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COMPARISON BETWEEN THE CERVIX UTERI CYTOLOGY PATTERN OF HIV POSITIVE WOMEN AND THAT OF THEIR AGE-MATCHED HIV NEGATIVE WOMEN IN SOUTH EASTERN NIGERIA.

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This study was undertaken to compare the relationship of the cytology of the uterine cervix patterns seen in HIV positive women (HPW) and that of their age-matched HIV negative women (HNW) in Anambra State of Nigeria, a sub-Saharan African community. The results showed higher abnormal smears in the HPW than in the HNW (p=<0.05). This study showed strong evidence that HIV positivity has effects on the cervix as a precursor for premalignant conditions and increased risk of cervical cancers in such patients. It is therefore, recommended that any HIV positive woman must be screened for cervical cancer and also all women who are sexually active irrespective of their HIV status be informed on the importance of both cervical screening and HIV screening periodically.

KEYWORDS: HIV Positive women (HPW), HIV Negative Women (HNW), cervical uteri cytology, Squamous Intraepithelial Lesion (SIL), Human Papilloma Virus (HPV**).**

INTRODUCTION

The cervix of the uterus is the cylindrical, narrow inferior portion of the uterus, which has a supravaginal part between the isthmus and the vagina. It serves as a neck that connects the uterus to the vagina through the endocervical canal. (Moore and Agur, 2007). The size and shape of the cervix vary widely with age, hormonal state, and parity. In addition, age and hormonal status are the most important factors influencing location of squamo-columnar junction (Pierre et al,). The live of the cervix has always been riddled with troubles. It must serve as a barrier to the ingress of air and the microflora of the normal vaginal tract yet must permit the escape of menstrual flow and sustain the buffeting of intercourse and the trauma of childbirth. No wonder, it is often prone to disease. Many diseases of the cervix are associated with constant activities in the area such as sex or parturition (Ellenson and Pirog, 2010). Most of the diseases of the uterine cervix are common in young sexually active females (Cervical cancer, www.cdc.gov/cancer/knowledge 1-800-CDC-INFO). Fortunately, most cervical lesions are relatively banal inflammations although it is also the site for some benign, pre-malignant and malignant lesions (Ellenson and Pirog, 2010). Tumours of the cervix include benign tumours, cervical intraepithelial neoplasia and malignant tumours. They all may manifest as abnormal bleeding per vagina, which may be postcoital, intermenstrual, and postmenopausal or may manifest as vaginal discharge (Abularach and Anderson, 2005).

Cervical carcinoma is the second most common cancer in women worldwide after cancer of the breast in frequency and is a major contributor to female morbidity and mortality (2014 African Cervical Cancer Multi Indicator Incidence & Mortality Score card). Chronic infection with human papilloma virus (HPV) is a necessary event in the evolution of cervical carcinomas (American College of Obstetricians and Gynecologists, 2010). Moreover, some studies showed that the prevalence of cervical intraepithelial neoplasia (CIN) has been shown to be higher among HIV-positive women than

among HIV-negative women especially in developing countries and some have demonstrated the presence of CIN in about 20% of HIV-positive women and only in 5% of the HIV-negative women (Duerr et al, 2001; Massad et al, 1999; La Ruche. et al, 1998). Conversely, the incidence of cervical cancer, which is predominantly of the squamous cell type, is now on the decline in developed countries because of effective cervical screening programmes available in those countries (Sulaiman et al, 2014). We embarked on this study to accept or reject the hypothesis which states that females with HIV infection have higher chances of developing cancer of the cervix.

METHODS

This study was conducted in Anambra State and the study population was stratified into three clusters according to the three senatorial zones in Anambra State. The total percentage coverage was estimated at 95% per selected stratum. This study was carried out in a specific period of time covering one year between October 2009 and September 2010. The study design involved explaining to the HIV positive patients the advantage and importance of the pap smear which would have cost the participant about N5, 000.00. However, enrollment would guarantee free of charge screening and the results made available to enrollees with free consultation. The same was done to the non-HIV (control) patients attending ante-natal, infertility and family planning clinics for the controls. All the participants in the non-HIV clinics were made to undergo HIV screening and only those who were HIV negative were used as controls. Screening for HIV was performed on both groups free of charges after counseling and informed consents were obtained. Pap smear was taken from all the participants using the Ayres spatula and smeared on frosted end slides which were immediately fixed in 95% ethyl alcohol. Thereafter, Papanicolaou stain was done for the slides using standard procedure as described by Papanicolaou in 1945 (Trott, 1989). The slides were examined with an Olympus Light Microscope and were classified and reported by the investigators. Bethesda Classification 2001 was the basis for classification of the results from the slides (Stoler, 2002). This is a WHO universally accepted standard of classification (Stoler, 2002). Some positive Pap smear samples reported by the investigators were given to other pathologists in his practice centre to compare results as an internal quality control and to pathologists in Lagos as an external quality control. The information obtained was coded and recorded on data sheets designed for the study and analyzed using SPSS statistical soft ware version 16. Test of significance were based on $p< 0.05$ using the appropriate tests.

