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Colposcopic findings in human immunodeficiency virus positive patients in Port Harcourt

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ABSTRACT

Background: Colposcopy is an outpatient procedure that involves visualization of the cervix, vagina and vulva using a magnifying optical instrument called the colposcope. Human Immunodeficiency Virus infection is associated with increased incidence of cervical malignancies which can be detected by colposcopy.

Objective: To determine prevalence of premalignant and malignant lesions of the cervix using colposcopic assessment among HIV positive women at the University of Port Harcourt Teaching Hospital (UPTH), Alakahia between June 2015 and August 2015.

Materials and Methods: One hundred HIV positive women were recruited by simple random sampling (by balloting) with an uptake rate of 97%. Informed consent was obtained from each individual and data was collected using a semi-structured interviewer administered questionnaire. They all had colposcopic examination. Data analysis was done using SPSS. Ethical approval was obtained from the hospital's ethical committee before the research was commenced.

Results: Ninety seven out of one hundred subjects had satisfactory colposcopy. The prevalence of premalignant lesions from colposcopy was 53.6%. The mean age respondents; 37.44 ±7.20 years, mean age for premalignant lesions; 37.73 ±7.49 years.The age range was 21-56 years.

Thirty-four (35.4%) had coitarche before eighteen years of age, fifty-five (57.3%) had it after the age of eighteen, seven (7.3%) had no idea. Majority (68.8%) have had two or more sexual partners in their lifetime. The mean CD_4 count was 543.77cells/mm^3.

Conclusion: There was high prevalence of premalignant lesions among the HIV positive women. This indicates that a routinely scheduled colposcopic examination of the cervix, together with directed may aid early detection and treatment of the lesions, which will further decrease the incidence of cervical cancer among this population.

1. Introduction

Colposcopy involves examination of the cervix, vagina and vulva using magnifying optical instrument called the colposcope. A colposcope works on the hypothesis that by magnifying the cervix and applying good illumination, early stages of cervical cancer can be detected.[1] Following its introduction in Germany by Hans Hinselmann in 1925, Schiller introduced the concept of applying iodine in 1929, and this was based on the fact that the non-glycogen

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containing areas on the cervix do not stain and these are the abnormal areas suspected to be carrying the early cervical cancer.[2–5] The instrument gives stereoscopic magnification from 6 to 40 times.[5]

Cervical cancer is regarded as a sexually transmitted disease due to its association with the highly oncogenic sexually transmitted Human Papilloma Virus (HPV), which is the known causative agent in about 99.7% of cases.[6–8] HIV infection has been associated with increased risk of CIN and invasive cancer of the cervix as a result of immunosuppression and opportunistic infection with oncogenic strains of HPV.[9–12] This has further been strengthened by the inverse relationship between $CD4^+$ count and the prevalence of neoplastic lesions of the cervix, as well as the direct relationship between viral load and the disease. There is high prevalence of HPV infection among HIV-positive women with high viral load and low $CD4^+$ count.[13–15]

Cervical cancer is a highly preventable disease due to its long premalignant phase as progression to cervical cancer usually takes about 10-15 years.[16] This further necessitates effective screening for early detection and prompt treatment of the disease.

The screening modalities for cervical cancer include; cytology which could be conventional, using the Pap smear or liquid based, visual inspection of the cervix after application of Lugol's iodine or 3-5% acetic acid (VILI or VIA respectively), HPV testing and colposcopy.[6] The primary screening technique is the Pap smear and those found to be abnormal are referred for HPV testing and colposcopy however, in areas where Pap smear screening is not feasible, VILI or VIA is done as the primary test.[1,2,17]

Colposcopy is an outpatient procedure requiring no anaesthesia.[18] When abnormal areas are detected, a colposcopically directed biopsy is taken for histological confirmation of diagnosis.[19] Unlike the Pap smear which scrapes tissues from the entire cervix, colposcopy allows the examiner to take biopsies from specific areas that look abnormal.[20] It is however said to be unsatisfactory when the squamocolumnar junction cannot be visualized, and in such cases, an endocervical curettage is done for histology.[21]

Immunosupression as in HIV infection is one of the indications for immediate colposcopy following any form of abnormal cytology report, and this may be attributed to the rapid progression of premalignant lesions in women with HIV.[18,22]

