Cervical cancer prevention and screening in Africa

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Epidemiology of HPV and cervical cancer

- Global burden of cervical cancer is ~500,000 cases, with > 270,000 deaths annually\(^1\)
- In Kenya ~ 2,400 women die every year from cervical cancer\(^2\)
- ~99.7\% of cervical cancers are attributable to HPV\(^3\)
- Up to 80\% of women acquire HPV infection in their lifetime\(^4\)
- Among the 15 oncogenic types, HPV 16, 18, 45 and 31 most commonly associated with cervical cancer, including cervical adenocarcinoma, worldwide\(^5,6\)

1. Globocan 2000  
2. Globocan 2002  
The most frequent cancers in women: incidence and mortality

Africa

**Incidence**
- Cervix: 29.3
- Breast: 23.4
- Liver: 6.2
- Stomach: 4.9
- Kaposi’s sarcoma: 4.6
- Ovary: 4.3
- Colon/Rectum: 4.2

**Mortality**
- Cervix: 23.1
- Breast: 16.2
- Liver: 6.2
- Stomach: 4.6
- Kaposi’s sarcoma: 4.3
- Colon/Rectum: 3.7
- Oesophagus: 3.2

Factors that increase risk of progression to cervical cancer

• Persistent infection with oncogenic HPV is the necessary cause of cervical squamous cell cancer
  – About 70% of cervical cancers worldwide associated with HPV types 16 and 18
  – HPV types 16 and 18 persist for longer than low-risk HPV types

• Co-factors
  – Environmental, e.g. smoking
  – Sexual exposure, e.g. parity, multiple partners, early onset of sex
  – Hormonal, e.g. long-term use of oral contraceptives
  – Immunosuppressive, e.g. HIV, long-term systemic steroid use
  – Genetics e.g. HLA gene polymorphism

• HIV and HPV have high prevalence in the same populations

HIV/AIDS

• After 3 decades, HIV now a generalized epidemic
• About 33.3m people living with HIV globally, >50% women 15 y and older
• More than two thirds live in sub-Saharan Africa
• Kenya, 1.1 -1.5m people living with HIV
• Declining from >10% in late 1990s to 7% by 2008

1. UNAIDS 2006  2. UNAIDS/WHO 2008
HIV, HPV and Cervical Neoplasia

• Cervical cancer included as an AIDS-defining illness in 1993 (CDC)
• HIV & Cancer registry linkages increased risk of cervical neoplasia in HIV infected women\(^1,\,2,\,3\); Variable results in Africa\(^3,\,4,\,5\)
• HIV-associated immunosuppression increases risk, promotes reactivation, permits HPV persistence\(^6,\,7\)
• CIN occurs earlier, progresses faster, does not regress even after HAART\(^7,\,8\)

CORRELATION BETWEEN HUMAN IMMUNODEFICIENCY VIRUS AND HUMAN PAPILLOMAVIRUS CO-INFECTION ON CERVICAL NEOPLASIA IN A SEMI-URBAN POPULATION IN TIGONI

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Justification

• Cervical cancer, attributable to human papillomavirus (HPV), is a common cause of death among women

• Immunosuppression due to HIV infection increases the risk of HPV-associated neoplasia and accelerated progression to invasive carcinoma

• Local data on both HPV and HIV scanty

• Screening of HIV and HPV, & early intervention important health strategies
Main objective:
To determine the correlation between HIV and HPV co-infection and cervical neoplasia in a semi-urban population in Tigoni, Kenya.
Materials & methods

• **Study Site**: Tigoni District Hospital, Limuru Division, Kiambu West District (2004-2007)
• **Study Designs**: cross-sectional survey
• **Population**: Women 25-60 years invited for HIV & cervical cancer screening
• **Sample size**: About 6,000 women (25-60y) eligible for screening (1999 Pop census), out of which 4,500 were recruited. A total of 4,363 women had both a HIV test and a satisfactory pap smear.
• A subset, 438 women had HPV results
Data Collection & Analysis

- Pre-tested questionnaire to collect socio-demographic, sexual & reproductive health, life-style data
- HIV Voluntary pre- and post-test counseling
- HIV testing by ELISA, +ve confirmed by 2\textsuperscript{nd} ELISA
- Pap smear by liquid based
- HPV testing on residual sample by RT-PCR in Antwerp
RESULTS

