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

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Background:

Anal Cancer Statistics in HIV

- 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.
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- 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:

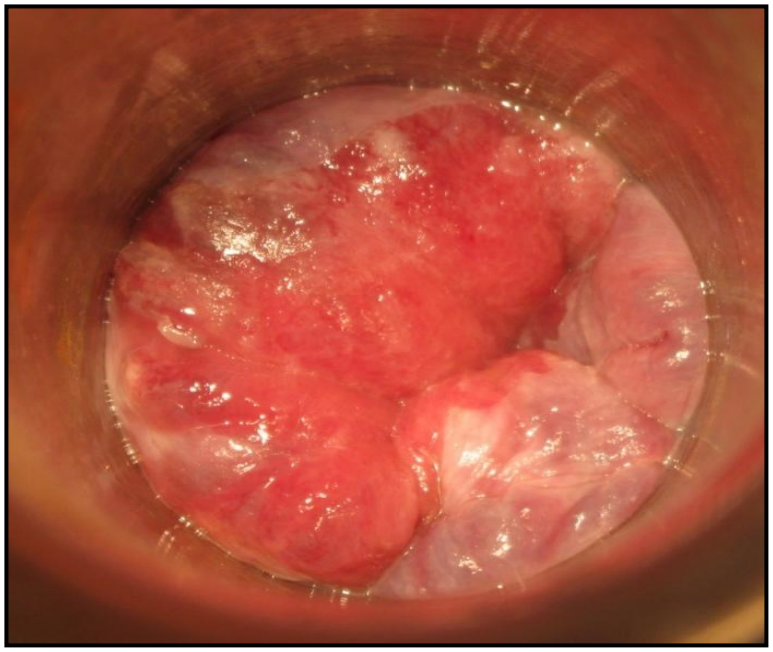
The inclusion criteria

- 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 Anospcopy was performed on all participants with abnormal anal cytology and a confirmatory colopscopic biopsy done.



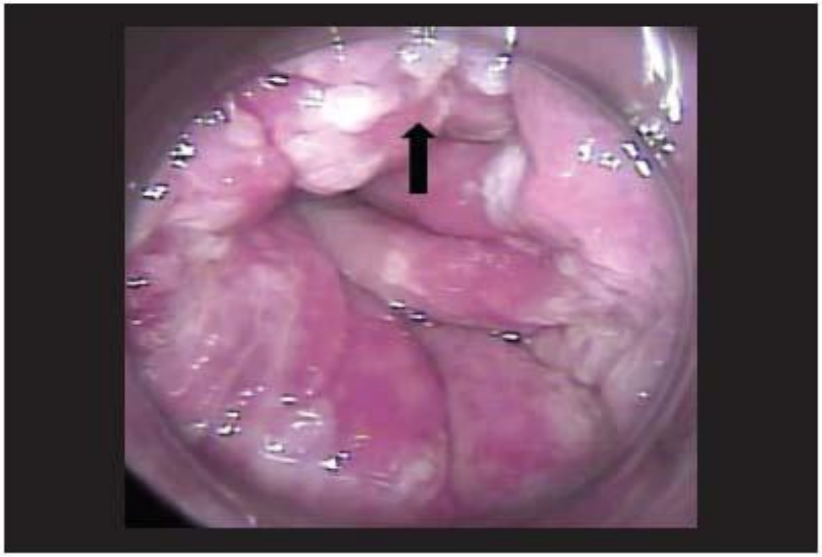


FIGURE 3. Acetowhite lesion, dense, coalescent, slightly elevated, papillary, HPV positive. Histopathology: LSIL

High resolution anoscopy showing squamocolumnar junction after application of acetic acid

Quality Assurance:

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 **c**ytology 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).

STASTITICAL 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

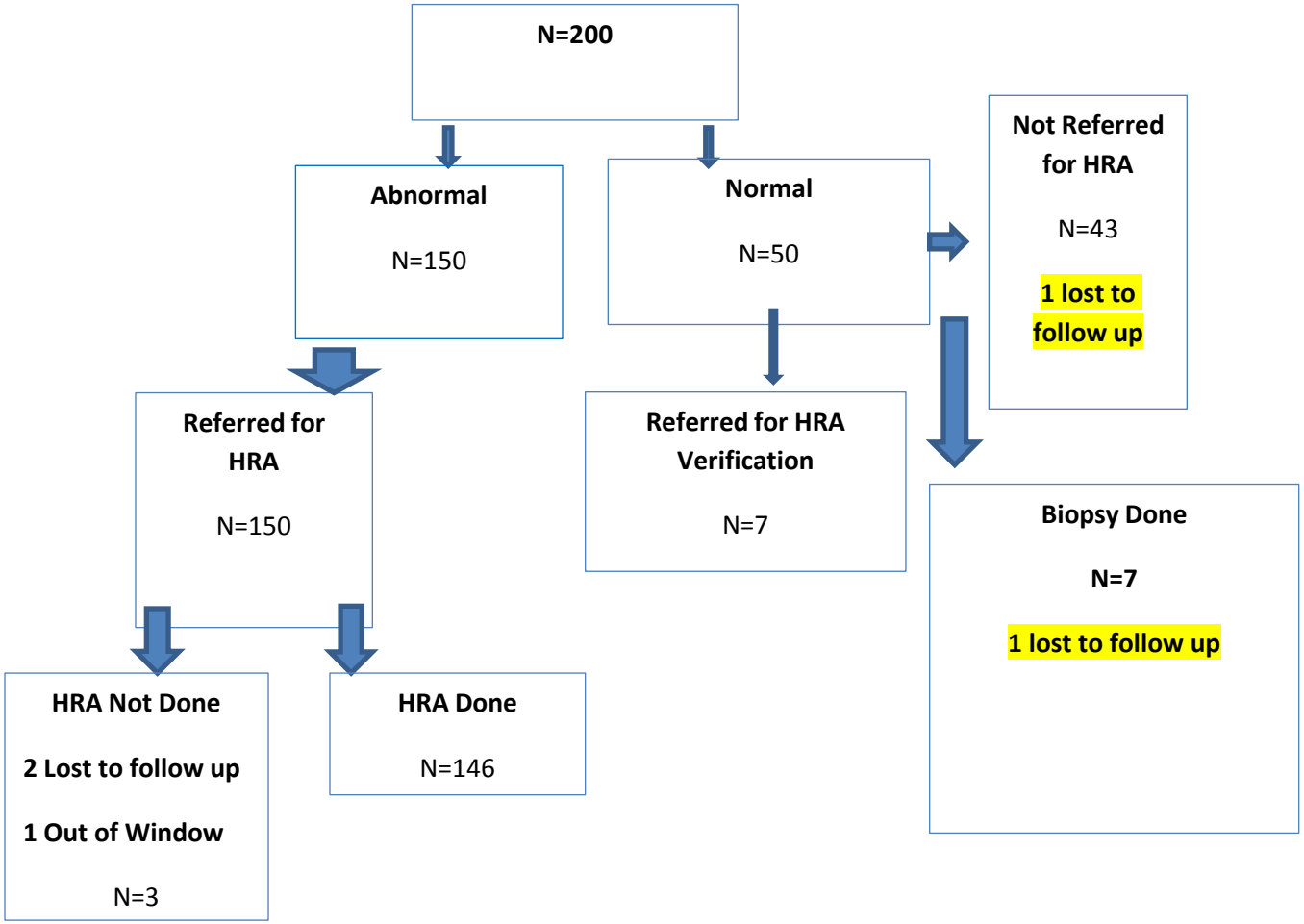


Table 1 Baseline characteristics of participants

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

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

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

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

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

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!