RISK FACTORS FOR CERVICAL DYSPLASIA IN AMINU KANO TEACHING HOSPITAL

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ABSTRACT

Background: *Cancer of the cervix remains the commonest cancer of the female genital tract in developing countries. Ironically, it is preventable by a well established screening program. A study of the risk factors will be needed in order to determine the group of women among whom cervical cancer screening should be further emphasized.*

Objective: *To determine the risk factors of dysplasia among a cohort of women in Aminu Kano Teaching Hospital, Kano Nigeria.*

Method: *A cohort study of 550 women, who attended the gynaecological clinic of Aminu Kano Teaching Hospital, between January 2008 and December, 2010.*

Results: *The period incidence for abnormal pap smears in this study was 11.6%. Age ≥ 35years and parity ≥ 5, age at coitarche, first marriage and first childbirth ≤ 18 years, multiple marriages, divorcees, low educational and socioeconomic statuses, family history of cervical cancer, previous history of excessive vaginal discharge, and Human Immunodeficiency Virus infection (HIV) /Autoimmune Deficiency Syndrome (AIDS) did confer some risk of dysplasia, while women in first order marriage, single, widows, use of hormonal contraception, intermenstrual vaginal bleeding, cigarette smoking, history of genital warts did not.*
Conclusion: *These groups of high risk women should be encouraged to have mandatory cervical cancer screening 3 years after coitarche.*

Key words: *Pap smear, risk factors, Aminu Kano Teaching Hospital.*

INTRODUCTION

Cancer of the cervix still remains the commonest cancer in developing countries like Nigeria, because of high prevalence of sexually transmissible diseases (STDs), and poor awareness about and paucity of cervical cancer screening programs in most of the communities, with a resultant effect that most of the women present late, with invasive cancer of the cervix, when curative treatments are usually not feasible[1-4]. In developing countries, low socioeconomic status put strain on the moral virtues that have been acquired by the men and women[1].

The role of sexually transmissible infections as causative agents in cancer of the cervix, is gaining prominence with the recent evidences that some serotypes of Human Papiloma Virus (HPV) (types 16 and 18), are responsible for the malignant transformation that occur at the transformation zone of the cervix in affected patients[5,6]. The causal link between cancer of the cervix and specific serotypes of HPV (16 and 18), is because the Deoxyribonucleic acid (DNA) of these serotypes of the virus has been found in majority of the cases[5,6].

Early girl marriage, which refers to any form of marriage that takes place before a girl child has reached 18 years, is common in developing countries[7]. In early girl marriage, the young girls who are particularly vulnerable to cancer of the cervix, are most likely to be forced into having sexual intercourse with their usually older husbands, who are more likely to be sexually experienced and HPV infected, because HPV is a very common infection, and over 75% of sexually active men and women are thought to

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have acquired the virus at one point or another[8] and these young girls are particularly vulnerable to cancer of the cervix, because of their softer vaginal membranes which are more prone to infections, and the dynamic nature of the transformation zone during this period of life[8].

The social structure in developing countries where there is gender inequality, which makes the men take primary responsibility and dominate in their households, encourage multiple sexual partners for men inside and outside of marriage, with reluctance to use condoms during casual sex, while women are required to be faithful and monogamous. Such socio-cultural practices and norms make marriage to put women at the greatest risk of HPV infection instead of protecting them[8].

Further, masculinity demands that men be sexual risk-takers, with reluctance to use condoms during casual sex, because of lack of knowledge of HPV, and these practices put men and female partners at risk of HPV infection. In this context, the dangers of multiple sexual partners, relates to the fact that if one person among the partners gets infected with HPV, there is a very high likelihood that all persons involved will be infected[8].

Among the sexual risk factors or manifestations, that have been reported to be associated with increased risk of precancerous lesions called squamous intraepithelial lesion (SIL) or cervical intraepitheliail neoplasia (CIN), or early stage of cancer of the cervix, include, age more than 35 years, low socioeconomic class, women with low literacy levels, early age of coitarche/marriage/first childbirth, high parity, women who engaged in risky sexual behaviours like multiple sexual partners, polygamous marriages, divorce and remarriages, drug abuse like alcoholism, cigarette smoking, use of hard drugs, family history of cervical cancer, vaginal discharge/abnormal bleeding, use of hormonal contraceptives, previous/present history of sexually transmissible infection(s), especially genital warts, HIV infection/AIDS[6].