Colposcopic evaluation and guided biopsy remains a critical diagnostic step for women with cervical neoplasia and it also gives the opportunity to offer immediate treatment where necessary.[19] Visualization of the transformation zone is the most crucial step in colposcopy, since majority (about 90%) of cervical dysplasias arise from this area.[2,23,24] The normal colposcopic findings include the original squamous epithelium, the transformation zone and the columnar epithelium of the endocervical canal. The abnormal findings include leukoplakia or hyperkeratosis, acetowhite epithelium, mosaicism or punctuation, and atypical vessels.[1] The colposcopic findings can be graded using the Reid colposcopic index[25,26] or the international normenclature for colposcopy.[27,28] The international federation of cervical pathology and colposcopy in 2002, classified colposcopic findings into three groups; those suggestive of low grade disease which corresponds to CIN 1/LGSIL, those suggestive of high grade disease corresponding to CIN 2 and CIN 3 and those suggestive of invasive disease. The indications for colposcopy include; abnormal cytology, positive HPV testing, suspicious-looking or clinically abnormal cervix, unexplained intermenstrual or postcoital bleeding among others.[1] Before the procedure, the patient is adequately counseled and consent obtained. Sexual intercourse, vaginal medications/instrumentations, douching and use of tampons should be avoided at least for 24 hours, as these may cause irritation and subsequently affect the interpretation of the result.[29] The procedure may be complicated by vaginal bleeding (if biopsy is done). Although colposcopy is said to be safe in pregnancy, directed biopsies are not encouraged as this may be complicated by torrential bleeding. This is because the pregnant cervix is highly vascularized.[30]

This study was conducted to examine the cervix and determine the prevalence of cervical lesions among HIV positive patients receiving care at University of Port Harcourt Teaching Hospital, Port Harcourt using colposcopy. This was important because it could serve as a direct screening method rather than cytology before referral for colposcopy among this population.

2. Materials and Methods

This was a cross-sectional study conducted at the oncology unit of the Department of Obstetrics and Gynaecology of University of Port Harcourt Teaching Hospital (UPTH) between June 2015 and August 2015.

The sample size was calculated using the formula, $(N= Z^2 P(1-P)/ d^2)$[31] where, N- Sample size, Z- Proportion of normal distribution corresponding to the required significance level (5%) which is 1.96,P- Prevalence of abnormal cervical smears among HIV-positive women in University of Port Harcourt Teaching Hospital from a previous study (0.344)[32] and d- Margin of error (0.1).

Thus, $n= 1.96^2 \times 0.34 (1-0.34)/ 0.1^2 = 0.862/0.01= 86.2$. An attrition rate of 10% (8.6) was added to the minimum sample size of 86.2, giving a total of 94.8. This was approximated to 100.

One hundred HIV-positive women attending the Sexually Transmitted Disease (STD)/infectious disease clinic who fulfilled the eligibility criteria (women who are HIV-positive receiving care at UPTH, those that have not had sexual intercourse or douching in the preceeding 24 hours,

those who gave consent) were recruited by simple random sampling (through balloting) after adequate counselling. Informed consent was obtained from each of them, and they were then referred to the oncology unit of the department of obstetrics and gynaecology for the study.

The procedure was again explained to each patient and a written consent obtained. A detailed history was obtained using a pre-structured interviewer administered questionnaire and vital information such as biodata, history of present illness, past medical history, menstrual history, family and social history, husband's HIV status, socioeconomic status, previous sexual relationship, current medications (if on HAART) and duration, and latest $CD4^+$ count (done in the last three months and documented in their case notes) were entered.

The video colposcope, SLV-101, class 1, Type B, 2010 manufactured by Medelkom Ltd, Graiciuno, Europe, attached to a 17.0" LCD monitor was used and it was positioned at a distance of about 25cm from the patient. It was focused on the cervix which was viewed with the white light and then the green light to assess the vascular pattern. A cotton ball on a sponge holding forceps was then soaked in freshly prepared 5% acetic acid solution and the cervix viewed on the screen for the presence of aceto white changes. The same procedure was repeated but with cotton ball soaked in Lugol's iodine solution which differentiated the dark- brown staining glycogen-filled cells (normal, iodine positive) from the paler glycogen-free areas (abnormal, iodine negative). Pictures were taken after each procedure and colposcopic grading was done using the modified Reid's colposcopic index. Two of the patients among those with suspected high grade lesions had cervical biopsy and the specimens were processed by the histotechnologist and reported by the histopathologist. Data analysis was done using SPSS. Ethical approval was obtained from the hospital's ethical committee before the research was commenced.

