-hit in the face of vulnerability. How can program interventions be tailored to serve the peculiar needs of the female OVC (FOVC)?

Methods: USAID-funded CUBS, a new project of Management Sciences for Health provides community based support to OVC in 11 states of Nigeria. From all children pre-enrolled, the OVC Vulnerability Index was used to select OVC to be enrolled while the Child Status Index tool was employed to screen OVC for service delivery. Baseline data of OVC enrolled and served with psychosocial support in August to December, 2010 in Rivers and Akwa Ibom states were 2,457 males and 2,361 females. In offering health services, the peculiar needs of girls were taken into cognizance by including Sanitary towels (STs) into the Basic Care Kits (BCK) that were distributed and by December, 704 FOVC over 597 male OVC (MOVC) were fully served BCK in the area of health promotion and hygiene. 49% MOVC and 51% FOVC representation was also considered while rendering Educational support while 30 FOVC were offered protection services over 20 MOVC.

Results: FOVC who opted for psychosocial support mainly recreational support and counseling in October and November were 1,615 less than 1,632 MOVC who opted for both. After the gender-tailored interventions, FOVC who opted for psychosocial support dramatically increased to 2,072 over 2,005 MOVC in December.

Conclusion: Mainstreaming gender as well as addressing the peculiar needs of girls when designing OVC programs addresses vulnerability issues amongst female OVC as well as increases the short-term and possibly long-term positive impact on the psychosocial and health-seeking behavior of the girl-child.

No conflict of interest
Abstract: A_13

Comprehensive Pediatric HIV care


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Background: Despite the implementation of programmes aimed to prevent mother-to-child transmission (PMTCT) and provide antiretroviral therapy (ART), scaling-up comprehensive care for HIV-infected children encounters many barriers in West Africa. We describe morbidity patterns and healthcare resource utilisation among non-ART-treated, HIV-1-infected children.

Methods: HIV-infected children enrolled prospectively in an HIV care programme in two health facilities in Abidjan, Côte d’Ivoire (2004-2009) were eligible. The children were followed-up from date of inclusion until database closeout, death, ART initiation, or loss to follow-up (no clinical contact for >6 months). Characteristics were compared by Fisher and Chi-square tests.

Results: Overall, 405 children were included, entering care at a median age of 4.5 years, 66.9% were receiving cotrimoxazole prophylaxis, and 27.7% met 2006 WHO criteria for immunodeficiency by age. The median follow-up time was 12 months (IQR: 1.5 – 30.7). Overall, 384 events occurred in 170 children (42%). Morbidity occurred more frequently among older (p<0.0001) and immunodeficient (p=0.003) children. 25% of clinical events led to in-patient day care, 8% to hospitalisation and 3.4% to death. In-patient day care usually required intravenous therapy (89%) and one-third lasted ≥4 hours. In-patient day care was less common among immunodeficient children than among the less impaired ones (18% vs 28%, p=0.002). In 33% of the cases, further medical examinations were made allowing to confirm diagnoses; this was more frequent among children aged < 1 year than among older ones (50% vs 27.5%, p =0.01).

Conclusion: Untreated HIV-infected children required substantial inpatient and outpatient care. Resource utilisation was highest among younger and non-immunodeficient children despite an inverse occurrence of morbidity patterns. Reassuringly, mortality was low following medical care inception. Given recent reports suggesting reduced mortality as well as short-term resource utilisation reductions for children treated with ART, it is urgent to improve early paediatric diagnosis, access to healthcare and ART.

No conflict of interest

Abstract: A_14

Comprehensive Pediatric HIV care

The psychosocial aspects of children in adolescence in dealing with their HIV status

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Background: Many children born with HIV are entering into adolescence and there are few services where the psychosocial needs of these children are specially met.

Materials & Methods: Twenty four children born with HIV taking treatment from INGOs in Yangon and their 21 caretakers were interviewed with a structured qualitative questionnaire during Oct and Nov 2010.

Results: Ten of 24 children were female and age-range was from 11 to 16 years. 21% of the children were out of school. More than half of them (58%) had at least one sibling infected with HIV. Majority of the children had correct knowledge on HIV transmission yet most of them had low level of knowledge on AIDS. Though 33% of them have been on ART for 5 years and more, none of them named the ARV drugs they are taking. Two children who said they could not
take ART on their own were both 11 years old but seven children, including older children, did not know their next clinic appointment day. Nearly half of them, mixed age group, stated not able to go to the clinic on their own. 49% of the children stated learning their HIV status from MD. Eleven children expressed feeling helpless on knowing their HIV status. 83% of the children were worried that they might transmit HIV to others. Half of them were bothered by their delayed physical development. 42% of them had disclosed their HIV status to no one, apart from their families and the medical team. Five children stated they had experienced discrimination and felt sad about it. Eight children discussed about feelings related to HIV with their MDs and nine with their counselors. Four children had discussions on HIV with their siblings, all of whom were also HIV infected. Half of them said they did not discuss with anyone when feeling angry or sad. Among those who discussed, majority were with their caretakers. Two-third of the children said their siblings were aware of their HIV status and almost all of them stated their siblings helping or protecting them. With friends, only two children mentioned having peer friends and only one child mentioned having difficulties in making friends. Two third of the children expressed their wishes to have more peer friends. Half of the children were orphans, where 7 lived with elderly grandparents (6 of whom were above 60 years). Nearly half of the caretakers identified themselves as not infected with HIV, and they represented majority of the group who showed poor knowledge in HIV, AIDS and their children’s AIDS status and treatment. All caretakers mentioned twice a day treatment of ART. 71% of the caretakers discussed about HIV with their children, mostly with emphasis on taking regular treatment. Only three caretakers touched psychological topics with the children.

Conclusions: Though adolescences with HIV were receiving medical treatment, the caretakers and the medical teams seem to be inadequate in meeting the psychosocial needs of these children to adjust well into their adulthood.

No conflict of interest

Abstract: A_15

Comprehensive Pediatric HIV care

Impact of In-reach home visits on adherence and virologic outcomes for pediatric patients in Botswana with previous poor adherence to ART

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Introduction: The Botswana-Baylor Children's Clinical Centre of Excellence (COE)'s In-reach program is an intervention strategy for challenging patients. It utilizes a nurse and social worker team to visit patients' homes - meeting family members, assessing the home environment, and ensuring that children and caregivers have support beyond the clinic at family and community level. This study's objective was to assess the impact of In-reach on ART adherence and virologic outcomes in children at high risk of treatment failure.

Materials & Methods: Retrospective chart review of all 19 children visited at home from January-June 2009 by In-reach on a priority basis due to persistently inadequate adherence to ART and/or non-suppressible viremia despite intensive counselling at clinic. Variables analyzed included last documented viral load (VL) and adherence to ART at time of In-reach visit and upon follow-up in December 2009, as well as line-of-therapy; 2/19 had unclear documentation of VL at 12 months and were excluded from VL analysis. Data were analyzed for statistically-significant differences (p<0.05) after intervention.

Results: At In-reach visit, 0/19 children (age range 3-16yrs, median age 12yrs) were noted to have good adherence to ART (95-105%). 12/17 had detectable VL (>400 copies/mL; if persistent, defines virologic failure in Botswana national ART guidelines). At follow-up (mean time-from-In-reach visit:8 months), 14/19 patients were noted to have good adherence (95-105%, p<0.05). 8/12 patients with previously detectable VL were noted to have suppressed VL at follow-up (p<0.05); 2
additional patients had achieved \( \text{VL} < 1,000 \) copies/mL. All 8 patients with detectable \( \text{VL} \) on non-first-line ART at time of In-reach had suppressed \( \text{VL} \) at 12 months follow-up.

**Conclusions:** In-reach visits generate substantial and sustained improvements in adherence to ART in complicated paediatric patients at high risk of treatment failure, with many patients previously unable to achieve viral suppression able to do so after In-reach intervention, including those who have already moved beyond first-line regimens. Wide inclusion of In-reach in national paediatric ART programmes should be considered as resources allow. Additional data will help inform such decisions, including assessing need for repeat In-reach visit; cost-effectiveness analysis of In-reach at both specialized centres such as the COE as well as district health sites; and prospective evaluation of its impact.

No conflict of interest

**Abstract: A_16**

**Comprehensive Pediatric HIV care**

**Family involvement status about HIV-infected children in China**

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**Background:** More and more HIV-infected children are receiving antiretroviral therapy (ART) globally and the importance of family-centered care for children infected with HIV has been emphasized consistently. Although family characteristics may have considerable impact on treatment outcomes, little attention has been paid to children's family status in China.

