

Full Length Research Paper

Correlates and risk factors for abnormal papanicolaou smear among HIV infected and HIV non infected women in Northeastern Nigeria

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Abstract

Background: Universal access to antiretroviral therapy has resulted in increased life expectancy among HIV infected women clients, however the risk of certain clinical conditions including premalignant lesion of the cervix may remain or enhanced compared with HIV negative control. **Objectives:** To compare the prevalence and the risk factors of abnormal Pap smear among HIV positive and HIV negative women attending clinics of two tertiary hospitals in Northeastern Nigeria. **Methodology:** This was a hospital based case control cross sectional study involving three hundred and sixty-five consecutive consenting HIV infected women and three hundred and sixty-five HIV non- infected women. Socioeconomic and clinical variables, abnormal Pap smear and CD4 cell count of all the HIV positive women were recorded. **Results:** Abnormal Pap smear among HIV infected women of 47.94 % (18.1% epithelial and 29.8% benign cells abnormalities) in this report was higher than 31.78% (8.0% epithelial and 23.78% benign cells abnormalities) among HIV non-infected women. A negative correlation was observed between CD4 cell count and the abnormal Pap smear. Other correlates of abnormal Pap smear include early coitache, multiple sexual partners and low social class. **Conclusion:** HIV infection is associated with increased risk of abnormal Pap smear in women. Other risk factors associated with abnormal Pap smear, include early coitache, multiple sexual partners and low social class. **Recommendation:** Cervical screening should be included among investigations in evaluating HIV infected women.

Key words: Abnormal Pap smear, HIV, CD4 cell count, risk factors, HPV.

INTRODUCTION

Cancer of the cervix is a common genital malignancy afflicting women worldwide especially in the developing countries (UNAIDS/WHO, 2014; Federal Ministry of

Health [FMOH] Abuja, 2010; American Cancer Studies [ACS], 2015; Sexana, 2014). About 530,000 new cases are diagnosed every year worldwide and approximately 275,000 women die of the disease and 80% of these occur in developing countries (Sexana, 2014; UNAID/WHO, 2014; FMOH Abuja, 2010). Fortunately, Cancer of the cervix is preventable with an organized

Papanicolaou smear (Pap smear) screening and treatment of early lesions. (UNAID/WHO, 2014; Lehtovirta et al., 2008; Basseyet al., 2014).

Cancer of the cervix is among the malignancies associated with HIV infection. Nigeria is located in sub-Saharan Africa; the region that bears most of the global burden of HIV infection. As at the end of 2014, the UNAIDS/WHO estimated the global burden of HIV infection in 36.9 million persons, approximately 68% of the global estimates were contributed by sub-Saharan Africa (UNAIDS/WHO, 2014). Nigeria with population of approximately 170 million had about 3.4 million people living with HIV infection (FMOH Abuja, 2014). Available estimates of abnormal Pap smear, a harbinger or premalignant condition closely linked to cancer of the cervix vary widely. The prevalence of abnormal Pap smear among HIV positive women was reported to be 33% (Lehtovirta et al., 2008) in Finland and 15% in Malawi (Chalermchockcharoenkit, 2006). In Nigeria, it was reported as 22.6%,14.3%, and 12.6% in Port Harcourt (South south region), south west Nigeria and Enugu (south east region) respectively (Basseyet al. 2014; Ezechi et al., 2014; Dim et al., 2011) while in Jos (North central) 68.3%; out of which 29% was cervical dysplasia (Patricia et al., 2009) was reported. Although a prevalence of 31.3% was earlier reported from our centre (Chama et al., 2005), this current study intend to validate or refute the reported correlates and risk factors for cervical cancer such as, early sexual exposure, multiple sexual partners, promiscuous male partners, sexually transmitted disease, HIV infection, smoking and use of combined oral contraceptives (COCP).

MATERIALS AND METHODS

Background of the study areas

The study was conducted in the Departments of Obstetrics and Gynaecology of the University of Maiduguri Teaching Hospital (UMTH), Maiduguri, Borno State and Federal Medical Centre Yola (FMC), Adamawa State, Northeastern Nigeria.