• HIV prevalence was 14.3% (national prevalence 8.7% in 2007\textsuperscript{1} with reported declining figures, urban, peri-urban & rural areas\textsuperscript{1,2})

• For 96.1% women, study provided first ever pap smear

• Abnormal pap result (ASCUS or greater) – 8.6%

• About 25.5% HIV+ women had a cervical lesion, compared to 5.7% in HIV-ve

• Among those who had a cervical lesion, 42.3% were HIV positive

HIV co-infection on the HPV genotype distribution & cervical neoplasia

• Out of 438 samples, 32.7% were positive for single or multiple HPV infections (prevalence reported highest among women in East Africa 31.6%\(^1\))

• Significant factors for HPV infection: age, number of lifetime sex partners, HIV infection, CD4 counts (for HIV+ women); oral contraceptive use

1. Bosch et al 2006
HPV prevalence and risk by HIV status among women in Tigoni (n=438)

<table>
<thead>
<tr>
<th>HPV</th>
<th>HIV STATUS</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Population (n=438)</td>
<td>Sero-negative (n=324)</td>
</tr>
<tr>
<td>Status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- negative</td>
<td>298(68.0)</td>
<td>261(80.6)</td>
</tr>
<tr>
<td>- positive</td>
<td><strong>140(32.0)</strong></td>
<td>63(19.4)</td>
</tr>
<tr>
<td>Oncogenic risk type</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- High</td>
<td>91(20.8)</td>
<td>48(14.8)</td>
</tr>
<tr>
<td>- Intermediate</td>
<td>44(10.0)</td>
<td>14(4.3)</td>
</tr>
<tr>
<td>- Low</td>
<td>5(1.1)</td>
<td>1(0.3)</td>
</tr>
</tbody>
</table>
Type 16 common in all diagnostic categories, highest in HSIL
Epidemiologic HR-HPV include 16,18, 31,33, 35, 39, 45, 51, 52, 56, 58, 59
(Munoz et al, 2003)
Comparison of HPV infection & abnormal cytology in HIV sero-positive and sero-negative women versus CD4 counts (cells/µl)

Discussion

- HIV prevalence in this female peri-urban was high, 14.3%, compared to declining national HIV prevalence currently at about 8%; reasons uncertain
- CIN prevalence was high, 8.6%; 25.5% in women who were HIV+, 5.7% in those who were HIV- (not unexpected findings)
Discussion cont´d

• High HPV prevalence, 32.7% in a population with high HIV prevalence consistent with IARC studies.

• Abnormal smears associated with HPV prevalence 52% (50-85%\(^1\)).

• HPV 16 most prevalent, type 18 frequent elsewhere had a low prevalence of 2.9%.

1. Bosch 2006
Conclusion

• HIV and cervical neoplasia are both highly prevalent in the peri-urban female population in Tigoni
• HIV is a major risk factor for HPV infection and cervical neoplasia
• HPV types found in study pop vary slightly from other geographical regions
Overall policy implications of study findings

1. High prevalence of HIV & HPV-related cervical neoplasia in this peri-urban population – need for a public health strategies for prevention, including HPV vaccination

2. Continuing basic & epidemiological research – relevance of current & appropriate future generations of HPV vaccines
Cervical Cancer Screening of Women Living with HIV-1: in the era of HAART

- Increased survival with HAART
- Increased risk for HR HPV infection for women living with HIV/AIDS
  - Increased progression to CIN-2/3 and invasive cancer
  - Increased disease recurrence post treatment for pre-malignant lesions
  - HAART has not reduced prevalence of cervical cancer

The Kenya Situation - Screening

• Currently over 100 sites are regularly screening across the country
• Screening Methods: cytology- pap smear, VIA/VILI
• HPV testing – mainly in research and private sector
Kenya situation - Treatment

- Treatment of dysplasia available in only 30% of screening sites
- Hence in many cases patients with dysplasia are over treated or not treated at all (e.g. TAH for CIN I!!)
- About 100 sites now offer cryotherapy equipment for treatment of dysplasia
Overview of the National Cervical Cancer Strategic Plan 2011 -2015
NCCPP 2011-2015