**Material and Methods:** The pediatric ART program was initiated in 2005 and a cross-sectional survey about family background was conducted from July 2005 to July 2009 at 4 HIV/AIDS clinics in Henan, Guangxi, Yunnan and Xinjiang provinces. General patient demographics were collected, including information about the children's surrounding family members, caregivers and drug administrators. Self-reported treatment challenges and medication adherence were also collected, as well as school attendance. SPSS 15.0 was used to analyze the data.

**Results:** 483 HIV-infected children were enrolled across the 4 sites. 62% were male, mean age at HIV diagnosis was 5.7 years, and mean age at time of survey was 10 years. 85% of mothers and 62% of fathers were also HIV-positive and 26% of mothers and 19% of fathers had died. Over a third (35%) of families had multiple children, with 46 (9.5%) having more than one HIV-positive child. Over 70% in all children listed their mother as their primary drug administrator with the rest administered by grandparents, other relatives, or themselves. 27% of patients reported difficulty in taking their medication, with pill burden as the key reason for adherence trouble. 32% of patient caregivers reported difficulty in picking up antiretroviral drugs, primarily due to transportation challenges. 324 children were of school age (7-8 years). Of these, 77.8% were currently enrolled in school, 33 (10.2%) had left school, and 39 (12%) had not yet begun school.

**Conclusions:** HIV positive children and their family were closely involved in dealing with disease as well as in bearing social burdens. The family care context may affect children's antiretroviral adherence. Hence, community based comprehensive care, including adequate assistance, stigma reduction, and psychological support should be provided for families with multiple HIV-positive family members.

No conflict of interest
Abstract: A_17

Comprehensive Pediatric HIV care

Mortality associated with HIV after HAART implementation in children in a Brazilian cohort

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Introduction: In Brazil a public health program of large-scale, free-of-charge distribution of antiretroviral (ARV) drugs to all HIV-infected children who fulfill criteria established by an independent advisory committee was implemented in 1996. At present, this program provides treatment to over 130,000 Brazilians with HIV infection, and after that, the AIDS/HIV lethality rate decreased. However, several children were wrongly exposed to ARV monotherapy, adherence to ARVs is far from perfect in this age group, and deaths HIV/AIDS related are still common. The aim of this study is to evaluate the HIV related mortality, in a prospective cohort, followed at Instituto de Puericultura e Pediatria Martagao Gesteira – IPPMG, an important HIV-pediatric reference center in Rio de Janeiro, Brazil.

Methods: Prospective cohort from all children followed at IPPMG from 1996 until 2005. A survival curve was built, and the lethality incidence density rate (IDR) was calculated. Risk factors for death were evaluated among patients baseline characteristics, bivariate comparisons were performed with Student T-test and Chi-square test. A logistic regression model were fitted with variables with p-value<0.15 in the bivariate analysis.

Results: 351 children were followed from 1996 until 2005. By the end of follow up, the average age was 11 years, and they were followed for 35185 children-months. 43 (12%) died (IDR 1.22 per 1000 children-months), 32 (9%) were lost e 56 (16%) were transferred. The main causes associated with the death were: disseminated citomegalovirus infection – 1 patient, miocardiopathy - 2 patients, chronic diarrhea – 2 patients, Non-pulmonary tuberculosis (TB) – 2 patients, pneumonia – 3 patients, neoplasia – 3 patients, PCP pneumonia - 4 patients, pulmonary TB - 5 patients, bacterial sepsis – 6, and encephalopathy - 7 patients. The main risk factors associated with death were: baseline CD4+ cell count (OR=1.06, for each 50 cells drop, p=0.09); year of birth before 1996 (OR=11.60, p-value=0.06); not being caucasian (OR=4.76, p-value=0.11); father is infected by HIV (OR=4.25, p-value=0.11); classification C, by CDC at first clinical visit (OR=3.03, p-value=0.28); chronic diarrhea at the diagnosis (OR=13.44, p-value<0.01).

Conclusion: The lethality rate was comparable with other series, and the causes of death were also comparable. Although some baseline risk factors for death were the same as in other studies (baseline CD4+ cells, chronic diarrhea), others, mainly associated with lower socioeconomic status were not described before, in a Country where the treatment is free of charge.

Another important variable associated with death was if the child was born before or after 1996, when the children could have access to ARV (including highly active antiretroviral therapy).

No conflict of interest

Abstract: A_18

Treatment of pediatric HIV infection

Management of children failing second-line antiretroviral therapy at Botswana-Baylor and decentralized ART sites in Botswana

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Background: While most children in Botswana have achieved sustained favorable clinical outcomes on antiretroviral therapy (ART), failure of ART is increasingly common, including failure of ritonavir-boosted lopinavir (LPV/r) second-line regimens. While rare, LPV/r-resistance requiring salvage with advanced regimens containing ritonavir-
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boosted darunavir (DRV/r) and raltegravir, both recently made available in Botswana, has become more common. With >2,000 children-in-care, the Botswana-Baylor Children's Clinical Centre of Excellence (COE) is Botswana's largest pediatric ART site and principal referral centre, and maintains an annualized mortality rate of < 0.5%. At the COE, complicated patients failing second-line and salvage ART are managed with a multidisciplinary team approach termed Challenge Clinic (approximately 60 patients currently). In Botswana, the need exists for increased decentralized capacity to manage complicated pediatric patients failing second-line ART, including the use of advanced ART regimens.

Methods: Evidence-based approach to developing a framework for use of advanced ART regimens at the COE, driven by COE-based pediatric/infectious diseases/HIV/public health specialists, taking into consideration Botswana-specific data and experience. Ministry of Health (MOH)-guided approach to Challenge Clinic development at non-COE sites.

Results: Framework for use of DRV/r and raltegravir at the COE developed, with criteria including documented genotypic resistance to LPV/r; correction of underlying adherence concerns; and specialist review with MOH approval. COE specialist mentors participate in regular support of a large Challenge Clinic in Francistown, and are assisting Challenge Clinic development at national health facilities in Palapye and Maun which receive regular COE specialist support.

Conclusion: An approach to the management of complicated pediatric ART failure cases can be developed in resource-limited settings, including in district health settings outside specialized centres. In Botswana, further Challenge Clinic development is necessary. New sites should be prioritized by a combination of factors - including need, feasibility and sustainability - under the direction of the MOH. Many elements of the Challenge Clinic approach require study, including clinical outcomes, cost-effectiveness and quality-of-care improvements.

No conflict of interest

Abstract: A_19

Treatment of pediatric HIV infection

Use of lamivudine –based regimens in HIV infected children with isolates harboring M184V mutation

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Introduction: Lamivudine (3TC) has been widely used in first-line regimes for the treatment of pediatric HIV. In this population, some evidence suggests that adherence may be a major issue especially in adolescents. The inadequate use of 3TC or FTC can precipitate the emergence of M184V mutation. Additionally 3TC resistance is rapidly acquired if the other components in the regimen are not effective. Among pediatric patients with drug resistance mutations, TAMs, M184V/I, and NNRTI resistance mutations are commonly observed. The evidence of benefits of continuing 3TC as part of a new regimen in patients harboring M184V mutation is scarce in pediatrics. The aim of this study is to describe the rate of virologic failure of new regimens in pediatric patients harboring M184V.

Material & Methods: A retrospective study was conducted reviewing clinical charts of HIV-1 infected children in our site who had M184V. Clinical profile, antiretroviral therapy and virological response to a new regimen with and without 3TC were captured. Patients with documented non adherence were excluded.

Results: From a cohort of 28 patients harboring the M184V mutation, 5 (17.8 %) patients were excluded of the analysis because of poor adherence documented. Eighteen (78.2%) patients received a 3TC-based regimen. At 24 weeks, the mean reduction in HIV-RNA was 1.32 log10 in the 3TC group and 1.16 log in the non 3TC group. Fourteen of 18 patients on 3TC and 3/5 with no 3TC had < 400 copies/ml at 24 weeks. No remarkable differences were found between groups in median time from HIV diagnosis (7 vs. 5 years) mean number of previous regimens received (2.7 vs. 2.6) and mean number of previous clinical AIDS events (0.2
vs. 0) Three patients in the 3TC group received new drugs (2 patients received darunavir and 1 patient raltegravir plus enfuvirtide).