The UMTH Maiduguri is a 500 bed tertiary health institution serving Adamawa, Bauchi, Borno, Gombe, Taraba and Yobe States in Northeast Geo-political zone of the country and neighboring countries of Chad, Niger and Cameroun. Federal Medical Centre Yola, a Tertiary health facility is a 150 bed capacity and provides services to residents of northeastern region and neighboring Cameroun.

Inclusion criteria

Participants included in this study include HIV positive women as cases and HIV negative women control that willingly consented to participate in the study.

Exclusion criteria

Established cases of cancer and non consenting women

Study design and study instrument

This was a prospective hospital based case control cross sectional study conducted in the two aforementioned tertiary health facility in northeastern Nigeria between 10th January 2013 and 19th June 2013. A validated structured questionnaire was used to document information obtained from each participant.

Sampling size

The minimum sample size required for the study was estimated to be 365 using Tailor's formula and 365 to serve as control.

Sampling procedure

Convenient sampling through approaching all the consenting women who satisfied the inclusion criteria that presented to the clinics of the two tertiary institutions was used. The subjects first received voluntary counseling and testing for HIV, those that were known to be HIV positive whether on Anti-Retroviral Therapy (ART) or not attending HIV clinics of the two institutions were also recruited. All Nurses and doctors who assisted in the data collection were trained on the sample collection technique. The procedures and the purpose of the study were well explained in clear terms to the consenting subjects and they were reassured of utmost confidentiality of the results. The Patients were counseled either in group or one on one basis on the importance of the Pap smear test. No personal identification information was included in the questionnaire. Those who needed interpretation of the questionnaire into local languages were assisted.

Data collection and Pap smear technique

Data collected include the age, Abnormal Pap smear result based on Bethesda classification, social class, age at first marriage or onset of sexual exposure, premarital sexual affairs if any, number of sexual partners and duration of HIV diagnosis and treatment in years and CD4 cell count of the HIV cases only. After obtaining consent, smears were obtained in the dorsal position, a bivalve speculum was introduced into the vagina to expose the cervix under good light, and any obscuring mucus substances were wiped off with a clean water wet swab. The extended tip of the Ayre's spatula was introduced gently into the external cervical Ostium and rotated through 360 degrees to scrape the entire squamo-columnar junction, and the material collected was immediately smeared evenly on a pre-labeled glass

slide and the slide was submerged immediately into a coupling jar containing 95% alcohol to fix the smeared material collected. The specimens were taken to histopathology laboratory for cytologic analysis in conjunction with Histopathologist. All unsatisfactory Pap smears were repeated.

Those that their results were found to be positive for abnormal Pap smear were counseled and referred for further diagnostic procedure such as colposcopy and treatment. Data was analyzed using SPSS (SPSS version 16 inc. Chicago. USA 2006). Statistical significance was set at $P < 0.05$ and results were presented in tables and proportions.

Ethical consideration

Ethical clearances were obtained from the research and ethical committees of the two institutions.

RESULTS

Seven hundred and thirty women (365 as cases and 365 as control) with complete information were analyzed. The mean age of the study population was 30.58(SD \pm 6.4) among the cases and 29.82(SD \pm 7.9) among the control group. The difference was not statistically significant. $X^2 = 5$, $P = 0.060$. Table 1 showed the prevalence of abnormal Pap smear among the cases and the control. 175 (47.9%) among the HIV positive and 116 (31.8%) among the HIV negative women. The abnormal Pap smear comprised of 66 (18.1%) epithelial abnormalities and 109 (29.9%) benign changes among the HIV positive women, while that of HIV negative women include 29 (8.0%) epithelial cells changes and 87 (23.8%) benign cells abnormalities and the difference was statistically significant. $P < 0.001$.

Table 2 shows some risk factors of abnormal Pap smear. Younger age at first coitus, $P < 0.001$, multiple sexual partners $P = 0.014$, low social class $P < 0.001$ and high number of co-wives $P < 0.011$, appeared to be associated with high abnormal Pap smear, the contribution of contraceptives usage $P = 0.079$ was not statistically significant.

