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Factors Influencing Cervical Intraepithelial Neoplasia and Cervical Cancer Development among Women in Lokoja, North Central Nigeria

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***Abstract*:** Cervical cancer is increasingly becoming a high cause of cancer deaths in Nigeria; it has a high prevalence in Nigeria, as it is the case in most developing countries. This study was aimed at screening for Cervical Intraepithelial Neoplasia (CIN) using Papanicolaou screening procedure, and identifying the influencing factors amongst women in Lokoja, North central Nigeria. This was a cross sectional study involving women between the ages of 16-65 years, selected through convenience sampling of patients and staff that attended the Federal Medical Centre. Interviewer- administered questionnaire and clinical report form were also used to collect data, and data was analyzed using correlational analysis. Results showed that of the 203 women in the study, 193 (95.07%) had normal cytology (they were negative for intraepithelial lesion or malignancy), while 10 (4.93%) women had CIN. Socio-demographic characteristics showed that there were significant relationships between the age of the correspondents and the development of CIN ($p = 0.015$), significant association was also obtained between male partner circumcision ($p=0.0262$), coitarche ($p=0.0046$), parity ($p=0.0019$), alcohol usage ($p=0.0026$), age of first pregnancy ($p=0.0326$), use of steroid contraceptive ($p=0.0104$), number of sexual partners ($p=0.0001$) and the development of CIN. CIN present were low grade squamous intraepithelial lesions, atypical squamous cell of

uncertain significance, and squamous cell carcinoma. The major risk factors associated with cervical intraepithelial neoplasia development indicated in this study include; parity, alcohol usage and multiple sexual partners.

Keywords; Cervical Cancer, Intraepithelial, Neoplasia, Nigeria, Women

Introduction

Cervical cancer has become an important problem affecting Nigerian women, it is the commonest malignancy of the female genital tract in Nigeria [1] and it is the second most common cause of cancer death amongst Nigerian women, second only to breast cancer [2]. There are 36.59 million Nigerians aged 15 years and older who are at risk of cervical cancer [3]. Cervical cancer is regarded as the second most common cancer amongst women worldwide, and it accounts for 250000 deaths and 500000 new patients worldwide annually [2].

These figures are hospital based and are grossly underestimated. Despite these figures, researches into human papillomavirus which is the principal organism associated with the development of cervical cancer in Nigeria is quite limited. Cervical cancers are principally associated with prolonged infections with species of high-risk human papillomavirus (HPV). The high HPV prevalence of 26.3% in women and 24.8% in women with normal cervical cytology correlate with the high cervical cancer incidence of 16.7 per 100,000 women and age standardized incidence rate of 28.5% as indicated by Ferlay et al [4]. Over 150 different genotypes of Human Papillomavirus (HPV) have been identified, of which about 40 are known to infect the anogenital tract. HPV's are DNA viruses that infect cutaneous and mucosal epithelia, manifesting as non-genital or genital warts, and pre-invasive and invasive lesions [5]. HPVs infecting the anogenital tract are divided into high-risk and low-risk types, based on their association with malignant or benign disease. HPV infection is associated with almost all cervical cancers, but also with other cancers of the anogenital tract including cancer of the vulva, vagina, anus, penis and some head and neck cancers.

Over 80 % of cervical cancers in sub Saharan Africa are detected in late stages, this is largely due to lack of information about cervical cancer and prevention services [2]. The control of cervical cancer is directly linked to prevention of HPV infection, identification of precancer cases through screening and subsequent management of identified invasive diseases. These are generally not available in Nigeria. In cases were cervical cancer screening are done, Papanicalaou test are often the only screening test done, the use of HPV DNA typing which is a major tool used in developed countries is hardly utilized in Nigeria.

Various risk factors such as smoking, alcohol, sexual life style, have been attributed to the development of CIN and cervical cancer, thus the objective of this study was to screen for Cervical Intraepithelial Neoplasia (CIN) and cervical cancer using Papanicolaou screening procedure, and identifying the factors influencing the development of CIN and cervical cancer amongst women in Lokoja, North central

Nigeria. This will help in providing information that will help in improving the advocacy for more voluntary screening with a view to reducing cervical cancer burden in the state.