Conclusions: The use of 3TC as a part of post failure regimen in children harboring M184V mutation has shown a reasonable viral load suppression in our patients. These results may contribute to consider keep using of 3TC as part of a new regimen in order to delay the use of new drugs, especially in pediatrics where the availability of adequate formulations and approval of new drugs is limited.

No conflict of interest

Abstract: A_20

Treatment of pediatric HIV infection

Scale up of early infant diagnosis- feasibility and operational issues in Karnataka, South India

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Introduction:
HIV-infected infants are the most vulnerable of all patients ~ mortality > 50% by age 2 in untreated patients. Karnataka has HIV prevalence of 0.81 percent, compared with national average of 0.36 percent (as per NFHS). Annual pregnancies in Karnataka are around 1.2 million. Prevalence of HIV among ANC's is 0.44, as per ICTC's ANC data in 2009-10 resulting in nearly 5000 HIV exposed babies annually. Objective was to study the operational feasibility of EID programme in Karnataka and recommend steps to improve it.

Methodology: EID was rolled in Karnataka during March 2010 DNA PCR Dry blood sample collection is done in 139 identified ICTCs out of 565 functional ICTCs and whole blood sample collection in 26 ART centers out of 41. NIMHANS, Bangalore is testing site for Karnataka. National algorithm for diagnosis of HIV-1 infection in infants and children < 18 Months are followed.

Steps Operational at ICTC & ART centers:
1. Dried Blood Spot Specimen collection
2. Exposed baby presents at ICTC (A & B: HIV-1 DNA PCR testing algorithm is followed)
3. Counseling done and consent form filled
4. Child made comfortable and records filled
5. Availability of materials required for collection ensured
6. Preparation of collection
7. Dried blood spot specimen collected
8. Drying and packaging
9. Storage and transportation to the Testing Laboratory
10. Report to ICTC as HIV-1 DNA detected within 7 days of receipt of specimen at lab
11. If positive referred to ART Centre for Whole blood HIV-1 DNA PCR testing
12. Evaluated for ART eligibility and initiated on ART
13. Follow up baby as per guidelines

Observations: Roll out of EID began with Capacity building and setting up of identified ICTC/ART facilities for HIV DNA PCR sample collection. 131 out of 139 identified ICTC sites are functional. 181 samples were found to be reactive out of 1694 DBS samples tested by end of December 2010. Only 60%(105) had undergone confirmatory HIV-1DNA PCR test with the whole blood specimen. 80% of WBS+ve babies currently alive had received NVP before 72 hrs of birth and 80% of them are below 12 months of age and less than 6 received LPV/rtr based ART regimen.

Conclusion and Recommendations: EID testing is the mainstay to diagnose HIV in children, scale-up to all functional ICTCs and ARTs is crucial. As 85% of babies found reactive were already exposed to NVP, decentralized availability of alternate regimen (LPV/rtr) is the need of the hour.

No conflict of interest
Abstract: A_21

Treatment of pediatric HIV infection

Care and treatment of child coming from PMTCT: case of côte d’ivoire, from ACONDA’s experience

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Introduction: With a HIV prevalence of 8.6% among pregnant women and 661,000 births per year, Côte d’Ivoire has an estimated 55,000 HIV-infected women delivering per year who need PMTCT services. Without intervention, 40 per cent of children can be infected. The national HIV program’s strategic plan calls for integration of PMTCT services into antenatal clinics, maternity and Family Planning units. ACONDA’s extension of decentralized prevention and care for pregnant women and PLHWA is based on a district approach that integrates basic health care, PMTCT, and ART services in maternal and child health centers. In 2008, ACONDA implemented this approach in 90 ANC clinics and child health center in the 26 health districts of Côte d’Ivoire

Methods: Health workers were trained. After, the program strategy consisted in coaching the care providers at the sites in VCT techniques with rapid HIV testing for women with unknown HIV status in ANC, labor-and-delivery rooms and Family Planning unit also. Drawing up and spreading simple technical procedures helped the care providers in the implementation of PMTCT. ARV drugs are packed up at the sites to get PMTCT kits ready to be distributed. The combined prophylaxis was offered to HIV-infected pregnant women and their newborns systematically, as recommended by national program, and then she got initial biological exams. Those who were eligible received a readjusted treatment. Those who were ineligible continued the current disease prevention. Nutritional advices were provided to the mother and the follow-up of the exposed child was systematic. After delivery, a folder is opened for the newborn. Nevirapin (in 72 H), Zidovudin (during 7 days) and Cotrimoxazol are given (at 6 week). Appointments are also given according to national vaccinal calendar. A child’s early HIV diagnosis by PCR is made after 6 weeks of postnatal follow up. The infected children received ART according WHO recommendations. A reference and counter-reference system links all HIV-infected women and their children to the medical doctors in the reference health centers.

Results: From October through September 2010, PMTCT services were integrated into 97 ANC clinics covering 31 districts, with 100 trained health workers. Of 79,618 pregnant women using antenatal services, 67,227 (84.43%) received HIV counseling and testing; 4391 (6.53%) were HIV-positive; and 4,215 infected pregnant women (96%) received their test results. 1789 of HIV-infected women received the mother and child combined prophylaxis and 638 under ART. 85% of children of infected mother who received correctly the prophylaxis were not infected.

Conclusion: The care and treatment of child coming from PMTCT must imply their father and even more their mother. A good prophylaxis can reduce the transmission of the virus of the mother to child and it is possible to pass on scale this disease prevention.

No conflict of interest

Abstract: A_22

Treatment of pediatric HIV infection

HIV-1 reverse transcriptase inhibitors resistance in vertically infected infants in Senegal

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Background: Preliminary data generated from children under antiretroviral (ARV) therapy in Dakar showed a high rate of virological failure after 24 months median follow up. Drug resistance mutations found in this population (80%) could suggest there may be gaps in the efficient delivery of ARV prophylaxis in Prevention of Mother To Child Transmission
program that can be a factor in development of early drug resistance in infants. Our objective was to assess HIV-1 drug resistance in vertically infected infants in Senegal.

Methods: Resistance analysis was carried out on dried blood samples for newly diagnosed children and not yet under HAART. A fragment covering the 700 first bp of reverse transcriptase gene was sequenced by the Agence Nationale de Recherche Sur le SIDA (ANRS) technique. Drug resistance was analysed according to the Stanford University HIV db algorithm and IAS USA list 2010.

Results: The study population was composed of 13 male and 7 female with a median age of 8 months (1 to 17). Eight out of 20 mothers were on prophylaxis including NVP. In 5 cases, regimen was AZT-3TC-NVP. Five infants born from these 8 mothers received AZT-NVP. Eight out of the 20 children were resistant to at least one reverse transcriptase inhibitor. Among them 5 children were born from mothers having received prophylaxis and 4 out of the 5 children received AZT-NVP. In children with sensitive viruses, 3 were born from mothers with prophylaxis and 2 out of the 3 children received AZT-NVP. Major mutations conferring NNRTI resistance were found in all the 8 children: V106M in 4 cases, Y181C in 2, and K103N, Y188L, P225S were found each in one case. NRTI major resistance was found in 2 children with D67N.

Conclusion: These results showed that ARV prophylaxis may have an impact on early acquisition of HIV-1 drug resistance in children. Thus there is a need to perform genotyping in children before starting HAART.

No conflict of interest

Abstract: A_23

Treatment of pediatric HIV infection

Quantification of CD4 responses to highly active antiretroviral therapy over five years among HIV-infected children in Kinshasa, DR Congo

Abstracts

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Introduction: The long term effects of highly active antiretroviral therapy (HAART) on CD4 cell percentage in HIV-infected children are incompletely understood. Evidence about this relationship from resource-deprived areas is particularly scarce, despite the fact that most children with HIV live in such settings.

Material & Methods: We analyzed observational data from HAART-naïve children enrolled between December 2004 and May 2010 into an HIV care and treatment program in Kinshasa, Democratic Republic of Congo. To estimate the effect of HAART on CD4 cell percentage while accounting for time-dependent confounders affected by prior exposure, a marginal structural linear mean model was used.

