

Original Research Article

Papanicolaou smear usage and Prevalence of premalignant cervical lesion among women living with HIV attending a Federal Teaching Hospital in South-West Nigeria: A Comparative study

Key words: HIV-Positive women, Papanicolaou Smear; Premalignant cervical lesions, prevalence.

ABSTRACT

Aim: Cancer of the cervix is the third most common cancer among women worldwide, and in Nigeria it is the second most common female cancer. Infection with the Human immunodeficiency virus (HIV) is associated with an increased risk of prevalent, incident and persistent squamous intraepithelial lesions (SILs) of the cervix. The aim was to determine the level of awareness of cervical cancer screening test and the development of premalignant cervical lesions among HIV positive women.

Study Design: A Hospital based comparative cross-sectional study.

Place and duration of the study: the study was carried out in the HIV clinic and general outpatient clinic of Federal Teaching Hospital Ido-ekiti, Ekiti state Nigeria. it was carried out from July to September 2015.

Methodology: The study was carried out among 65 HIV-positive and 65 HIV-negative women. Data were gotten through participants'™ interview. Participants also had Pap smear. Data collected were analyzed using statistical package for social sciences version 19.

Result: The mean age was 39.73 ($\hat{A}\pm 8.57$) and 40.98 ($\hat{A}\pm 10.68$) among the HIV positive and negative women respectively. Only 27.7% of the HIV-positive women compared to 56.9% of the HIV negative women had heard of cervical cancer with $P= 0.001$. The level of awareness of cervical cancer screening test was 15.4% and 50.8% among the HIV positive and negative women respectively ($P= 0.001$). The prevalence of premalignant cervical lesions among the study and control groups was 26.2% and 16.9% respectively. This showed that premalignant cervical lesion was more prevalent among HIV-positive women though not statistically significant ($P=0.201$). However, using risk ratio (RR), the risk of developing cervical lesions is 1.55 times more in HIV exposed women than HIV negative women.

23 Conclusion: There is therefore need for the Physicians to use every opportunity to counsel their clients on the need for routine
24 cervical cancer screening especially in adult HIV clinics.

25 *HIV-Positive women, Papanicolaou Smear; Premalignant cervical lesions, prevalence.*

26 Introduction

27 HIV infection is associated with an increased risk of diverse cancers and has emerged as a single major factor in the recent accelerated
28 burden of cancer in Sub-Saharan Africa.^[1] It is the best example of the close relationship between infection, immune dysfunction and
29 evolution of malignancies. Classically, the Centers for Disease Control and Prevention (CDC) designated Kaposi sarcoma (KS),
30 cervical cancer (CC) and non-Hodgkin's lymphoma (NHL) as AIDS defining cancers (ADCs) because of the association of these
31 cancers with increased risk of HIV infection.^[2] Of the three cancers, only cervical cancer can be screened for.

32 Carcinoma of the cervix is the second most common cause of malignancy in women in Nigeria accounting for up to 30.8% of all
33 female malignancies.^[3] It is also the second most common malignancy in women worldwide, second only to breast cancer; and it
34 remains a leading cause of cancer-related deaths for women in developing countries.^[4] Women with HIV/AIDS are at a greater risk of
35 developing cervical intraepithelial neoplasia (CIN) which is a precancerous lesion that often precedes the development of cancer of the
36 cervix. CIN occurs in about 20% of women with HIV/AIDS, and may be associated with Human papilloma virus (HPV) infection as
37 compared to 4% in HIV Negative women.^[5] In addition, high-grade CIN can progress to invasive cervical cancer, and women with
38 AIDS are therefore at higher risk of developing this cancer.

39 CIN is common in HIV infected women because both HIV and HPV are sexually transmitted, HIV infected women are more
40 likely to have persistent HPV infection and Persistent infection with one or more oncogenic HPV subtypes is a major factor in the

41 pathogenesis of premalignant and malignant cervical disease.^[6] Many studies worldwide have shown a higher prevalence of cervical
 42 intraepithelial neoplasia (CIN) among HIV-positive women than among HIV-negative women. In the HIV Epidemiology Research
 43 Study (HERS, a US observational, multisite cohort study) one of the larger studies of HIV-positive women, CIN was present in 19%
 44 of HIV-positive women and only in 5% of the HIV-negative women. Similar results were found from the Women's Interagency HIV
 45 Study Group (WIHS) and from a large study of women in Abidjan, Ivory Coast.^[7] Also, in a study done at the Lagos University
 46 Teaching Hospital (LUTH), Prevalence of squamous intraepithelial lesion (SIL) was higher in those who were HIV positive than in
 47 those who were HIV negative, 10.9% vs 4.3% ($p=0.00798$). Prevalence of high grade SIL was higher in HIV positive than HIV
 48 negative subjects, 7.9% vs 2.6% ($p=0.0115$).^[8]