Table 3 shows the relationship between abnormal Pap smear and CD4 cell count of the cases (HIV infected women) only. It was observed that the higher the CD4 cells count the lower the abnormal Pap smear, $P < 0.001$. When subjected to Pearson correlation coefficient there is negative correlation between the CD4 cell count and the abnormal Pap smear.

Table 4 detailed the relationship of abnormal Pap smear and the duration of ARV treatment. It was observed that the longer the patients were on antiretroviral therapy the less the prevalence of abnormal Pap smear. There were only two patients who were not on ART which were too few for statistical comparison with those on ART.

DISCUSSION

In this study, the incidence of abnormal Pap smear was 47.9%. It was not unexpected to find no significant differences in the mean age of the cases from that of the control as they come from the same population attending the same clinics. This was similar to the findings reported previously in the same centre (Chama et al., 2005). The prevalence of 47.9% (18.1% epithelial and 29.9% benign cells abnormalities) among the HIV positive women which represent 60.1% of the 291 total numbers of women who had abnormal Pap smear in the study, was significantly higher than 31.8% (8 epithelial and 23.8%) among the HIV negative women which also represent 39.9% of the total number of 291 who had abnormal Pap smear. $P < 0.001$. The prevalence of 18.08% epithelial cells abnormality is smaller than 31.3% previously reported among the HIV sero-positive Gynaecological patients from the same population (Chama et al., 2005). This might suggest the positive impact of the ART in our centre (Bukar et al., 2009, Chama et al., 2005). However this findings was lower than the prevalence reported from Finland (Lehtovirta et al., 2008), Port Harcourt (Bassey et al., 2014) and Jos (Patricia et al., 2009) but much higher than the prevalence reported from Enugu (Dim et al., 2011) Malawi (Chalermchockcharoenkit et al., 2006) and South Western Nigeria (Duru et al., 2015; Ezechi et al., 2014). This study also showed that age at first coitus ($P < 0.001$), multiple sexual partners ($P < 0.014$), co-wives ($P < 0.011$), low socioeconomic class ($P < 0.001$) were associated with high prevalence of abnormal Pap smears. These findings were comparable to the previous studies (Bassey et al., 2014; Dim et al., 2011; Duru et al., 2015; Ezechi et al., 2014; Zaporozhan et al., 2010, Katki et al., 2011) while, the use of oral contraceptives in this study does not seem to have significant association with abnormal pap smear.

It was also observed that the higher the CD4 cell count the lower the abnormal Pap smear (Pearson's correlation coefficient $-1, p < 0.001$). Similarly, those who had been on antiretroviral drugs for 5 years and above had lower prevalence of abnormal Pap smear than those that were on treatment one year or less ($P = 0.0358$). This suggests that as the individual immunity improves the risk of abnormal pap smear reduces. Hence, reducing the prevalence of cancer of the cervix amongst these group of patients. This findings was similar to the study reported earlier (UNAIDS/WHO 2014; ACS 2015; Chama et al., 2005, Patricia et al., 2009, Katki et al., 2011, William et al., 2009).

The strength of this study was that the prevalence of abnormal Pap smear among HIV infected and HIV non infected women were determined and those women found to have positive epithelial abnormality were referred for colposcopy and subsequent treatment. However the pitfall of study was that it was a cross sectional study, the association between CD4 cell count and the abnormal Pap smear would have been stronger

Table 1. Abnormal Pap smear results of the HIV positive and HIV negative women.