Results: 790 children were active for a total of 2090 person-years and a median of 31 months. The median age at baseline was 5.9 years; 405 (51%) were in HIV clinical stage 3 or 4 and 528 (67%) had advanced or severe immunodeficiency. During observation, 80 (10%) died, 76 (10%) were lost to follow-up, and six (1%) transferred care. HAART was initiated by 619 children (78%). The absolute rise in CD4 percentage was 6.8% (95% CI, 4.7%–8.9%) after six months of HAART, compared to no therapy, with the difference increasing to 8.6% (95% CI, 7.0%–10.2%) at 12 months and 20.5% (95% CI, 16.1%–24.9%) at 60 months. Although HAART resulted in short and long term immunological increases across baseline CD4 cell percentage categories, gains were slower when the initial CD4 cell percentage was <15. The cumulative incidence of recovery to "not significant" immunodeficiency was lower if HAART was started when immunodeficiency was severe rather than mild or advanced.

Conclusions: HAART increased CD4 cell percentages among HIV-infected children in a resource-deprived setting, as previously noted among children in the United States. More gradual and protracted recovery in children with lower baseline CD4 cell percentages supports the earlier initiation of pediatric therapy.

No conflict of interest

Abstract: A_23

Treatment of pediatric HIV infection

Quantification of CD4 responses to highly active antiretroviral therapy over five years among HIV-infected children in Kinshasa, DR Congo

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Reviews in Antiviral Therapy & Infectious Diseases 2011_8
Abstract: A_24

Factors determining adherence in children on ART in the city of Ouagadougou

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Introduction: Adherence is one of the cornerstones for the success of any treatment. In order to determine factors influencing adherence in ART, a study was conducted among children in Ouagadougou.

Methodology: It is a cross-sectional survey among caretakers and children on ART, done in the four most important hospitals in the capital.

Results: The study was done on 152 children with a mean age of 7 years (age range 1-17 years). The sex ratio was 1.08. Orphans of at least one parent were 59. A simplified diagram using a combined tablet concerned 109 children. Reasons for not taking ART were Lpiv/r and DDI syrup bad taste, the big Lpiv/r tablet, taking DDI while fasting, and fatigue among adolescents. The mean adherence rate was 98.38% for those in the age range between 0-5 years, 97.67% for those between 6-10 years and 92.59% for those more than 10 years. Adherence was better in children who had their father as the caretaker followed by those who had their mother and then those who had a tutor as a caretaker. Children who were informed about their serostatus had better adherence. Patients who were living in a family where the mother was also taking ART adhered better.

Conclusion: In order to get more satisfying results on children on ART, it is important to develop strategies that would minimise reasons of non-adherence like forgetfulness, absence of care takers, stopping treatment, insufficient food.

No conflict of interest

Abstract: A_25

Prevention of Mother-to-Child transmission

Key considerations for successful implementation of the 2010 WHO guidelines for PMTCT in resources limited settings.

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Introduction: The new 2010 World Health Organization (WHO) guidelines for the prevention of mother-to-child transmission of HIV (PMTCT) present a major shift in the strategy for preventing post-natal transmission of HIV during breastfeeding. However operational barriers for successful implementation of these guidelines in resources limited settings need to be addressed.

Material & Methods: The guidelines promote early initiation (14 weeks of pregnancy) of lifelong highly active antiretroviral therapy (HAART) among eligible HIV+ pregnant women and offer two options to prevent HIV transmission during breastfeeding for HIV+ pregnant women not eligible for lifelong HAART:

Option A: [maternal AZT prophylaxis from 14 weeks gestation, intra-partum nevirapine (NVP) and daily infant NVP prophylaxis until one week after breastfeeding cessation]; or

Option B [maternal HAART prophylaxis from 14 weeks gestation until one week after breastfeeding cessation and either six weeks of daily infant NVP or AZT]. We used the WHO health system’s 6 building blocks as the framework of analysis to identify key considerations in implementing these guidelines in resources limited settings.

Results: In-country policy analysis to select between option A and B, should be guided by the following: coverage of existing PMTCT services by type of regimen; linkages with ART programs; human resource capacity and policy environment for task-shifting to facilitate service delivery at decentralized levels; existing laboratory capacity to perform CD4 cell counts testing and feasibility of strategies

Reviews in Antiviral Therapy & Infectious Diseases 2011_8
Abstract: A_26

Prevention of Mother-to-Child transmission

Mother-to-child transmission of HIV: an assessment of level of knowledge and attitude among women in rural Kenya

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Introduction: Vertical transmission of human immunodeficiency virus (HIV) remains the most important source of pediatric HIV infection. Without intervention, a third of exposed infants are at risk of infection. Adequate maternal knowledge and attitude remain key pillars in prevention strategies targeted at mother-to-child transmission (MTCT) of HIV. We sought to assess the knowledge and attitude on mother-to-child-transmission of HIV among women in a rural kenyan population.

Methods: Ninety five women in their reproductive age (19 to 49 years) and at least a single parity were recruited from Nyangena Division, Kisii district, rural Kenya using convenience sampling. Data was collected via a questionnaire and the aim explained to the respondents to obtain consent. Analysis for descriptive statistics was done using SPSS® 15.0 for Windows.

Results: Majority (74.3%) knew about MTCT with a similar proportion (74.7%) indicating awareness of its prevention. Only 25.4% correctly identified breastfeeding as a source of pediatric infection but over half of the respondents agreed that use of ARVs lowers transmission and makes breastfeeding safer.

Conclusion: While it is encouraging to note the high level of awareness about MTCT of HIV and the role of ART in prevention, little appreciation of breastfeeding as a source of pediatric infection is of concern. More effort should be geared towards highlighting proper infant and young child feeding practices in the context of HIV to improve safer PMTCT profile of this population.

No conflict of interest

Abstract: A_27

Prevention of Mother-to-Child transmission

One body, one test, two lives: patient centered strategy to increase HIV testing in pregnant women and their partners

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Background: Neighborhood Health Services Corporation (NHSC), an urban community-based Federally Qualified Health Center located in Central New Jersey, USA, provides healthcare services to 25,000 uninsured, underprivileged/impoverished and minority persons. Prenatal services, labor and delivery, are provided to 750 women annually. Given that NJ has the third highest number of HIV women in USA and the highest number of children with HIV, early HIV detection in pregnant women and timely intervention become paramount. NHSC historically struggled with sub-optimal OB HIV testing rates (60%) and needed to make radical program changes to comply with CDC
recommendations to ensure HIV testing is offered to 100% pregnant patients.

Methods: A PDSA (Plan-Do-Study-Act) cycle was conducted to test a new approach to HIV testing among OB patients: professional HIV Counselors are physically located in OB department; HIV counseling and Rapid testing is done at the time of OB registration via HIV Counselors; daily OB registration schedules are available to HIV Counselors; HIV results become part of OB medical records immediately upon result availability; HIV educational DVDs are utilized in OB patient waiting areas to increase awareness/interest in getting tested.

Results: Resulting from PDSA-improved OB HIV testing strategy, NHSC observe sustained 100% compliance with CDC recommendations. Furthermore, with proper pre-test counseling 100% of pregnant women and 91% of accompanying partners consent to HIV testing. Rapid HIV testing and Rapid-on-Rapid positive result confirmation allow for smooth/timely transition from HIV testing to care/treatment services for newly diagnosed HIV pregnant patients and partners.

Conclusions: The collected/analyzed data suggests that coordinated, convenient, on-location, patient-centered approach to HIV testing of OB patients and partners help to: identify HIV positive pregnant patients in the first/second trimesters; immediately connect them to prenatal and HIV specific care to minimize a chance of vertical HIV transmission; provide prevention and/or treatment services for partners including prevention for positives.

No conflict of interest

Abstract: A_28

Prevention of Mother-to-Child transmission

Integrating ART in to ANC services improves ART access and reduces MTCT: Experience from Kakamega, Kenya

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Background: Integrating HIV care and treatment into ANC (“MCH Model”) was approved for provincial hospitals in Kenya in 2009 to increase ART access for pregnant women. The model includes opt-out counseling and testing for pregnant women, partner testing, WHO clinical staging and CD4 testing. HIV positive mothers, their partners and exposed infants receive HIV services at MCH until the baby is 18 months. In Kakamega Provincial General Hospital (KPGH) during the six months before initiation of the MCH model, 47% of the 113 referred ANC HIV+ mothers registered for HIV services and only 15% returned after registration.

Method: In 2008, MCH staff from KPGH were trained in ART in preparation for the integration. They also observed a functional MCH model at the national referral hospital. Routine follow-up and supervision were provided by the APHIA II Western project team located in Kakamega. MCH nurses were routinely mentored by hospital gynecologists to administer ARVs for prophylaxis and treatment.

