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Our Issues, Our Drugs, Our Patients

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PREVALENCE OF ANAL DYSPLASIA IN HIV-INFECTED WOMEN IN JOHANNESBURG, SOUTH AFRICA

DR. BRIDGETTE GOEIEMAN
Incidence of anal cancer is **40-80x higher in HIV + population**

Most HIV-infected individuals live in sub-Saharan Africa, but prevalence of anal disease is unknown

ART use has shown little effect on cervical and anal dysplasia and a high prevalence of persistent infections with oncogenic HPV types despite ART use

Factors implicated in Anal Cancer in HIV+ persons include HPV, sexual habits and smoking

High risk HPV16 and receptive anal intercourse (RAI) increase risk of anal cancer by 33% over the general population

In general population, rate of anal cancer is 0.9 per 100,000

In cases of RAI rate +- 35cases per 100,000

Smokers are 8x more likely to develop anal cancer
METHODS:

Study Design:
• A prospective cohort study of 200 HIV-infected women age 25-65
• Participants recruited from an HIV clinic in Johannesburg, South Africa.
• Women were educated regarding the screening study, signed consent and completed a questionnaire.
• Cervical and Anal swabs were taken for conventional cytology and HPV testing by Digene HC2/Geneprobe) from each woman.
• Women with abnormal anal cytology were seen for high resolution anoscopy (HRA).
• To adjust for verification bias, 20% of women with negative anal cytology had HRA biopsy done for verification of the negative cytological results.
METHODS:

The inclusion criteria
• Documentation of HIV infection
• Able to give consent
• Able to participate in study related procedures.

Exclusion criteria
• Pregnancy
• Clinically active sexually transmitted diseases (defined by clinical symptoms and/or signs)
• Previous hysterectomy with removal of the cervix
• Significant medical/mental illness
High Resonance Anoscopy was performed on all participants with abnormal anal cytology and a confirmatory colposcopic biopsy done.

High resolution anoscopy showing squamocolumnar junction after application of acetic acid
Each HRA was recorded by digital photography for quality assurance and reviewed quarterly by the study team for accuracy of interpretation with an experienced anoscopist.

- Cervical and anal cytology was reported using the Bethesda system

Cytology results were classified as:
- normal,
- atypical squamous cells of uncertain significance (ASCUS)
- low-grade squamous intraepithelial lesion (LSIL)
- high-grade intraepithelial lesions (HSIL) and
- atypical squamous cells of uncertain significance where a high-grade lesion could not be excluded (ACSUS-H)
- squamous-cell carcinoma (SCC).

HRA histology results were classified as:
- normal
- atypia (condyloma),
- LGAIN (AIN 1) and
- HGAIN (AIN 2-3).
STATISTICAL ANALYSIS

• Baseline characteristics, prevalence of anal dysplasia and different grades of dysplasia were summarized using descriptive statistics and were presented with 95% confidence limits.

• For statistical purposes, cytology results were stratified into 4 categories: Negative, ASCUS, LSIL and HSIL (ASCUS-H combined with HSIL).

• Histology results were stratified into 4 categories: Negative for intraepithelial lesion and malignancy (NILM), No biopsy obtained (no lesions observed on HRA, inadequate biopsy taken or lost to follow up), atypia/LGAIN and HGAIN.

• If multiple biopsies were taken, the most severe result was taken as the final diagnosis.

• HRA results were compared to those of anal cytology using Chi square for proportions.
RESULTS:
CONSORT DIAGRAM