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 50 Despite the high mortality from cervical cancer in developing countries, these morbidity and mortality could be greatly reduced using
 51 preventive health methods such as safe sexual practice and early detection of the disease through the Papanicolaou (Pap) smear test.
 52 The Pap smear test is currently the most widely used approach for preventing progression of cervical cancer, and is considered the best
 53 approach to reduce cervical cancer incidence worldwide.^[9] it is however surprising that the level of awareness of cervical cancer and
 54 its screening is below average in Nigeria. In a cross sectional survey done at the university of Nigeria Teaching Hospital, it was
 55 reported that ninety (30%) respondents were aware of cervical cancer. This included 33 (22.0%) HIV-positive women and 57 (38%)
 56 HIV-negative women. Twenty-nine (87.9%) women from the study group who were aware of cervical cancer did not know their risks
 57 of developing the illness, while the remaining 4 (12.1%) thought that their risk was the same as that in the general population. For the

58 HIV-negative women, 43 (75.4%) had no idea of their risk, 10 (17.5%) thought it was same as in the general population, and 4 (7.0%)
 59 felt that their risk was reduced.^[10] It is obvious from their study that HIV positive women have low level of awareness and knowledge
 60 of risk factors for cervical cancer.

61 This study therefore aimed at assessing the level of awareness, current usage of pap smear test and prevalence of premalignant
 62 cervical lesion among HIV positive women.

63

64 **Methodology**

65 The study was conducted in the HIV clinic and the General Outpatient (GOP) clinic of the Federal Teaching Hospital, Ido-Ekiti
 66 (FETHI). It was a comparative cross sectional study which was carried out over a period of three months (May, June and September
 67 2015).

68 The study population consisted of HIV positive women receiving care at the HIV clinic of FETHI, and comparatively matched against
 69 HIV negative women attending the GOP clinic of the same hospital. The sample size was calculated based on the national prevalence
 70 rate of HIV which was 4.1% as at 2012, ^[11] using the formula $n = \frac{z^2 pq}{d^2}$. With an attrition rate of 10%, the minimum sample size was
 71 63, which was rounded up to 65. So 65 consenting HIV patients were used for the study. Similarly 65 consenting HIV negative
 72 women attending the GOP clinic of FETHI was used as control.

73 Systematic random sampling of consenting HIV positive women who have been attending clinic and were seen during the study
 74 period was used for the study. The inclusion criteria were consenting HIV positive women ages 18 to 65 years who were sexually

75 active and consenting HIV negative women of same age range while the exclusion criteria were Pregnant HIV positive women,
76 severely ill patients and patients with clinical features suggestive of sexually transmitted infections as at the study period. Women who
77 had previously been treated for cervical neoplasia/cancer or had had total hysterectomy or were menstruating at time of the study
78 enrolment were also excluded.

79 A semi-structured interviewer administered questionnaire was administered to both the HIV positive and HIV negative women to
80 determine the risk factors for development of premalignant lesions. Both were also screened for premalignant lesions with Pap smear
81 test. The specimens were sent to the histopathology department of FETHI for cytology and the results were categorized as either
82 normal, ASCUS (**Atypical squamous cell of undetermined significance**), AGUS(**Atypical glandular cell of undetermined**
83 **significance**) , LSIL(**Low-grade squamous intraepithelial lesion**), HSIL(**High-grade squamous intraepithelial lesion**) or cancer.
84 Participants whose samples were positive for premalignant cervical lesions were informed, counseled and referred to the
85 gynaecologist for expert management.

86 Ethical clearance was obtained from the ethical committee of FETHI. Informed consent (verbal and written) was obtained from
87 willing participants. The participants were assured of confidentiality and also that their participation were voluntary.

88 Data were analyzed using SPSS version 19. Statistics such as mean, mode, median and standard deviation were determined.
89 Association between dependent and independent variables were compared using Pearson's chi square and Fischer exact test as
90 appropriate. The level of statistical significance is taken as $P \leq 0.05$.

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92 **Results**

93 A total of 130 respondents (65 each for study and control groups) who fulfilled the inclusion criteria and were recruited from the HIV
94 and GOP clinics over 12 weeks were studied. They were aged between 21 and 65 years [mean 40.98 ±10.68 years].