Results: KPGH launched the MCH Model in July 2009, but structured follow-up for infants commenced in January 2010. Up to December 2010, 315 HIV positive mothers (of 6,720 tested) have been diagnosed: all had CD4 counts, clinical staging and Prevention-with-Positives counseling. Of the 79 women needing treatment, 100% initiated HAART and 82% are continuing: one client died before delivery, seven transferred to another location, one transferred to HIV services at KPGH (the infant was negative at 18 months) and 5 were lost. 63 mothers on HAART delivered and all their infants tested negative by PCR at 6 weeks.

Conclusion: The MCH model improved access to ART and related HIV services for mothers and infants and appears to reduce MTCT in Kakamega. Implementation of this Model is feasible in Kenyan public hospitals if staff are well trained and local expertise is available.

No conflict of interest
Abstract: A_29

Prevention of Mother-to-Child transmission

Prevention and control Program of the vertical transmission of the HIV/AIDS in Cuba (January 1986-August 2010)

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Background and aims: Since 1986, a controlled program has been established in the primary health care system in order to reduce HIV vertical transmission in Cuba.

Methods: The usual approach since 2008, applied to every HIV+ pregnant woman who decides to keep her pregnancy, is to administer HAART independently of her immunological status, from week 14 to the time when the caesarean section is carried out (week 38). Breastfeeding is strongly discouraged. The newborn child receives ZDV (2mg/Kg/dose) every 6 hours for the first 6 weeks. The children are followed-up at the IPK outpatient office, where their HIV infection status is determined. Infected children are treated with antiretrovirals according to the presence of opportunistic diseases, CD4 cell count and viral load.

Results: A total of 2520 seropositive women have been reported since January 1, 1986 to August of 2010 (18.8%) of all the seropositive cases of the country (2520/13346), 398 (15.7%) have given birth a total of 432 children (27 women have delivered twice and 7 have twins); 37 of 432 are HIV+ (8.5%), 34 classified as AIDS (34/37=91.8%) , 24 are under treatment with HAART ; 2 are asymptomatic and 11 (11/37=29.7 %) have died. No infection was demonstrated in 319 children by PCR and Western Blot (319/432=73, 8%) and 76 (76/432=17, 5%) are still under study.

Conclusion The Program for Prevention and Control of HIV Vertical Transmission is effective since the number of infected children is low, similar to the figures reported for developed countries.

No conflict of interest

Abstract: A_30

Prevention of Mother-to-Child transmission

Prevention of Mother To Child Transmission In côte d’ivoire, from ACONDA’s experience.

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Background: With a HIV prevalence of 8.6% among pregnant women and 661,000 births per year, Cote d’Ivoire has an estimated 55,000 HIV-infected women delivering per year who need PMTCT services. ACONDA’s extension of decentralized prevention and care for pregnant women and PLWHA is based on a health district approach.

Methods: Health workers were trained. After, the program strategy consisted in coaching the care providers at the sites in VCT techniques with rapid HIV testing for women with unknown HIV status in ANC, labor-and-delivery rooms and Family Planning unit also. Drawing up and spreading simple technical procedures helped the care providers in the implementation of PMTCT. ARV drugs are packed up at the sites to get PMTCT kits ready to be distributed. The combined prophylaxis was offered to HIV-infected pregnant women and their newborns systematically, as recommended by national program, and then she got initial biological exams. Those who were eligible received a readjusted treatment. Those who were ineligible continued the current disease prevention. A psychosocial supports for treatment adherence, was provided by counselors and Nutritional advices also. A child’s early HIV diagnosis by PCR is made after 6 weeks of postnatal follow up.

Results: From October through September 2010, PMTCT services were integrated into 97 ANC clinics covering 31 districts, with 100 trained health workers. Of 79,618 pregnant women using antenatal services, 67,227 (84.43%) received HIV counseling and testing; 4391 (6.53%) were HIV-positive; and 4,215 infected pregnant women (96%) received their test results. 1789 of HIV-infected women received the mother and child combined prophylaxis and 638 under ART. 85% of
children of infected mother who received correctly the prophylaxis were not infected.

Conclusions: Providing the combined prophylaxis from the disclosure of test results is essential if we noticeably want to reduce the Mother to child HIV Transmission for the scaling up.

No conflict of interest

Abstract: A_31

Prevention of Mother-to-Child transmission

The outcome of admitted HIV exposed babies at Kanombe Military Hospital from June 2010 to March 2011

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Introduction: This study aimed at assessing the mortality in HIV exposed infants in the post ART era and to find out the causes of admissions and morbidity in the admitted HIV exposed infants at Kanombe Military Hospital.

Method: This analysis is part of a prospective study conducted at KMH Pediatric and Neonatology wards from among HIV exposed mother-infant pairs. 88 mother-infant pairs were admitted and recruited into the study between June 2010 and March 2011.

Results: The overall infant mortality rate was 16% (14/88) and the major causes of admission were neonatal infections (30%), birth asphyxia (23%). Of the 14 deaths, 8 (57%) occurred within the first 2 days (early neonatal deaths) and 13 (93%) within the first 7 days. Although the difference was not significant, early neonatal mortality rates were slightly higher among males than females (22% males, 18 females, p=0.674). Overall, neonatal mortality rate was slightly higher in males than in females (16.7% males, 14.3% females, p=0.091). Adjusting for infant age, maternal age and low birth weight, infants with birth asphyxia (RR=22.1, 95% CI: 1.45-338.32) and those with neonatal infections (RR=49.1, 95% CI: 1.34-1804.2) were significantly at risk of death.

Conclusion: Most likely that the high early neonatal mortality rate seen in this population is due to selective recruitment of a high-risk group of infants referred for special care. However, our finding of infections as important contributor to neonatal deaths that occur within 2 days of admission among patients referred for specialized care at the hospital emphasizes the importance of monitoring delivery, hospital and community acquired infection.

No conflict of interest

Abstract: A_32

Prevention of Mother-to-Child transmission

Characterization of HIV Perinatal Infected Children born in a Public Hospital in Argentina

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Background: Since 2003 the strategies for prevention mother-to-child transmission (PMTCT) have been intensified in our setting. Poor prenatal care, late HIV diagnosis and lack of exposure to antiretroviral treatment have all been well established.

Objective: To describe the clinical, virologic and immunologic outcomes of HIV-infected children diagnosed between 2003 and 2010. To describe the perinatal risk and current status of their mothers.

Methods: Retrospective chart revision of HIV+ children and their mothers, born at our hospital thorough 2003 to 2010.

vertically, and 1 horizontally infected. Media of Viral load and CD4 at baseline (1/13 missed data): 5.3 log and 28.5%, Media of Viral load and CD4 at last visit (10 results during 2nd semester 2010. 1 died, 2 lost to follow up): 3.2 log and 34 %. (6) Pneumonias, (1) severe anemia, (1) HIV encephalopathy, (1) MAI, (1) congenital toxoplasmosis and (1) disseminated fungal sepsis were diagnosed during their first year of life. 1 child was born with congenital anomalies and died at 1 month of life. All mothers (12) had at least 2 or more major perinatal risk to transmit HIV. 3 mothers died when their babies were under 2. Causes: poor adherence and advanced disease.

Conclusions: The trends of HIV vertical transmission (5.7 - 3.6) viral transmission (5.3 - 3.2 log) and immunological reconstitution (28.5 - 34.2% CD4) possibly reflect the efforts to implement the well known strategies of PMTCT and to improve the survive and QoL of infected children. Regardless of several improvements in the treatment and accessibility during the last years in our setting, it hasn't achieved in this cohort a mayor decline in the HIV transmission. This is due to social co variables, addictions, lack of controls and poor adherence to the ARV treatment during pregnancy. Much more efforts or new strategies will be needed to achieve the ideal of "transmission zero".

No conflict of interest

Abstract: A_33

Prevention of Mother-to-Child transmission

Risk factors for HIV vertical transmission: When should be considered more than one drug to an HIV vertically exposed newborn.

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Background: Risk factors for HIV vertical transmission are known. Several authors suggested based on those risk factors, that neonatal post-exposure antiretroviral therapy (TARV) should be done with more than one drug. The aim of this study is to evaluate in a Brazilian cohort of HIV vertically infected (HVC) and non-infected, but vertically HIV exposed children (NHVC), how important are the main known risk factors in prevent HIV infection before the labor and delivery in order to decide judiciously the use of more than one antiretroviral drug in the neonatal period.