3. Results

Out of one hundred patients that were recruited, three had unsatisfactory colposcopy leaving a total number of ninety-seven. The prevalence of premalignant lesions from colposcopy was 53.6%. The mean age of patients was 37.44 ±7.20 years and the mean age of those with premalignant lesions was 37.73 ±7.49 years. The age range of the patients was 21-56 years with the highest number of respondents (27.1%) in the 30-34 years group. This was closely followed by 35-39 years with 26.0%. Majority of the patients (49.0%) were married and the others were either single, divorced or widowed. Most of the patients had at least secondary education (38.5% and 37.5% for tertiary and secondary levels of education respectively). The parous women were more than the nulliparous women (62.5% and 37.5% for the parous and nulliparous women respectively). These are shown on Table 1.

Thirty-four (35.4%) of the respondents had their first sexual intercourse before eighteen years of age while fifty-five (57.3%) had it after the age of eighteen, however seven (7.3%) had no idea of their age at first sexual exposure.

Majority of the women have had more than one sexual partners in their lifetime; nineteen (19.8%) of them have had five and above while sixty-six (68.8%) have had two to four sexual partners. Only six (6.2%) have had one sexual partner in their lifetime, however five (5.2%) did not respond. These frequencies are shown in Table 2.

Seventeen (17.7%) of the respondents had CD4 counts less than 250 cells/mm^3, thirty (31.3%) had values between 250 to 499 cells/mm^3while forty-nine (51.0%) had 500 cells/mm^3 and above.

Table 1: Socio-demographic characteristics of the patients (N=97)

Variable	N	Percentage (%)
Age(years)		
20-24	1	1.0
25-29	11	11.3
30-34	26	26.8
35-39	25	25.8
40-44	21	21.7
45-49	7	7.2
>50	6	6.2
Marital Status		
Single	28	28.9
Married	48	49.5
Divorced	5	5.1
Widowed	16	16.5
Educational level		
None	3	3.1
Primary	21	21.7
Secondary	36	37.1
Tertiary	37	38.1
Parity		
0	36	37.5
1-4	51	53.1
≥ 5	10	9.4

Table 2: Sexual characteristics of the patients (N=97)

Variable	N	Percentage (%)
Coitarche		
< 18 years	35	35.4
≥ 18 years	55	57.3
Not specified*	7	7.3
Number of sexual partners**		
1	6	6.2
2-4	67	69.1
≥ 5	19	19.5
Not specified*	5	5.2

*Value not given **Lifetime number of sexual partners

Table 3: Colposcopy diagnosis

Colposcopy findings	N	Percentage (%)
Normal	39	40.2
Inflammatory/Cervicitis	5	5.2
Low grade lesion	28	28.9
High grade lesion	24	24.7
Glandular disease	1	1.0
Total	97	100.0