Materials and Methods

Study design

This was a cohort study conducted for a six-month period among women attending the obstetrics and gynecology clinic of the Federal Medical Center, Lokoja, a 500-bed government owned specialist and reference hospital. The hospital is in the city of Lokoja and is the major Federal government of Nigeria medical facility serving communities in the city and its environs.

Study population

The study was carried out among 203 women attending the Obstetrics and Gynaecology Clinic of the Federal Medical Centre, Lokoja, within the ages of 16 years (yrs) and 65yrs who were willing, and met the inclusion criteria. The sample size was determined using Fisher's formula for cross sectional study of a population greater than 10,000 as follows;

$$n = \frac{Z^2 pq}{d^2}$$

(Where N is the desired sample size)

Z=the standard normal deviation which is 1.96 (at 95% confidence interval)

P= the prevalence of HPV in the environment

A structured close ended questionnaire was administered to these patients after an informed consent had been obtained, followed by clinical examination.

Inclusion criteria

Female patients attending Obstetrics and Gynaecological unit, female patients between 16 to 65 years of age, female patients who consented to partake in the study and non-patients who meet other inclusion criteria and agree to participate in the study.

Exclusion criteria

Elderly female patients (greater than 65yrs), female patients below 16years, male patients, patients who do not give consent to partake in the study and patients that have had total abdominal hysterectomy.

Ethical considerations

Approval for this study was obtained from the Ethical Review Committee of the Federal Medical Centre, Lokoja. The study was done at no cost to the subjects, and information from the patients and/or parents and guardian were confidential.

Sampling technique

Convenience sampling techniques was used in which women who were willing and met the inclusion criteria were recruited consecutively during the period of the study, before applying a structured questionnaire after an informed consent had been obtained.

Data collection and preparation

A structured close ended questionnaire was administered to the participating population and after due consent had been taken; cervical smears were collected by a Gyneacologist after visual inspection. Sample collection was done as described by Mbamara et al [6] in which each subject was placed in a dorsal position with her legs flexed at the hip and knee and abducted. The labia were parted using a gloved thumb and index fingers with a non-lubricated disposable speculum passed and fixed to visualize the cervix under a bright light

source. An Ayre's spatula was then inserted at the external and swept through a 360º movement to scrape the entire squamocolumnar junction of the transformation zone.

The smears collected were immediately fixed to slides before being transferred to the laboratory for processing. The fixed smears were stained by the cytotechnologist using Papanicolaou staining procedure and read by a histopathologist using a light microscope. The Papanicolaou screening test utilized had a sensitivity of 52% and a specificity of 90%. The slides were reported as normal, inflammatory, abnormal (epithelial lesion). For simplicity, the results in the tables were regarded as positive or negative. Positive results were results that were classified and reported as abnormal, while negative results were results that were classified and reported as normal, or just inflammatory. The abnormal ones were classified using the Bethesda 2001 system. The samples were collected continuously for a three months period.

Data Analysis

Data were analyzed using statistical package for social science version 20.0 for windows. Both continuous and discreet variables were generated. The relationship between discrete variable and outcome of interest was tested using Chi-squared test. The p-value that will constitute statistical significance was set at < 0.05.

Results

The study population for this research comprised of 203 women with a mean age of 40.38years. Result of cytology shows that 193 (95.07%) had normal cytology, while 10 (4.93%) women had abnormal cytology. Out of the 10 women with cervical intraepithelial neoplasia (CIN), four of the women's cytology was reported as having atypical squamous cells of uncertain significance (ASCUS), one had squamous cell carcinoma, while the remaining five of the abnormal cytology was reported as having low-grade squamous intraepithelial lesion (LC).