Methods: Nested case-control study, of all children followed at a reference center in Rio de Janeiro, Brazil. Cases were defined as HIV vertically infected children, and controls were defined as HIV-vertically exposed, but not infected children. Risk factors for HIV vertical infection before labor/delivery were evaluated and a logistic regression model was fitted to demonstrate variables independently associated with the infection risk. Since in this cohort, several children were exposed to post-natal interventions to diminish the HIV infection risk and others not, the variables breastfeeding and use of zidovudine (ZDV) during neonatal period were forced in the model, in order to adjust to these variables.

Results: 1182 children were evaluated: 173 (15%) were infected. The risk factors evaluated were: Did not use TARV in prenatal care (OR=13.10 CI95%= 3.68-46.69); did not use ZDV in labor (OR=3.71, CI95%= 0.87-15.80); birth weight<2500g (OR=1.02, CI95%=0.82-12.55), vaginal delivery (OR=3.82, CI95%= 1.36-10.74) , amniorexis for more than 4 hours before delivery (OR=0.70, CI95%= 0.26-1.86), use of ZDV in neonatal period (OR= 21.82, CI95%=8.68-54.89), breastfeeding(OR= 2.42, CI95%= 0.78-7.49).

Conclusion: In conclusion, when analyzing all risk factors independently, the variables that must be considered when deciding to add antiretrovirals to the therapy to an HIV vertically exposed newborn are maternal use of TARV during prenatal care, use of ZDV in labor, and vaginal delivery.

No conflict of interest
Abstract: A_34

Prevention of Mother-to-Child transmission

Decentralization: A Tool to Scale-up Prevention of Mother to Child Transmission among Pregnant Women in Nigeria

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Background: Prevention of Mother to Child transmission (PMTCT) coverage in Nigeria has been sub-optimal. This may be due to the fact that interventions have been restricted majorly to tertiary and secondary health centers.

In 2009, only 13% of pregnant women were tested for HIV while ARVs for PMTCT reached only 22% of pregnant women living with HIV/AIDS. Scaling up access to prevention, treatment, care and support interventions remains a major challenge in tackling HIV/AIDS, especially PMTCT in Nigeria as majority of pregnant women living with HIV give birth without access to PMTCT services. Availability of access to care, treatment, prophylaxis, counseling and trained personnel are reflected as the predictor variables for the success of this HIV/AIDS program.

Method: Data was obtained from health care providers in 25 districts offering PMTCT in 2009 while in 2010 data was obtained from an additional 8 health care providers making 33 districts in total. This data represented number of HIV+ pregnant women who received PMTCT prophylaxis (Zidovudine and lamivudine at antenatal visits and single dose nevirapine SD-NVP during labour). All babies born received SD-NVP at birth and zidovudine for 6 weeks. Data from both years were compared and trends derived utilizing bi-variant analysis. A logistic regression analysis was also used to compute the predictor variables of the therapy initiated.

Results: Cumulatively, 1124 HIV+ women received prophylaxis in 2009 while 1144 received prophylaxis in 2010. A frequency distribution shows that the trend in percentage of HIV+ pregnant women receiving ARVs for PMTCT (2009-2010) fell by 9% while the number of sites had increased by 30.7% (2009-2010). All the PMTCT sites are secondary (private) health centers. Of the 33 health centers: 21(62%) are faith based, 9(29%) are private-owned while 3(9%) are government owned. Faith based health facilities had 1037(92%) and 995(87%) of the total PMTCT coverage in these health centers in 2009 and 2010 respectively.

Conclusion: The primary health care system in Nigeria still needs to be strengthened while use of faith-based health centers, mission homes and traditional birth attendants for PMTCT sites should be adopted.

No conflict of interest

Abstract: A_36

Co-infections in HIV-infected children

Grade 3 anal intraepithelial neoplasia in a HIV-infected African girl

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Background: Women with HIV infection are at increased risk for intraepithelial cancer of the inferior genital tract and the anal canal. Seventy percent of vulvar intraepithelial neoplasia (VIN) are related to a human papillomavirus (HPV) infection and frequently involve cervical and vaginal mucosa. The anal intraepithelial neoplasia (AIN) is the precursor lesion of anal squamous carcinoma; it is also associated with the oncogenic types of HPV. These neoplasms are nevertheless just rarely described in HIV-infected girls and no treatment has been thoroughly examined in paediatric patients. A case of a ten-years-old African girl, living in a very poor and large family and vertically HIV-infected is presented.

Case Report: Since the age of about eight the emergence of several similar condylomatous lesions was observed, extending from the perianal region and the anal canal to the vulvar surface and rapidly reaching a considerable size. On observation a large, smelly and somewhere bleeding neoformation extending from the anal canal and the intergluteal sulcus
Abstract: A_37

Co-infections in HIV-infected children

The clinical manifestations and outcomes of HIV infected children with Cryptococcus neoformans at Tygerberg Children’s Hospital

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Background: Cryptococcus neoformans (CN) is an encapsulated yeast which causes infection in both animals and humans. A laboratory based study performed in South Africa in 2002-2004 found that children under the age of 15 years accounted for 1% of the total number of cryptococcal infections encountered in the 2 year period. The aim of this study is to determine the occurrence, clinical presentation and outcome on treatment of HIV infected African children with Cryptococcal disease.

Materials and methods: This is a descriptive, retrospective case series. All HIV infected children diagnosed with Cryptococcus neoformans disease at Tygerberg Children’s Hospital from January 2004 till December 2010 were included. Data was collected on the clinical characteristics of Cryptococcal illness, laboratory data and radiological investigations. Data was also collected on the dose and duration of antifungal and antiretroviral (ARV) drugs.

Results: 7 HIV infected children presented with Cryptococcal disease during the study period. 3 of the 7 patients were on ARV therapy, and 2 had lower than detectable viral loads at the time of presentation. As in adults severe CD4 depletion was a common finding with 5 (71%) of children having fewer than 50 cells/mm³ at presentation. 4 children presented with meningitis, and 3 with sepsis. 2 were subsequently found to have lung involvement as well. 2 patients died during first admission (both had undetectable viral loads) and 3 had a relapsing course despite Fluconazole prophylaxis and ARV therapy.

Conclusion: Children with HIV infection are at risk of developing Cryptococcal disease. In our
Abstract: A_38

Co-infections in HIV-infected children

39 Cases of Tuberculosis in HIV-infected children - clinical, radiological and microbiological features

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Background: Tuberculosis (TB) is a major cause of morbidity and mortality among HIV-infected children. Diagnosis of TB is notoriously difficult in HIV-infected children. There are few large cohorts describing the clinical features of TB in HIV-infected children. Here we describe the clinical, radiological and microbiological features of all definite and probable cases of TB in children enrolled in an INH prophylaxis study during the period from January 2003 up until the end of 2007.

Objective: To describe the clinical, radiological and microbiological features of definite and probable TB.

Methods: A descriptive analysis was done within a prospective, double-blinded placebo-controlled trial of INH compared to placebo in HIV-infected children in Cape Town, South Africa, a high TB incidence setting. Definite TB was defined as culture positive for Mycobacterium tuberculosis on a sputum or other sample; Probable TB was defined as a chest radiograph (CXR) suggestive of TB (lymphadenopathy, miliary pattern, pleural effusion, bronchial compression or parenchymal infiltrate) plus at least one of the following: a positive tuberculin skin test (TST), a history of a close contact with an adult with TB, loss of weight or failure to gain weight within the previous 3 months, or a positive smear microscopy for acid fast bacilli on sputum.

Results: 39 /298 (13%) children were diagnosed with TB from January 2003 to December 2007. 22 /39 (56%) were male, 22/ 39 (56%) were on placebo. 2 children died. 74% of children were between 2 and 4 years old. 2 children had more than one episode of TB. At time of TB diagnosis 9/39 (23%) of children were on HAART. 2 children had MDR TB. 1 had a contact with MDR and 1 was on INH prophylaxis. 19 children were classified as having definite TB and 20 probable TB. 19 had a household TB contact. 5 children had a positive TST. 7 had prior TB. 30 had clinical symptoms.

Conclusions: TB is common in HIV-infected children, even in those on HAART. Access to CXR and culture improves diagnosis and management. HIV-infected children with culture positive TB can have normal chest radiographs and can be asymptomatic so regular screening is crucial.

No conflict of interest

Abstract: A_39

Co-infections in HIV-infected children

Cytomegalovirus myocarditis presenting as immune reconstitution inflammatory syndrome in an HIV-1 infected child.