The study had some strength and limitations. Strict inclusion and exclusion criteria for selection with simple non-replacement random sampling were adopted to eliminate such problems. Due to the low level of awareness and acceptance of Pap smear in the society, some of the subjects were unwilling to participate. Women who had active genital tract infection were excluded and were told to go for treatment at their own expense and we lost most of them as they never turned up again for their pap smear.

RESULTS

Majority of the patients in the test group (65.2%) have a negative smear which included NIL and NIL-BCC. ASCUS accounted for 3.4% and ASC-H accounted for 3.7%; LSIL accounted for 11.3% and LSIL-HPV accounted for 6.3%; and HSIL accounted for 3.2%. In the control group, NIL and NIL-BCC accounted for 81.4% of the total sample size, ASCUS accounted for 6.9%; ASC-H accounted for1.5%, LSIL for 2.9%; and LSIL-HPV for 2.6%; and HSIL for 2.2% as shown in Figure 1. Table 1 compares the CD4 count of patients with the cytologic pattern seen on Pap smear on the HPW (test group). The CD4 count was grouped into counts of 200cells/mm^3 and below and those CD4 count above 200cells/mm^3. Of the 278 HIV positive patients with known CD4 count, cytology of 202 cases showed NIL. Of these, 9.9% had a CD4 count of 0-200 cells/mm^3 while the remaining 90.1% had a CD4 count of over 200cells/mm^3. Among the 15 cases with ASCUS, 6.7% had CD4 count of 200cells/mm^3 and below while 93.3% had CD4 count of 200cells/mm^3 and above. However, among those with low grade lesion, 48.4% had a CD4 count of 0-200cells/mm^3 and 51.6% had a CD4 count of 200cells/mm^3 and above. Majority of patients with high grade lesion (57.1%) have a CD4 count of below 200cells/mm^3 and 42.9% had CD4 count of 200cells/mm^3 and above. These figures showed that high grades of dysplasia are seen more with those with lower CD4 count (p-value < 0.001) as shown in Table 1.

In comparing age group of the participants with their cytologic patterns, the cytologic pattern has been grouped into two broad categories namely normal and abnormal smears. Normal smears are those with cytology result of NIL while abnormal smears are all other results put together. In Table 3, the age group 20 – 30 years of the HIV positive patients showed 74.3% as normal smear and 25.7% as abnormal smear. Those in age group 31-40 showed 71.2% normal smear and 28.8% abnormal smear. Of the 38 patients who were 41-50 years 67.5% of them had a normal smear and 32.5% abnormal smear. Fifteen patients were 51 years and above and 75% of them had a normal smear while 25% had an abnormal smear. The results for the control cases show a similar pattern in all age groups. Testing for level of

significance using the chi square, it showed that there is no significant relationship between age of the patients and abnormal cytologic pattern, (p-value = 0.856) as shown in Table 2.

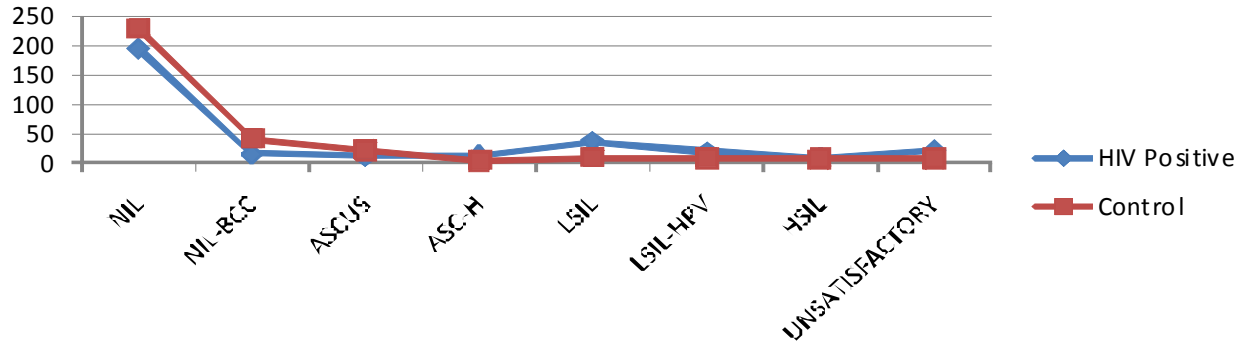

Figure 1: Cytologic Patterns of Pap smear results among the 324 HIV Patients and the 334 Control Cases.