Table 1 shows the social demographic characteristics of the study population. Table 2 presents the association between the age, marital status and type of marriage of the subjects and presence of CIN. There was a statistical difference (p=0.015) between the age of the subjects and CIN, with subjects within the ages of 46-55yrs accounting for 60% of CIN amongst the subjects. Marital status (p=0.542) and type of marriage (p=0.347) were not statistically significant to the development of cervical intraepithelial neoplasia among the subjects.

Table 3 shows the association of the sexual attitudes of the subjects, with regards to the development of CIN. Male partner circumcision (p=0.0262), coitarche (p=0.0046), and number of sexual partners (p=0.001), all constituted potential risk factors, while subjects having a history of genital infection (p=0.8744) had no statistical association to the development of CIN.

Reproductive factors among the subjects are represented in Table 4. Although majority of the subjects (67.49%) of the subjects had their first pregnancy at ages between 26-35yrs, 80% of CIN was found among subjects who had their pregnancy at ages between 16-25yrs.

This constituted a risk factor of statistical significance (p=0.0326). Also, the use of steroid contraceptive (p=0.0104) as well as parity (p=0.0028), constituted risk factors of statistical significance.

Table 5 shows the association between tobacco and alcohol usage, and the development of CIN. While tobacco usage (p=0.6429) did not represent a risk factor, alcohol usage (p=0.0026) constituted a potential risk factor.

Table 1 Socio-demographic characteristics of the study population

Socio-demographic characteristics	Study population(percentage)
Age	
16-35 years	70(34.48)
36-55 years	118(58.13)
56-65 years	15(7.39)
Type of education	
Formal	178(87.68)
Informal	25(12.31)
Level of education	
Primary education	16(8.99)
Secondary education	57(32.02)
Post-secondary education	105(58.99)
Religion	
Christians	105(51.72)
Muslims	90(44.33)
Other religion	8(3.94)
Region of residence	
North Central region	187(92.12)
South South region	1(0.49)
South West region	15(7.39)
Marital status	
Married	170(83.74)
Single	2(0.99)
Divorced	10(4.93)
Widowed	21(10.34)
Occupation	
Middle class civil servants/	
Small scale business women	68 (33.50)
Junior staff/ petty traders	120(59.11)
Other jobs	15(7.39)

Table 2 Association between age, marital status, type of marriage and cervical intraepithelial neoplasia

	Positive (%)	Negative (%)	X^2	df	p Value
Age(N=203)			12.346	4	0.015
16-25yrs	0(0.00)	10(4.93)			
26-35yrs	0(0.00)	60(29.56)			
36-45yrs	2(0.99)	68(33.50)			
46-55yrs	6(2.96)	42(20.69)			
56-65yrs	2(0.99)	13(6.40)			
Marital status(N=203)			2.150	3	0.542
Married	10(4.92)	160(78.82)			
Single	0(0.00)	2(0.99)			
Divorced	0(0.00)	10(4.92)			
Widowed	0(0.00)	21(10.34)			
Type of marriage(N=203)			0.883	1	0.347
Polygamous	1(0.49)	43(21.18)			
Monogamous	9(4.43)	150(73.89)			

P < 0.05 is significantly different
df- degree of freedom
X^2– Chi square
N- Number of participants

Table 3 Association between sexual attitudes and cervical intraepithelial neoplasia

	Positive (%)	Negative (%)	X^2	df	p Value
Male partner circumcision(N=203)			4.942	1	0.0262
Yes	9(4.43)	191(94.09)			
No	1(0.49)	2 (0.99)			
Coitarche (Years) (N=203)			8.013	1	0.0046
<15	7(3.45)	54(26.60)			
≥15	3(2.46)	139(68.47)			
Previous genital infection(N=203)			0.025	1	0.8744
Yes	8(3.94)	151(74.38)			
No	2(0.99)	42(20.69)			
Number of sexual partners			16.693	1	0.001
< 2	4(1.97)	168(82.76)			

≥ 2	6(2.96)	25(12.32)			