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Background: Cytomegalovirus (CMV) is a common opportunistic infection in HIV disease causing a wide range of clinical pathology. There is considerable diagnostic difficulty and poor access to therapy in resource limited settings. CMV is well described as a cause of myocarditis in both HIV infected and

No conflict of interest
uninfected adults and children. CMV myocarditis can present as part of the Immune Reconstitution Inflammatory Syndrome (IRIS) and this has been described in adults. No childhood cases of CMV IRIS myocarditis have been reported in the literature. We present a case of CMV IRIS myocarditis in an HIV infected toddler managed at Tygerberg Children's Hospital in South Africa.

**Results:** A 22 month old HIV positive girl presented with severe malnutrition, acute gastroenteritis and significant proteinuria. At the time of diagnosis she had no features of cardiac dysfunction. She was severely immune suppressed with a CD4 count of 222 cells/mm3 (5.7%) and a viral load of more than 10 000 000 copies/ml (>6.7 log). She was initiated on highly active antiretroviral therapy (HAART): abacavir, lamivudine and lopinavir/ritonavir.

Twelve days after initiating HAART she developed a tachycardia with poor perfusion, hepatomegaly and a gallop rhythm. Echocardiography confirmed a dilated left ventricle with poor function. Admission to the Paediatric Intensive Care Unit was needed for inotropic support and intensive monitoring. Polymerase chain reaction (PCR) for CMV confirmed a concurrent CMV viraemia with a viral load of 3400 copies/ml (log 3.5). She was treated with systemic ganciclovir (GCV) but due to continued deterioration this was followed by a course of steroids with good response. Cardiac function recovered with an ejection fraction of 63% 18 days later. There was no retinitis and a renal biopsy was not performed.

She received a total of 6 weeks of gancyclovir and oral valganciclovir in therapeutic doses. Proteinuria, complicated by hypertension persisted and this was treated with a calcium channel blocker.

**Conclusion:** Myocarditis can occur in children as part of IRIS. CMV should be considered as a possible etiology and promptly treated. Current reports and research on IRIS in children focus on management of the more common tuberculosis IRIS. Management and access to therapy for other serious but rarer forms of IRIS is still lacking.

*No conflict of interest*

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**Abstract: A_40**

*Implementation research on PMTCT and pediatric treatment programs*

**The role of a patient escort service as an integral part of the referral system within an HIV program in Nigeria**

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**Background:** Jhpiego is implementing a CDC-funded HIV prevention project in 15 Nigerian hospitals. The project refers all identified HIV+ clients from their point of testing to the closest comprehensive sites for further care and treatment. Referred clients are encouraged to provide feedback to the testing sites after accessing care. Data from three randomly selected facilities out of the 15 hospitals showed that fewer than 20% of referred clients ever arrived at referral sites and of those who did arrive, 42% gave feedback to the testing sites. The project subsequently trained, supported and provided incentives to volunteers to escort HIV+ clients to their various referral sites and to ensure feedback. Over 80% of the escorts were community volunteers with the remaining 20% constituted by the facilities’ staff to coordinate the entire escort services.

**Methods:** Using data from one-year before and after the escort intervention, the study team reviewed, compared and analyzed aggregated data and specific targeted indicators from the three randomly selected facilities out of the 15 facilities. The two groups: (One-year before and One-year after the intervention) were then compared to show significant differences between them.

**Results:** One-year after escort services implementation, 93% of clients referred were seen at referral sites compared to 19% one-year before the intervention. This difference was found to be statistically significant. Also after the intervention, 96% of clients returned back to their primary site to provide feedback after accessing care and management at the
comprehensive sites, compared to just 42% before the intervention (p<.001)

**Conclusion:** Implementation of escort program demonstrated the value of trained escorts in ensuring that HIV+ patients access referral services and provide feedback to primary sites. This intervention also demonstrates escort service as a valuable addition to the continuum of care in HIV program implementation especially to the non-comprehensive HIV sites.

No conflict of interest

**Abstract: A_41**

*Implementation research on PMTCT and pediatric treatment programs*  

**Strengthening Information Systems for Community OVC Programs in Nigeria: The CUBS experience**

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**Background:** Since 1990, the number of Orphans and Vulnerable Children (OVC) have stealthily increased in Sub-saharan Africa and was projected at over 18million in 2010 (COTB,2004). With this phenomenal increase, program evaluators have demanded painstaking documentation of activities that mirror the quality of services delivered and wellbeing of OVC which on the other hand have proved to be a hurculean task for program implementers. CUBS a USAID funded project which provides community based (CB) support for OVC in 11 states of Nigeria, provides a blueprint of milestones achieved by scaling the hurdle of data gathering and verification.

**Materials & Methods:** In order to strengthen the community and national systems for quality data generation and reporting, CUBS trained 16 Community Based Organization (CBO) staff and 6 OVC desk officers of Federal and State Ministries of Women Affairs (FMWASD) on OVC monitoring and evaluation (M&E) tools. M&E tools used included OVC Vulnerability Index (OVI), Pre-enrollment register, Child status Index (CSI), Enrollment card and register, Service form and register, National referral form, Training register and Monthly Summary form (MSF). CUBS partnered with these CBOs to enroll and screen OVC according to vulnerability priority, provide service delivery, gather data and report same in a bottom-up approach by using these tools. All tools were administered as guided by the National M&E framework, National Guidelines and Standard of Practice (SOP) on OVC service delivery. CUBS provided monthly mentoring, monitoring and supervisory visit to these CBOs in company of the OVC desk officers, verified generated data using a simple Excel spreadsheet monthly and Data Quality Assessment periodically. Findings were on a 6-month study period in two focal states of Nigeria.

**Results:** Before the project CBOs had little or no concrete documentation on OVC activities, the few available were saddled with errors, the FMWA had no database or directory on OVC, no monthly reports from CBOs were available at the SMWA, OVC service delivery was quantitatively-based and monitoring of OVC wellbeing at the community level were almost absent. 6 months into the CUBS project, 2,457 males and 2,361 female OVC enrolled in Rivers and Akwa Ibom states between August to December by 6 CBOs were offered services within the 6+1 service areas with complete documentation, all OVC had a Client Folder with all M&E tools duly filled for each child, first and second level verification by CUBS reduced error by 95%, an OVC database/directory now developed by the FMWA with technical assistance from CUBS, all monthly reports of CBOs working on the CUBS project are now available at the ministry, OVC service delivery is now based on needs while the well being of the OVC is now qualitatively monitored with the CSI tool.

**Conclusion:** Reiterating data gathering and verification processes using a bottom-up approach can enhance the quality of services rendered by CBOs and public health workers to the OVC at the community level. The wellbeing of especially most vulnerable OVC would also be enhanced all of which lies in the triage intervention of the CUBS project.

No conflict of interest
Abstract: A_42

Implementation research on PMTCT and pediatric treatment programs

On-site mentoring & Quality Improvement initiatives as strategies to scale up paediatric ART: a pilot programme in 3 rural districts in Tanzania

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Introduction: Although combination antiretroviral therapy (cART) reduces mortality in HIV-infected infants and children, ART initiation rates remain unacceptably low, despite training. Data to support clinical mentoring as a means to build capacity are sparse. We piloted a 5-day clinical mentoring intervention by 1 experienced HIV/AIDS nurse to increase paediatric cART enrollment rates at rural clinics.

Materials & Methods: In March 2010, 3 Tanzanian district/regional sites were identified for intervention. Assessments included quality improvement (QI) review, direct observation of care, and discussions with staff. Gaps identified resulted in same-day targeted mentoring interventions. Mentoring topics included conventional clinical knowledge/skills (e.g. early infant diagnosis (EID), staging, growth charts, safe ART prescribing, weight-based dose adjustment) and systems-strengthening activities (e.g., documentation).

Results: Baseline QI review found that 35% (130) of eligible children had not started cART. Through provider mentoring, 51 (39%) of these children were found and initiated on treatment; 79 (61%) were lost to follow-up. Providers reported increased confidence in EID, staging, initiating cART, and dose adjustment.

Conclusions: Short term (5 day) targeted clinical mentoring can increase provider competence and confidence in pediatric cART, and increase pediatric cART initiation.

Interventions to identify infants and children eligible for treatment and to retain them in care are urgently needed.