N=200

Abnormal
N=150

Referred for HRA
N=150

HRA Not Done
2 Lost to follow up
1 Out of Window
N=3

HRA Done
N=146

Normal
N=50

Referred for HRA Verification
N=7

Biopsy Done
N=7

1 lost to follow up

Not Referred for HRA
N=43

1 lost to follow up

2 Lost to follow up
1 Out of Window
### Table 1 Baseline characteristics of participants

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Median [IQR] or No. (%)</th>
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<tbody>
<tr>
<td>Age</td>
<td>38 [33-44]</td>
</tr>
<tr>
<td>1 or more sex partners in prior 6 months</td>
<td>157 (78%)</td>
</tr>
<tr>
<td>No prior cervical Pap</td>
<td>95 (48%)</td>
</tr>
<tr>
<td>Current tobacco use</td>
<td>5 (2.5%)</td>
</tr>
<tr>
<td>No prior pregnancy</td>
<td>22 (11%)</td>
</tr>
<tr>
<td>Current CD4 count</td>
<td>430 [311-600]</td>
</tr>
<tr>
<td>Nadir CD4 count</td>
<td>158 [74-227]</td>
</tr>
<tr>
<td>Current ART use</td>
<td>193 (97%)</td>
</tr>
<tr>
<td>Length of ART use (years)</td>
<td>3.0 [1.6-5.3]</td>
</tr>
<tr>
<td>Plasma HIV RNA &lt;400 copies/mL</td>
<td>166 (89%)</td>
</tr>
<tr>
<td>History of anal condyloma</td>
<td>13 (6.5%)</td>
</tr>
<tr>
<td>Current anal symptoms (pain, itching or bleeding)</td>
<td>73 (37%)</td>
</tr>
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</table>

None of the women in the study reported a history of receptive anal intercourse and 83% (N=165/199) reported barrier contraception (condoms).
Table 2: Anal HPV versus Anal Cytology

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>ASCUS</th>
<th>LSIL</th>
<th>ASC-H/HSIL</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anal HPV+</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>17 (33%)</td>
<td>11 (34%)</td>
<td>40 (42%)</td>
<td>14 (74%)</td>
<td></td>
<td>82/198 (41%)</td>
</tr>
<tr>
<td><strong>Anal HPV-</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>34 (67%)</td>
<td>21 (66%)</td>
<td>56 (58%)</td>
<td>5 (26%)</td>
<td></td>
<td>116/198 (59%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>51 (100%)</td>
<td>32 (100%)</td>
<td>96 (100%)</td>
<td>19 (100%)</td>
<td>198 (100%)</td>
</tr>
</tbody>
</table>

*Anal cytology and HPV digene results were missing from 1 and 2 participants respectively.
### Table 3: Factors associated with cervical HPV, anal HPV and anal HSIL

<table>
<thead>
<tr>
<th></th>
<th>Anal HSIL N=31/199 (15.6%)</th>
<th>Anal HPV</th>
<th>Cervical HPV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Multivariable</td>
<td>Multivariable</td>
<td>Multivariable</td>
</tr>
<tr>
<td>Age per 10 years</td>
<td>--</td>
<td>0.51 (0.32-0.79)</td>
<td></td>
</tr>
<tr>
<td>CD4 (per 100 cells/mm3)</td>
<td>--</td>
<td></td>
<td>0.67 (0.54-0.81)</td>
</tr>
<tr>
<td>Anal HPV infection</td>
<td>5.1 (2.0-13)</td>
<td></td>
<td>4.4 (2.2-8.6)</td>
</tr>
<tr>
<td>Anal symptoms</td>
<td>2.5 (1.1-5.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cervical HPV infection</td>
<td>--</td>
<td>4.9 (2.5-9.7)</td>
<td></td>
</tr>
</tbody>
</table>
RESULTS:

• Prevalence of abnormal anal cytology was 74% (n= 148/199)

• Prevalence anal HPV positivity was found in 41% (n=82/198)

• High-grade lesion (HSIL) of the High-grade lesion (HSIL) of the anus was confirmed by HGAIN biopsy results in 8.5% of women.

• Concomitant anal and cervical HPV infection was detected in 52/198 (26%)

• A high CD4 count >=500 and a long duration on ART >= 3-5 years were shown to be protective against anal HPV infection and dysplasia.

• The HIV viral load had no effect on anal cytology.

• We found no association between smoking and abnormal anal cytology
CONCLUSION:

• We found significant burden of anal HPV infection and abnormal anal cytology.

• HGAIN has been shown to be very common and on the increase in HIV + women regardless of the absence of traditional risk factors for HPV and sexual practices.

• High grade (SIL) on anal cytology was found in **9.5%** of our women which is **2-4X** higher than studies of men who have sex with men (MSM).

• An important risk factor for anal dysplasia in women is cervical dysplasia and /or poorly controlled HIV.

• A high CD4 count >=500 and a long duration on ART >= 3-5 years were shown to be protective against anal HPV infection and dysplasia.

• We found no association between HIV VL, smoking and abnormal anal cytology
THANK YOU!