P < 0.05 is significantly different
df- degree of freedom
X^2– Chi square
N- Number of participants

Table 4 Association between reproductive factors, and cervical intraepithelial neoplasia

	Positive (%)	Negative (%)	X^2df	p Value	
Age of first (N=203)				10.513	4
0.0326					
pregnancy					
16-25yrs	8(3.94)	58(28.6)			
26-35yrs	2(0.99)	135(66.50)			
36-45yrs	0(0.00)	0(0.00)			
46-55yrs	0(0.00)	0(0.00)			
56-65yrs	0(0.00)	0(0.00)			
Use of steroid (N=203)				6.565	1
0.0104					
contraceptive					
Yes	5(2.46)	34(16.75)			
No	5(2.46)	159(78.33)			
Parity (N=203)				11.792	2
0.0028					
≤2	1(0.50)	44(21.89)			
≥3 to5	3(1.49)	117(58.21)			
>5	6(2.99)	32(14.93)			

P < 0.05 is significantly different
df- degree of freedom
X^2– Chi square
N- Number of participants

Table 5 Association between tobacco usage, alcohol usage and cervical intraepithelial neoplasia

	Positive (%)	Negative (%)	X^2df	p Value	
Tobacco usage			0.215	1	0.6429
Yes	0(0.00)	4(1.97)			
No	10(4.93)	189(93.10)			
Alcohol usage			9.042	1	0.0026
Yes	4(1.97)	18(8.87)			
No	6(2.96)	175(86.21)			

$P < 0.05$ is significantly different
df- degree of freedom
X^2– Chi square

Discussion

The prevalence of 4.93% abnormal cytology in this study is similar to that reported by Durowade et al [7] in Kwara state, who reported a prevalence rate of 5% for CIN. Results from this study shows that 50% of the CIN present were made of low grade squamous intraepithelial lesions (LSIL). The high level of LSIL is in tandem with results obtained by Obaseki and Nwafor [8] where LSIL accounted for the highest percentage (66.27%) of abnormalities found. Unlike in the works of Obaseki and Nwafor [8], Odusolu et al [9] and Thomas et al [10], high grade squamous intraepithelial lesion, atypical endocervical cells not otherwise specified, atypical endocervical cells neoplastic and adenocarcinoma were not present in this study.

Majority of the women who participated in this study were young and middle-aged women which is largely due to the fact that majority of women attending the Obstetrics and Gyneacological clinic belong to the child bearing age, which is largely embedded in this age group. Also, in a similar study, Odusolu et al [9] and Mbamara et al [6] recorded 66.6% and 80.6% respectively, for the occurrence in subjects within this age group of 25-44yrs. A large proportion of the subjects had a form of education. This is largely due to the fact that nurses in the Federal Medical Centre participated in the study in large numbers, as the test was made at no cost to the participant. Obaseki and Nwafor [8] acknowledged that University of Benin Teaching Hospital staffs were among the first major set of participants in a similar study. The presence of high number of participants with formal education corresponds to those that participated in a similar study as reported by Mbamara et al [6] where over 98% of the study population had formal education. Religion among the subjects was almost evenly split between Christians and Muslims, which reflected the prevailing religions in the study area which is largely dominated by Christians and Moslems. There was a statistical difference ($P<0.05$) between the religions of the subjects. This supports the result of Oche et al [11]

were Christians, Muslims and other religion accounted for 52.7%, 46.4% and 0.9% respectively. The region of residence also shows that 92.12% of the study population resided in the North central region of Nigeria. This is attributed solely to the location of the hospital where the study was carried out, which is in Lokoja a city in the North central region.

Age is usually regarded as a critical risk factor in HPV infection and CIN and cervical cancer development. In this study, there was a statistical relationship ($p = 0.015$) between the incidence of abnormal cytology and the age of the respondents. There was a clear indication that the incidence of CIN increased with age, with the only case of squamous cell carcinoma present in subject within the ages of 56-65yrs. It clearly follows the pattern described by Clifford et al [12] and is in consonance with the works of Plummer et al [13].