95 Table 1. The mean age of both groups were within same range (study group 39.73, control group 40.98). The control group had more
96 respondents with tertiary education (64.6% vs 41.5%). The study group had no professionals as against the control group with 16.9%
97 of the respondents being professionals. Majority of the respondents in both groups were married (84.6% and 92.3%), more than half of
98 the respondents (52.5%) in the study group had been married for 10-20 years and both groups had ≥ 4 children (35.4%).

Table 1. Comparison of socio-demographic characteristics between the study and control groups.

Variables	Subject category		χ^2	df	P value
	Study	Controls			
Age (years)					
21 – 30	11 (16.9)	9 (13.9)	0.265	3	0.966
31 – 40	28 (43.1)	29 (44.6)			
41 – 50	16 (24.6)	16 (24.6)			
> 50	10 (15.4)	11 (16.9)			

Mean ± SD	39.73 ± 8.57	40.98 ± 10.68	-0.736	128	0.463*
Religion					
Christianity	57 (87.7)	59 (90.8)			
Islam	7 (10.8)	6 (9.2)			0.778**
Others	1 (1.5)	0 (0.0)			
Educational status					
Primary	20 (30.8)	13 (20.0)			
Secondary	18 (27.7)	8 (12.3)			0.010**
Tertiary	27 (41.5)	42 (64.6)			
No education	0 (0.0)	2 (3.1)			
Occupation					
Professionals	0 (0.0)	11 (16.9)			
C/S, Teachers	18 (28.1)	28 (43.1)			
Traders, Artisans	39 (60.9)	23 (35.4)			0.001**
Farmers	2 (3.1)	2 (3.1)			
Students	5 (7.8)	1 (1.5)			

Marital Status

Single	6 (9.2)	3 (4.6)			
Married	55 (84.6)	60 (92.3)			0.411**
Separated / Divorced	4 (6.2)	2 (3.1)			

Duration of Marriage (years)

> 10	43 (72.8)	39 (62.9)			
			1.378	2	0.240
≤ 10	16 (27.2)	23 (37.1)			

Number of children

<4	42 (64.6)	42(64.6)			
			0.336	2	0.854
≥ 4	23 (35.4)	23 (35.4)			

* Independent samples t test,

** Fisher's exact test

99 Table 2 below shows that only 4.6% of the study group and 12.3% of the control group had ever done Pap smear. Of the respondents
 100 who had done Pap test, 33.3% of the study group had done 50% of the control group had done it more than once.

Table 2. Usage of Pap smear among study subjects.

Variables	Subject category		Fisher's	exact
	Study	Controls	P	
Ever done Pap smear				
Yes	3 (4.6)	8 (12.3)	0.206	
No	62 (95.4)	57 (87.7)		
Number of Pap smear ever done				
One	2 (66.7)	4 (50.0)	0.152	
Two	0 (0.0)	4 (50.0)		
Three	1 (33.3)	0 (0.0)		

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107 In table 3 below, abnormal cervical lesions were present in 26.2% of the study group while it was present in 16.9% of the control
108 group. This was not statistically significant with a p-value of 0.201. However, using risk ratio (RR), the risk of developing cervical
109 lesions is 1.55 times more in HIV exposed women than HIV negative women.

110 **Table 3 cytology results**

Cytology	Study	Control	χ^2	P value	RR	CI
Abnormal	17(26.2)	11(16.7)	1.639	0.201	1.545	0.786-3.038
Normal	48 (73.8)	54(83.1)				

111 **note, cytology results stating ASCUS,AGUS, LSIL HSIL were classified as abnormal*

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114 In table 4, none of the 3 respondents from the study group who had ever done pap smear had abnormal cervical cytology while
115 17(27.4%) of those who had never done pap smear had abnormal cervical cytology. Of the 8 respondents from the control group who
116 had had pap smear, 3(37.5%) had abnormal cervical cytology.

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Table 4. Relationship between usage of Pap smear test and development of pre-malignant cervical lesions among the study group and controls

Variables	Premalignant cervical lesion (cytology) study group			Premalignant cervical lesion (cytology) control group		
	Abnormal	normal		abnormal	Normal	
Ever done Pap smear						
Yes	0 (0.0)	3 (100.0)	3 (100.0)	3 (37.5)	5 (62.5)	8 (100.0)
No	17 (27.4)	45 (72.6)	62 (100.0)	8 (14.0)	49 (86.0)	57 (100.0)
	Fisher's exact $P=0.561$			Fisher's exact $P =0.126$		