KEY

NIL = NEGATIVE FOR INTRAEPITHELIAL LESION
ASCUS = ATYPICAL SQUAMOUS CELL OF UNDETERMINED SIGNIFICANCE
ASC-H = ATYPICAL SQUAMOUS CELL – HIGH GRADE
LSIL = LOW GRADE SQUAMOUS INTRAEPITHELIAL LESION
HPV = HUMAN PAPILLOMA VIRUS
BCC = BENIGN CELLULAR CHANGES
HSIL = HIGH GRADE SQUAMOUS INTRAEPITHELIAL LESION

Table 1: Comparison of the CD4 Count with Cytologic Pattern among the 278 HIV Patients with Known CD4 Count

	0-200Cells/mm^3		
CYTOLOGIC PATTERN	**Frequency**	**Percentage)**	**TOTAL**
NIL	20	9.9	202
ASCUS	1	10	10
ASC-H	-	-	5
LSIL	15	50	31
HSIL;	8	57.1	14
UNSATISFACTORY	2		16
TOTAL	**46**		**278**

Chi-square value =48.04, p-value <0.001,

Table 2: Comparing the age of the 324 HIV patients and the 334 Control cases with their Cytological patterns

	HIV patients			**Control cases**		
Age	**Normal (%)**	**Abnormal** (%)	**Total**	**Normal** (%)	**Abnormal** (%)	**Total**
20 – 30 years	74.3	25.7	124	76.4	23.6	71
30 – 40 years	71.2	28.8	145	77.5	26.5	140
41 – 50 years	67.5	32.5	40	70.8	29.2	108
50 & above	75	25	15	67.2	32.8	12
Total			**324**			**334**

Chi-square value =0.77, p-value <0.856,

DISCUSSION

The present study is in agreement with data obtained from the other parts of the country, other African countries and some parts of the world which basically concluded that cervical abnormalities has an association with HIV positivity. A study performed in Maiduguri (North Eastern) Nigeria by Chama et al in 2005 showed that HIV infection is a risk factor for cervical abnormalities with resultant pre-malignant and malignant conditions (Chama et al, 2005). In that study, patients attending the gynaecology clinic of the University of Maiduguri Teaching Hospital were screened for HIV and also had their pap smears taken. Cervical abnormalities (dysplasia) were significantly commoner among HIV positive women than those that were HIV negative (31.3% versus 7.8% respectively). The incidence of cervical dysplasia was also proportional to the degree of immunosuppression as women with low CD4 count had higher incidence of cervical dysplasia (Chama et al, 2005). In another related study done in Ibadan, South-west Nigeria Campbell et al recruited patients with cancer of the uterine cervix and screened them for HIV seropositivity before and after radiotherapy. They compared the severity of the disease in terms of clinical staging and histological grading of HIV seropositive women and seronegative women. Their result showed a prevalence rate of 4.2% for HIV seropositivity which was similar to the rate quoted for the general populace in Nigeria. The study however showed that HIV seropositive women present with more severe disease state than the seronegative women. They opined that HIV infection increases the severity and progression of cancer of the cervix in Nigeria (Campbell. et al, 1999). Similar findings of this study were demonstrated by different researchers in other parts of Nigeria and Africa (Anorlu. et al, 2004; Parham et al, 2015; Denny et al, 2000).

CONCLUSION

Control of infections and STD: Most cervical neoplasms are related to sexually transmitted infections. HPV (Human Papilloma Virus) and HIV (Human immunodeficiency Syndrome) infections which are now known to be strong aetiological agents in the pathogenesis of carcinoma of the cervix are mainly sexually transmitted. Improved moral lifestyle, faithfulness in marriages, sexual abstinence by the adolescents and youths, keeping to the doctrine of avoidance of premarital sex and keeping to one sexual partner and the use of condom or barrier contraceptives would go a long way in the control of STD.

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