No association was found between the marital status, type of marriage and development of CIN or cervical cancer amongst the subjects. The result is similar to that reported by Durowade et al [7] in Kwara state, which reported that there was no significant relatedness in the marital status and the development of abnormal cytology. Also, Ibrahim et al [14] in Sudan reported no significant correlation between marital status and the development of cervical cancer.

In this study, it is clearly shown that subjects whose male partners were not circumcised were at a higher risk of developing CIN or cervical cancer; this is similar to what was obtained by Durowade et al [6]. With 70% of subjects having CIN being among subjects who debuted sexually at ages lower than 15yrs, it was clear that coitarche was a major risk factor in the development of CIN and cervical cancer. There was a direct statistical correlation ($p=0.0046$) between the age of sexual debut of the subjects and development of abnormal cytology. This fully agrees with the works of Averette and Nguyen [15]; Durowade et al [6] and Schiffman et al [16].

Having a previous history of genital infection was not considered a significant risk factor ($p=0.8744$) for the development of abnormal cervical cytology in this study. Although this was in consonance with reports by Durowade et al [6] in Kwara State Nigeria and a similar study in Turkey [17].

It was observed in this study that the risk of developing CIN increased as the number of sexual partners of the subjects increase. There was a direct statistical correlation ($p=0.001$) between this risk factor and presence of abnormal cytology. This was a common phenomenon reported in similar studies of Ojiyi et al [18], Schluterman et al [19], Durowade et al [6], and Thomas et al [10].

The age of first pregnancy, steroid contraceptive usage as well as parity, were all regarded as potential risk factors for the development of CIN and cervical cancer. Despite a greater proportion of the participants 67.49% in this study had their first pregnancy between the ages of 26-35 yrs, 80% of CIN was found among subjects with age of first pregnancy between 16-25 yrs. This result agrees with the work of Reis

et al. [17] but is in contrast with the works of Thomas et al [10]. Although the percentage of the subject that utilized steroid contraceptive was generally low among the subjects, 50% of those with abnormal cervical cytology were found among these subjects. This study showed that respondents with parity greater than five had the highest number of abnormal cytology, accounting for 60% of the cases. Multiparity is believed to be a risk factor for cervical cancer, especially among human papillomavirus (HPV) positive women [20].

Tobacco smoking was not regarded as a considerable risk factor in the development of CIN in this study. Only 4 (1.97%) of the subjects indicated they had a history of tobacco use, with all 4 (1.97%) negative for abnormal cervical cytology. This was not consistent with hypothesis by Winkelstein [21], and results reported by Plummer et al [13] which found a direct relationship between smoking, HPV infection and cervical cancer. Alcohol usage was recorded as a critical risk factor in this study. With only 22 (10.84%) of the subjects indicating they utilized alcohol, 40% of the cases of abnormal cervical smear were found amongst this group which supports the works of Reis et al [17].

This study has clearly shown that women in Lokoja, Nigeria are increasingly becoming at a risk of developing cervical intraepithelial neoplasia and cervical cancer. Due to the low level of awareness about cervical cancer and low uptake of cervical screening, there should be a well-coordinated cervical cancer screening programme targeted at risk groups. The lack of a cancer registry in Nigeria WHO [5], means researchers have to rely on studies like this done in the country or other developing countries with similar developmental and socio-demographic status, for information and statistics with regards to the development of cervical cancer or CIN.

Conclusion

The major risk factors associated with development of CIN among the respondents are age of the women, male partner circumcision, age of first pregnancy, use of steroid contraceptive, alcohol usage and multiple sexual partners. A need thus exists for making a population based screening programmes readily available, increased opportunities such as this study which to the best of our knowledge is the first of its kind in the study location be used to help reduce cervical burden index. There is therefore the need to make the screening services more affordable, acceptable and accessible to the majority of women who need the services especially those who leave in the rural areas and the urban poor.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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