3.1. Olposcopy pictures showing high grade lesions

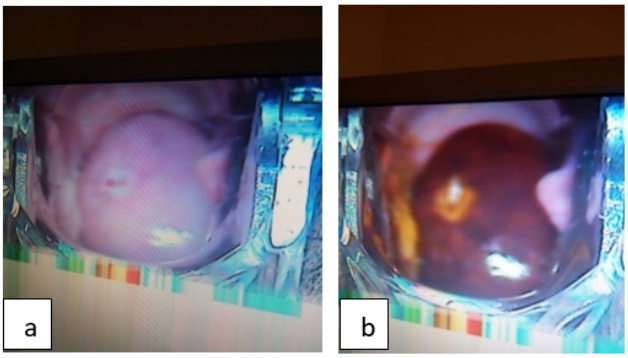

Fig. 1: a: Acetowhite reaction; **b:** Iodine negative areas

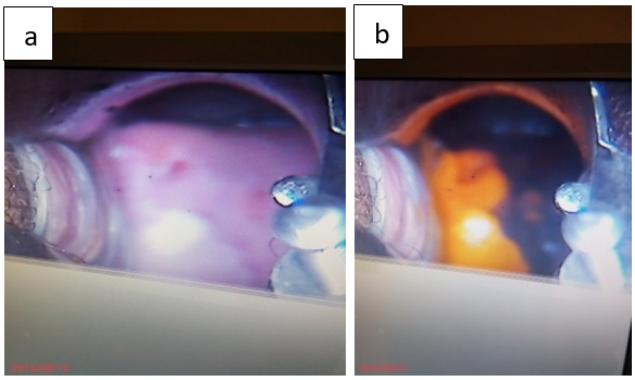

Fig. 2: a: Acetowhite reaction **b:** Iodine negative areas

3.2. Colposcopy pictures showing normal cervix

4. Discussion

The prevalence of premalignant lesions from colposcopy was 53.6% which was significantly high. This is probably due to the unsuspected aceto-white lesions that may mimic premalignant lesions on colposcopy leading to over diagnosis. There is however paucity of information on the performance of colposcopy in HIV positive women in Nigeria. Figures 1 and 2 show the cervix of patients with high grade lesion. Figure 1 a and Figure 2 a show areas of dense acetowhite changes in the areas of the transformation zone indicating coagulated proteins in the premalignant cells following application of 5% acetic acid. The acetowhite areas did not stain with Lugol's iodine (Figure 1 b and Figure 2 b; yellow instead of mahogany brown/blue black) also indicating areas of premalignant changes with defective glycogen store. Figure 3 shows a normal cervix with no reaction to acetic acid (Figure 3 a) and satisfactory staining with Lugol's iodine indicating the presence of normal mature glycogen filled cells in the cervix (Figure 3 b).

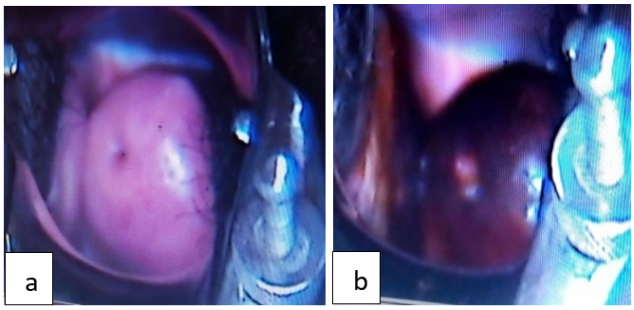

Fig. 3: a: No reaction to Acetic acid; **b:** Total iodine positivity

Colposcopy has been found to aid the identification of premalignant lesions of the cervix and allows for conservative treatment of abnormalities of the cervix that are unlikely to undergo malignant transformation.[31]

Colposcopic findings can be assessed using different indices such as the Reid's/ modified Reid's colposcopic index, 2011 international terminology of colposcopy, Swede/ modifiedSwede score, international federation for cervical pathology and colposcopy classification.

The agreement between colposcopic diagnosis and cervical pathology was reported to be 60.9% using the 2011 international terminology of colposcopy.[32] Another study reported moderate strength of agreement, 57.9% with overestimation occurring in 31.1% and underestimation in 11% of cases.[33] Kushwah et al. however reported good correlation between Reid score, Swede score and histology in the assessment of colposcopic findings.[34]

HIV infection has been shown to increase a woman's risk for cervical intraepithelial neoplasia,[35] however the use of antiretroviral therapy did not show reduction in the prevalence of cervical cancer.[35,36]

5. Conclusion

The prevalence of premalignant lesions was very high from this study compared to values gotten from Papanicolaou smear, therefore, colposcopy with directed biopsy may be an effective screening method for this population at risk of cervical cancer.

Cervical cancer screening programs have been difficult to implement and maintain especially in the low resource areas, however, the scale-up of antiretroviral therapy has

provided an opportunity to integrate these programs into the scheme as this will likely improve the uptake. Despite the overestimation associated with colposcopy, it is likely to detect the severe premalignant lesions that are more likely to undergo malignant transformation, therefore, it should be encouraged. Visual inspection with acetic acid or Lugol's iodine provides a low cost alternative and like colposcopy, gives the advantage of immediate biopsy of visualized lesions as well as the 'see and treat technique which will save time and long term cost.

6. Source of Funding

None.

7. Conflict of Interest

The authors declare no conflict of interest.

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