No conflict of interest

Abstract: A_43

Implementation research on PMTCT and pediatric treatment programs

Pregnancy, HIV and Prevention of Mother to Child Transmission (PMTCT) in Central Mozambique: Community influences on loss to follow up

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Background: Despite the expansion of PMTCT services in Sub-Saharan Africa, many women and children are lost to follow-up at each step of the continuum of care. Previous qualitative research findings in African settings have shown the importance of cultural and contextual factors in PMTCT enrollment and follow up. In order to better understand the universe in which HIV positive pregnant women circulate, we aimed to identify and describe community discourse, attitudes and norms concerning HIV testing and follow up during pregnancy, in a high HIV prevalence Mozambican community characterized by significant loss to follow up.

Materials & Methods: This abstract discusses the qualitative findings of in depth interviews and focus group discussions (FGDs) which constituted the community component of a larger research project that utilized mixed methods to explore PMTCT loss to follow up in Central Mozambique. This component of the study aimed to better contextualize women’s ability to take advantage of HIV prevention, care and treatment strategies, by exploring communities’ perceptions and experiences.
regarding universal HIV screening in ANC clinics, male partners’ and communities influences in women’s decision-making process around HIV/AIDS. In depth individual interviews (33) and FGDs (7) were conducted with women and men in the communities of the direct catchment area of 2 sites (Dondo and Munhava, Sofala Province) offering PMTCT services, and coded using AtlasTi.

Results: Main themes emerged from the interviews and FGDs that help understand women’s realities that ultimately interfere in their ability to enroll and follow up with HIV prevention, care and treatment activities especially during pregnancy:

- HIV is still a discomfiting topic in the community, especially when discussed in the context of pregnancy: people often referred to HIV as a forbidden topic, as a secret;
- HIV testing conversation in households elicits broader discussions around unfaithful relationships, male partner role, possibility of couples sero-discordance, fear of discrimination;
- There is common disbelief and distrust in health systems, mainly related to the benefit of drugs and accuracy of test results;
- Interviewees often referred to health systems’ poor ability to motivate, inform and support the community in HIV prevention, care and treatment activities.

Nevertheless, findings also showed that community mobilization efforts have had a positive impact in mitigating the effects of tradition and cultural practices that hinder care seeking and follow up.

Conclusions: PMTCT represents an important opportunity to engage women and their families in HIV prevention and treatment programs. Community insights around HIV/AIDS should be incorporated into the processes of rethinking and implementing policies and guidelines to improve outreach services and care for HIV-infected women and their households. Such activities include continuous health education and counseling, male involvement and the involvement of influential community leaders and stakeholders. Loss to follow up should be addressed taking into consideration structural, social and cultural factors, and should largely benefit from community participation, positively supported by health systems.

Abstract: A_44

Implementation research on PMTCT and pediatric treatment programs

Strengthening paediatric HIV test in rural health facilities in north east Nigeria

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1Management Sciences for Health, Nigeria.

Background: The MSH ProACT (Management Sciences for Health-Prevention Organizational Systems Strengthening and AIDS CARE) project - a USAID funded project providing treatment, care and support to HIV/AIDS. Paediatric HIV testing for exposed infants delivered by HIV infected mothers on HAART (highly active anti-retroviral therapy) during pregnancy and breastfeeding in the rural communities in North East Nigeria. The issue has been the transportation of DBS (dry blood spot) samples from health facilities in rural communities to the PCR laboratories which resulted to prolonged turnaround time of Paediatric HIV test results, delayed enrollment of HIV infected children into treatment and care. Mothers and healthcare providers reluctant to embrace the service as most samples collected are not sent to the PCR laboratory in good time and results of sent samples are not returned to facility within the expected TAT (turnaround time). The objective of this study is to appraise the performance of USG PEPFAR supported sites in North East Nigeria service delivery points to babies of HIV Mothers and develop strategy to address needs in a rural community.

Methods: Early infant diagnosis of exposed infant using the dry Blood Spot (DBS) for PCR (polymerase chain reaction) antigen technology for detection of HIV antigens in babies born to HIV infected mothers. Exposed infants delivered in health facilities are tested for 1st DBS from the delivery date to 6weeks of immunization and followed-up with 2nd testing at least 6weeks of weaning. During a program audit, it was discovered that 20 mothers presented their babies for Paediatric HIV testing in the facilities, only 5(25%) of them had their results in 3 months before the intervention due to delay turnaround time and uncoordinated samples transportation systems by facilities. DBS Samples collected from 5 different facilities were transported to PCR
laboratory for analysis and results expected with a TAT of 4-6 weeks. The following steps were taken: 1. Integrating DBS samples with other HIV sample logging transportation. 2. Integration of DBS sample transportation with Project Site support visits (3). Electronic transmission of results from central laboratory to facility by SMS printer.

**Result:** This resulted to 30 exposed infants being tested compared to 20 before the intervention which is an increase of 150% for HIV testing while 5 infants (25%) received result before the intervention and 24 infants (80%) received their results in these 5 different facilities in 3 months of intervention at the expected turnaround time, hence HIV positive babies were enrolled into lifesaving treatment in good time.

**Recommendation:** The increase by 150% in number of children being tested and returned test result rose from 25% to 80% emphasis the need for more commitment, increased collaboration to support HIV paediatric testing for effective care and lifesaving treatment of infected HIV Children and monitor the progress of PMTCT in exposed infants whose mothers received HAART during pregnancy. Health facilities in the rural communities should not be left alone to collect and transport DBS samples until the system is strengthened.

No conflict of interest

**Abstract: A_45**

**New technologies for diagnosis of HIV or co-infections**

**A Point of Care Early Infant HIV-1 Diagnostic Assay using the LiatTM Assay**

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**Introduction:** Early identification of HIV infection in infants is crucial so that prophylactic antiretrovirals (ARV) can be stopped to reduce the development of resistance and therapeutic ARVs can be initiated quickly. Ideally, this would be performed as a point of care assay to prevent delays in obtaining results, loss to follow-up, or early mortality. To address this need, the Liat™ Whole Blood HIV Assay (IQuum, Marlborough, MA), which targets HIV RNA and DNA in whole blood samples, is under development.

**Methods:** Samples being tested for HIV RNA in infected ARV-treated adults (n=30) or for HIV DNA in HIV-exposed infants (n=10) were tested in the Liat system. A 25ul sample of whole blood was placed into the Liat assay tube which was loaded onto the Liat Analyzer, which automatically performs all sample preparation, amplification and detection steps. The assay took 55 min from whole blood sample to viral load (VL) result. Liat results using 0.025mL of whole blood for adults were compared with HIV-1 RNA results obtained from the Abbott RealTime m2000 assay using 0.6 mL plasma, and for infants with the Roche HIV-1 DNA assay, version 1.5 using 0.2 mL whole blood.

**Results:** All infants had non-reactive HIV DNA and negative Liat results (100% specificity). Among the 30 HIV infected adults, 14 had Abbott undetectable HIV RNA, 8 had detectable Abbott VLs < 40 cp/ml, and only 8 had Abbott quantifiable VLs. In contrast, only 4 of the 27 adults had Liat undetectable results and all 4 were also Abbott undetectable. The remaining 26 samples were all Liat detectable. For the 18 adults with Abbott undetectable or <40 RNA cp/ml, Liat results were in the range from 2.61-4.03 HIV RNA/DNA log_{10} cp/ml. Of the 8 specimens with quantifiable VLs in both assays, correlation was fair. Four specimens with Abbott VLs of 4.19-5.34 log_{10} RNA cp/ml had Liat results that differed by less than -0.3 log_{10} RNA/DNA cp/ml (Liat-Abbott). However, 4 specimens with Abbott VLs of 3.5 log_{10} RNA cp/ml or less demonstrated differences of 0.84-1.42 log_{10} RNA/DNA cp/ml.

**Conclusions:** More samples are currently being tested, but this preliminary evaluation suggests that the Liat Whole Blood HIV assay might be suitable for infant diagnosis of HIV. Qualitatively, the assay was both very specific and sensitive in samples tested to date. This is important as virtually all infants, even in resource limited settings, receive ARVs as infant prophylaxis or via breast milk of mothers who are being treated. These drugs have the potential to lower an infected infant’s VL so very sensitive assays are required. Due to its
ease of use and requirement for only 25ul of whole blood, the assay could be performed from a heel stick sample. Quantitatively, the RNA/DNA cp/mL in a whole blood sample is significantly higher than that in the plasma for VL <4 log cp/ml, which may be due to the detection of intracellular HIV RNA and HIV DNA. As such, the clinical utility of VL from whole blood sample needs to be further established.

No conflict of interest
3rd International Workshop on HIV Pediatrics
15 – 16 July 2011, Rome, Italy

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