Variables	HIV+	HIV-	total
Normal Pap smear	190(52.1%)	249(68.2%)	439(100%)
Abnormal pap smear	175(47.9%)	116(31.78%)	291(100%)
Total	365(100%)	365(100%)	730(100%)
$X^2 = 29.93$ P < 0.001			
Normal Pap smear	190(43.3%)	249(56.7%)	439(100%)
Benign cellular changes			
Infections (inflammatory)	73(51.0%)	70(49%)	143(100%)
HPV assoc changes	36(67.9%)	17(32.1%)	53(100%)
Epithelial cell abnormalities			
ASCUS	23(63.9%)	13(36.1%)	36(100%)
LGSIL	27(73.0%)	10(27%)	37(100%)
HGSIL	16(72.7%)	6(27.3%)	22(100%)
Total	365	365	730(100%)

$X^2 = 29.93$, P < 0.001

Key-ASCUS- atypical squamous cell of undetermined significance.

LGSIL- low grade squamous intraepithelial lesion

HGSIL-high grade squamous intraepithelial lesion

SIL- Squamous intraepithelial lesion.

Table 2. Risk factors for abnormal Pap smear only among cases and the control.

1	Age of first coitus (years)	HIV +	HIV -	total
≤19	abnormal Pap smear	122(67.8%)	58 (32.2%)	180(100%)
>19	abnormal Pap smear	52(47.3%)	58 (52.7%)	110(100%)
$X^2 = 15.8$, P < 0.001				
2	sexual partners	HIV+	HIV-	total
1	Abnormal pap smear	80(51.9%)	75(48.1%)	154(100%)
≥2	Abnormal Pap smear	95 (70.4%)	41(29.6%)	135(100%)
$X^2 = 10.57$, P = 0.014				
3	Co-wives	HIV+	HIV-	total
	Normal pap smear	70 (52.2%)	64 (47.8%)	134(100%)
	Abnormal pap smear	75(68.2%)	35 (31.8%)	110(100%)
$X^2 = 6.5$, P = 0.011				
4	Contraceptive usage	HIV+	HIV-	total
No contraception				
	Abnormal pap smear	115 (65.0%)	62 (35.0%)	177(100%)
With Contraception				
	Abnormal pap smear	58 (51.8%)	54(48.8%)	112(100%)
$X^2 = 9.86$, P =0.079				
5.	Social class	HIV+	HIV-	total
Low				
	Abnormal Pap smear	123 (71.1%)	50 (28.9%)	173(100%)
Middle				
	Abnormal pap smear	42(46.2%)	49(53.8%)	91(100%)
High				
	Abnormal Pap smear	8 (32.0%)	17(68.0%)	25(100%)

$X^2 = 24.28$, P < 0.001.

if the study was a well-control longitudinal study. In conclusion, this study demonstrated that HIV infected women have higher prevalence of abnormal Pap smear

when compared to HIV negative women. We recommend that Pap smear test should form part of routine investigations performed for all HIV patients; this may

Table 3. Abnormal Pap smear and CD4 cell count among the HIV positive women.

CD4 count (cells/UL)	Abnormal Pap smear	Normal Pap smear	Total
<100	23(100%)	0 (0%)	23(100%)
100-199	41(83.7%)	8 (16.3)	49(100%)
200-299	31(53.4%)	27(46.6%)	58(100%)
300-399	30(38.4%)	48(61.6)	78(100%)
400-499	27 (35.1%)	50 (64.9%)	77 (100%)
500 and above	23(28.8%)	57(71.2%)	80 (100%)
Total	175	190	365 (100%)

Pearson correlation coefficient -1 P = 0.001

Table 4. Abnormal Pap smears and duration of ART among the sero positive women.

Duration of ART use	normal pap smear	abnormal Pap smear	total(100%)
Not yet on ART	1 (50.0%)	1(50.0%)	2(100%)
<1 year	8 (34.78%)	15(65.2%)	23(100%)
1-<2 years	21(42%)	29(58.0%)	50(100%)
2-<3 years	18(41.9%)	25(58.1 %)	43(100%)
3-<4 years	27(49.1%)	28(50.9%)	55(100%)
X 4-<5 years	30 (55.6%)	24(44.4%)	54(100%)
≥5 years	85 (61,6%)	53(38.4%)	138(100%)
Total	190 (52.05%)	175(47.95%)	365(100%)

$\chi^2 = 32.2$ P = 0.0358

*there were only two patients who were not on ART which was too few for statistical comparison with those on ART.

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