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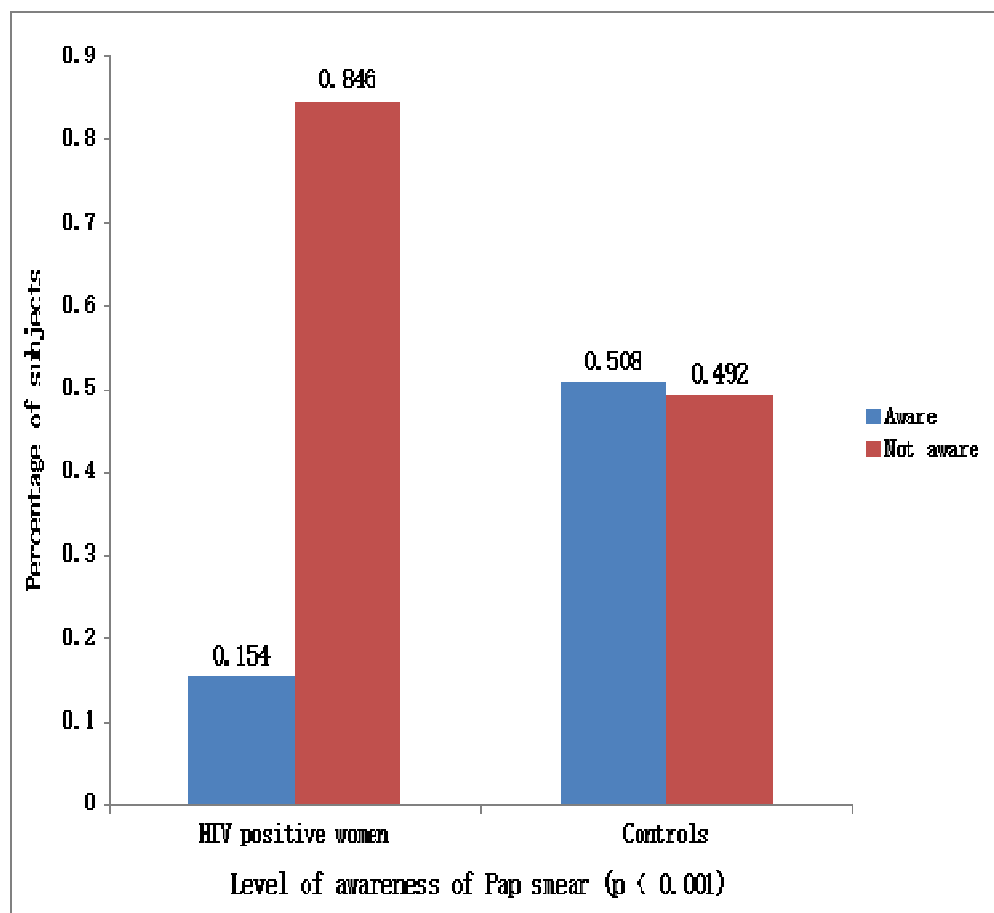


Figure 1: Clustered bar chart showing that the HIV positive women were significantly less likely to be aware of cervical screening tests compared to the control subjects.

134 **Discussion**

135 This comparative cross sectional study has determined the relationship between cervical cancer screening awareness and development
136 of premalignant cervical lesions among HIV positive women attending HIV clinic in FETHI, Ido-Ekiti, in the South-Western Nigeria.

137 **Socio-demographic characteristics of respondents**

138 The modal age group was 31-40 years and the mean age was 39.7 ± 8.5 and 41.0 ± 10.6 years for the study and control group
139 respectively. This was consistent with a study done in Abuja by Ononogbu *et al*^[12] where the mean age of respondent was 35 years.
140 Similarly, a study done in Kenya by Memiah *et al* showed a median age of 40 years amongst women receiving care in a resource
141 constraint setting which is consistent with most other studies around the globe.^[13 - 15] This could be attributable to the fact that most
142 women are recruited into HIV care through PMTCT programme, thereby leaving out the younger age group and the older ones.
143 Majority of the respondents in both the study (41.5%) and control group (64.6%) had tertiary level of education, however the control
144 group had higher educational status, which was statistically significant ($p=0.010$). This is not surprising as poverty and ignorance are
145 factors responsible for high prevalence of HIV in Nigeria due to low access to information and education about HIV/AIDS and
146 women with higher educational status are more prone to this information and therefore more likely to practice safer sex. This finding
147 is consistent with related studies in South-Eastern and Northern Nigeria.^[16, 17] The impact of education was evident in this study as it
148 might account for the observed significant differences in the awareness of cervical cancer and Pap test between the study group and
149 the control group. This is an important advantage of women empowerment.

