Risk factors for metabolic abnormality in a European cohort of HIV-infected children and adolescents

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Presented at the 2nd International Workshop on HIV Pediatrics
16-17 July 2010, Vienna Austria
• Increasing coverage of ART in HIV-infected children (WHO), with survival to adulthood in vertically-infected individuals
• HIV-infected children are increasingly exposed to ART at younger ages and for longer durations
• The impact of exposure to ART during key growth periods and of increasing cumulative exposure to different regimens remains unclear
• Metabolic abnormalities and body fat redistribution are well recognised as being associated with ART in HIV-infected adults
• Relatively few large studies have looked at lipodystrophy syndrome in children and adolescents
• *European Paediatric HIV Lipodystrophy Study* recruits children across 14 clinical sites
  - Paediatric HIV centres participating in the *European Collaborative Study* (Belgium and Poland)
  - *Italian Register of HIV Infection in Children* (Italy)
• Inclusion criteria: aged 2-18 years at recruitment
• Exclusion criteria: children on corticosteroid treatment
• Data collected included socio-demographics, anthropometric measures, drug regimens, markers of HIV infection and progression, metabolic profile, and body fat redistribution
• Prospective data collection
• Current analysis: cross-sectional data collected at enrolment
• Statistical analyses conducted using STATA version 10
LIPODYSTROPHY SYNDROME

BODY FAT CHANGES

METABOLIC CHANGES

Hypertriglyceridemia

Age/Gender defined

Hypercholesterolemia

Glucose intolerance

Definitions

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Objectives

• Describe the demographic, clinical and treatment characteristics of the study population

• Estimate the point prevalence of key metabolic outcomes (hypercholesterolemia and hypertriglyceridemia)

• Identification of potential risk factors for adverse metabolic outcomes, including specific ART drugs
Results: Socio-demographic characteristics

- 389 subjects enrolled
- 46% male
- Ethnicity:
  - 69% White
  - 27% Black
  - 4% “Other”
- Median age - 12.1 years (IQR; 9.0, 14.9 years)
- Tanner Staging
  - 25% Stage V
  - 37% Stage I
- Hepatitis C co-infection in 7%
- Most subjects (95%) were vertically infected with 2% infected through blood products
Results: Clinical characteristics

Nadir clinical status
- B: 35%
- C: 22%
- N+A: 43%

Nadir immuno-suppression
- Severe: 30%
- Moderate: 36%
- None: 34%

Clinical status at recruitment
- B: 5%
- C: 3%
- N+A: 92%

Immuo-suppression at recruitment
- Severe: 7%
- Moderate: 18%
- None: 75%
• All subjects were on ART at recruitment
• Median age at first exposure to ART
  – 2.8 years (IQR: 0.83, 6.10)
• Median duration of ART use
  – 8.4 years (IQR: 5.4, 10.7)
• Detectable viral load (HIV RNA > 50 copies/ml) in 38% subjects
Results: Drugs characteristics 2

Proportion of study population exposed to specific classes of ART

- NRTI: 50% (n = 193)
- NNRTI: 28% (n = 108)

Class of drug

Percentage of participants

Current-use

Ever-use

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Results: Drugs characteristics 3

Proportion of study population currently taking specific ART at recruitment

Drug:
- Lamivudine
- Kaletra
- Abacavir
- Zidovudine
- Tenofovir
- Efavirenz
- Stavudine
- Nevirapine
- Emtricitabine
- Ritonavir
- Fosamprenavir
- Atazanavir

Percentage of participants:
- 80
- 70
- 60
- 50
- 40
- 30
- 20
- 10
- 0

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Results: Prevalence of lipodystrophy outcomes

- No LS symptoms: 170
- Metabolic abnormality only: 53
- Fat redistribution and Metabolic abnormality: 63
- Fat redistribution only: 98

Metabolic abnormality: 31% (95% CI: 26, 35)
Lipodystrophy syndrome: 57% (95% CI: 52, 62)
Fat redistribution: 42% (95% CI: 37, 45)

n = 384

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Results: Prevalence of metabolic outcomes

- **Hypertriglyceridemia**
  - 24% (95% CI: 20, 29)

- **Hypercholesterolemia**
  - 13% (95% CI: 9, 16)

- **Glucose non-tolerance**
  - 1% (95% CI: 0, 2)
Results: Risk factor analysis 1

- Logistic regression models for several outcomes
  - Any metabolic changes
  - Any hypercholesterolemia
  - Any hypertriglyceridemia
  - Both hypercholesterolemia and hypertriglyceridemia
- Saturated model contained all covariates
- Backward and forward covariate selection
- Final optimal model contained covariates significant to ≤ 5%
- All models adjusted for age at recruitment and duration of drug exposure, with a random effect for clinical site
### Results: Risk factor analysis 2: AOR(95% CI)

<table>
<thead>
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*All models adjust for age and duration of drug use

*All models contain a random effect for clinical site

$p \leq 0.05$

*$p < 0.001$
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*p < 0.001*
Conclusions

• The prevalence of metabolic abnormality was 31%
  • 4 in 5 of these children had hypertriglyceridemia
  • 2 in 5 of these children had hypercholesterolemia
• Current use of protease inhibitors was a consistent risk factor for all metabolic abnormality outcomes
• Children on ritonavir and ritonavir-boosted PI regimens may warrant increased surveillance but atazanavir may be associated with better metabolic status
• Increasing need to investigate lipodystrophy syndrome as ART becomes more available to HIV-infected children, since the metabolic abnormalities may be important in the early stages of development of cardiovascular disease
We would like to thank the children and their families for participating in this study

- **United Kingdom**: C. Thorne, M Cortina Borja
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- **Belgium**: T Goetghebuer, J Levy, M Hainaut, B Brichard, J De Camps, N Thiry, G Deboone, H Waterloos, V Schnitz

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