Vision

Kenyan women free from cervical cancer

Goal:

• To reduce incidence, prevalence, morbidity and mortality from cervical cancer and improve quality of life of cervical cancer patients in accordance to the Health policy framework, the National RH policy and National RH strategy.
Objectives:

• To create an enabling environment for expansion of the National Cervical Cancer Program
• To create demand for cervical cancer prevention and control services.
• To provide high quality cervical cancer prevention and treatment services.
• To strengthen referral system for the cervical cancer program (linkages)
Components of cervical cancer control

- Primary prevention
- Early detection / screening
- Diagnosis and treatment
- Palliative care
Primary prevention strategies

- The following Primary prevention strategies are advocated for use in Kenya
  - Promote Abstinence or delayed sexual debut for adolescents (A)
  - Promote faithfulness to one partner for those in relationships, (B)
  - Promote Condom use - C
  - Promote HPV Vaccination
  - Promote male circumcision
PREVENTION: Will sub-Saharan Africa Realize the Promise of HPV Vaccination?

• Rwanda leading the way
  – School based programs
  – Think about the hard to reach & out of school girls
    • High risk for cervical cancer and likely to miss out
  – Data on efficacy among HIV-1 infected children

• Acceptability Studies
  – Over 90% among school programs
HPV Vaccination in Kenya

• Introduction of HPV vaccine for girls between 9-13 years
• Kenya GAVI eligible like many sub-Saharan African countries
• Request in by 2013
• Revision of National Immunization manual including HPV
Potential impact of the HPV 16/18 candidate vaccine

Potential reduction:
- ICC: 67–71%
- HSIL: 52–60%
- LSIL: 14–25%
- ASCUS: ~20%

ASCUS = atypical squamous cells of undetermined significance;
ICC = invasive cervical cancer; L/HSIL: low/high-grade squamous intraepithelial lesion

Screening Approaches

• The following screening approaches are recommended for public health use in Kenya
  – VIA/VILI,
  – Pap smear cytology
  – HPV testing

• Other screening approaches may be used for research or teaching purposes
Target Population

For screening to be cost effective, women in the high-risk age group have to be targeted.

- The recommended target group is women 25-49 years
- (Women outside this group who wish for screening or for whom screening is advisable will not be denied services)
- The recommended screening interval is 5 years for HIV negative women
Entry Points for screening

- Cervical Cancer Screening will be provided as an Integrated service at all KEPH levels.
- The recommended initial entry points for cervical cancer screening are:
  - the MCH/FP clinics,
  - the Comprehensive Care Clinics and
  - the Gynecology clinic.
- Cervical cancer screening will also be integrated into other RH outreach activities e.g. during integrated RH/FP camps, and campaigns in order to reach more women especially in hard to reach areas.
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MINISTRY OF HEALTH
Treatment of Pre-cancer

- The following are the recommended treatment strategies for precancerous lesions for the Kenya program:
  - Cryotherapy
  - Loop Electrosurgical Excision Procedure (LEEP)
  - Cold knife Conization
Treatment approaches

- The specific treatment of precancerous lesions will depend on the severity, size, and location of the lesion.
- The program recommends availability of cryotherapy from KEPH level 3.
- The programme recommends availability of LEEP at level 5 and above.
- As far as possible the Single Visit Approach should be employed.
Providers of treatment services

• It is recommended that Cryotherapy at district hospitals and below be done by appropriately trained non-physicians (nurses, Clinical Officers & doctors) provided they are competent in the procedure.
Data management

- A basic set of standardised data tools will be introduced to facilitate data management. These include:
  - Cervical cancer screening form
  - A daily register
  - A monthly summary tool
  - A data use poster
  - A support supervision tool
- Key indicators will also be incorporated into the routine HIS data capturing tools i.e. Mother Child booklet and the Longitudinal registers.
A team approach to cervical cancer prevention and control

- Cervical cancer control requires a multi-sectoral and multidisciplinary effort.
- It also requires strong linkages and teamwork between providers at all levels of the health care system.
Conclusion

- Cervical Cancer is a major public health concern in Kenya due to its prevalence, morbidity and mortality
- Overt cancer is expensive to treat
- Investing in cervical cancer prevention and control saves lives, improves the quality of the woman’s life and is cost saving to the country
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