150 **Current usage of pap smear among respondents**

151 Only 3(4.6%) of the study group had ever had Pap smear while 8(12.3%) of the control group had ever had pap smear. Of the three
 152 respondents in the study group who have had pap smear, 1(33.3%) has done it thrice while the other 2(66.7%) had done it once.
 153 Ezechiet *al* got control group a higher prevalence, 9.4%, amongst HIV positive women in Lagos.^[18] Ezem found that only 7.1% of
 154 women in Owerri had ever done pap smear, which is less than that found among the respondents in this study.^[19] Studies around the
 155 country have shown very low usage of pap smears test. Owoeye and Ibrahim found that 12.1% of their respondents have had pap
 156 smear test while Wright et al in Lagos found 8.5% among their respondents.^[20,21] These low uptake found in different studies could
 157 have been linked to the low level of awareness of cervical cancer screening test among these respondents, however, despite the high
 158 level of awareness shown by Owoeye and Ibrahim the uptake of cervical cancer screening test was still very low.^[20] Similarly,
 159 Gharoro and Ikeanyi also found a high cervical cancer and pap smear awareness (65% and 64%) but the uptake rate was very low
 160 (14.1%) among the respondents.^[22] this shows that awareness will not necessarily translate to usage if there is no provision of a
 161 national screening programme, especially for high risk groups like the HIV positive women. In developed countries where there are
 162 standard programmes for cervical cancer screening, awareness and uptake are very high. In a study done in Catalonia, Spain among
 163 HIV positive women, screening coverage was found to be 60.0% and the researchers considered this as low screening coverage in
 164 their study.^[23] In the study done by Ezem in Owerri, reasons ranging from unawareness, being unnecessary, fear of detection of cancer
 165 and anxiety were given as reasons for not doing the test.^[19] Fear and anxiety stems from poor understanding of the rationale behind
 166 cervical screening. Similarly, in a study done by Ndikom and Ofi among women in Ibadan, lack of awareness, illiteracy, nonchalant

167 attitude to health and financial constraints were factors identified to affect uptake of cervical cancer screening among the
 168 respondents.^[24] These reasons were however contrary in a study done among female nurses in Nnewi, where the rate of uptake was
 169 found to be 5.7% with majority of the respondents (37.1%) having no reason for not undergoing pap smear, 25% felt they were not
 170 candidate for cervical cancer while 15% gave fear of outcome as their reason.^[25] This shows that even among health workers where
 171 awareness is high uptake of cervical cancer screening is very low, therefore health workers especially females who should be at the
 172 forefront of this awareness campaign should be properly educated again that the benefit of early detection is the probability of a total
 173 cure.

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176 **Prevalence of premalignant cervical lesions among respondents.**

177 Recent guidelines recommend that, following two initial normal Pap-smears at a 6-month interval, all HIV-positive women should
 178 undergo annual cervical cytologic examination. In addition, it is recommended that all immunosuppressed women with atypical
 179 squamous cells undergo colposcopy.^[26] Out of the 65 HIV positive women screened for premalignant cervical lesions, 17 (26.2%) had
 180 abnormal cytology result which is higher than 11 (16.9%) among the control group though this was not statistically significant. This
 181 prevalence is higher than 12.6% and 4.6% found by Dim *et al* among HIV positive and HIV negative women respectively.^[27] Ezechi
 182 *et al* also found a similar prevalence with Dim, 14.3% and 3.3% among HIV positive and negative women respectively.^[28] Anorlu *et al*
 183 also got a similar prevalence of 10.9% and 4.3% among HIV positives and negatives respectively.^[8] However, Bassey *et al* in Port

184 Harcourt found a higher prevalence of 34.4% and 19.8% among HIV positive and HIV negative women respectively.^[29] The
 185 differences encountered in these studies might be due to the prevalence of HPV infection and level of immune suppression. The
 186 difference in the prevalence of abnormal cytology between the two groups in this study is consistent with the findings in other studies
 187 and supports the fact that compared with HIV negative women, HIV positive women are at greater risk of developing abnormal
 188 cervical cytology. A Brazilian study also found a high prevalence of CIN among HIV positive women to be 23.6% which is similar to
 189 the findings in this study.^[30] Moodley *et al* found a prevalence of 66% of cervical abnormalities among HIV positive women initiating
 190 HAART in South Africa.^[14] This is much higher than most studies in Africa and even in developed countries. However, the high
 191 prevalence was attributed to the low immune status of their respondents.

192

193 **Conclusion.** There was higher rate of cervical premalignant lesion found among HIV positive patients when compared with HIV
 194 negative women. In spite of this higher risk, the rate of uptake of Papanicolaou smear was abysmally low among HIV positive women.
 195 There is need for healthcare providers to be proactive in educating women on regular cervical cancer screening and structured
 196 screening programme should be put in place.

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