The risk of development of CIN III was 8 fold higher among women with multiple sexual partners, while among women whose coitarche was less than 20 years, the risk of development of CIN III was 2-5 times greater than among women whose age of coitarche was more than 20 years. Smoking of more than 20 sticks a day increases the risk of CIN III by 3-4 folds, hormonal contraceptives increases it by 2 folds, parity increased the risk from 0.8% among nullipara to 1.4% among para 5 or more[6,9,10].

The progression of CIN is variable, because it may regress back to normal, persist or progress to invasive cancer. Progression from CIN I to the invasive form also varies, and may be between 7-14 years, a window that leaves time for the detection of the lesion in the pre-invasive or early invasive stage when curative rather than palliative treatments can be offered in communities with good cervical cancer screening programs[10,11].

The Papanicolaou test, also called Pap smear, was invented by and named after the prominent Greek doctor, Georgios Papanikolaou in 1940, and has not been significantly modified since it was first discovered, is a screening test that is used to detect pre-cancerous and early cancerous processes in the endocervical canal (transformation zone) of the uterine cervix, at this stage when it can be treated, thus preventing development of invasive cervical cancer[10-13]. The test remains an effective, widely used method for early detection of pre-cancer and cervical cancer[11]. A regular program of cervical cancer screening, with appropriate follow-up, has reduced the incidence of invasive cervical cancer by up to 80% in developed countries[11-13].

The Pap smear screening is a routine test, which is recommended for females who have had sex, but it is advised to start 3 years after

coitarche, which corresponds to an average the age of about 21 years in the USA and 25 years in the UK[10-12]. It has not been found to be cost effective among women who have not had sex[11]. Guidelines on frequency vary from every three to five years following a normal test[12]. If results are abnormal, and depending on the nature of the abnormality, the test may need to be repeated in six to twelve months[10]. If the abnormality requires closer scrutiny, the patient may be referred for detailed inspection of the cervix by colposcopy[14].

No study has been conducted on the risk factors of abnormal pap smears at Aminu Kano Teaching Hospital. It is against this background that this study was designed to determine the risk factors of abnormal pap smears at Aminu Kano Teaching Hospital, in order to determine the group(s) that further emphasis should be placed in our cervical cancer screening program, and ensure that we reap the maximum advantages of cervical cancer screening in our community.

METHODS

A prospective cohort study of 550 women who attended the gynaecological oncology outpatient clinic of Aminu Kano Teaching Hospital with gynaecological problems, and were referred for pap smear between January 2008 and December 2010. The women were counseled about the study, and those that gave consent were recruited for the study. The exclusion criteria were women who did not give consent for participation, those who were menstruating or currently with abnormal vaginal discharge and those with invasive carcinoma of the cervix.

The Pap smears were collected in the cytological unit in our hospital, between day 10 and 20 of the menstrual cycle among premenopausal women. The women were told to avoid for at least 2 days, douching or vaginal insertion, like spermicidal foams, creams or jellies of vaginal medicines which could wash away or hide any abnormal cervical cells. The women were counseled about the procedure and informed consent was obtained.

The collection of the Pap smears were carried out with the women in dorsal position by inserting a speculum which was lubricated with sterile water, to avoid unnecessary discomfort, into the woman's vagina. This was used to spread the vagina open and allow access to the cervix. A sample of cells from the transformation zone was collected by scraping it with an Aylesbury spatula. An endocervical brush was rotated in the central opening of the cervix. The cells were smeared on glass slides and fixed in 95% alcohol, before they were taken to the Histopathology laboratory for cytological examination by the Pathologists.

The Bethesda terminology (2001) for cytologic reporting was used in this study. Normal smears were cases where there was no dyskaryosis, and were designated as negative smears, while abnormal smears were cases where there was dyskaryosis, and were designated as squamous intraepithelial lesion (SIL), with two sub-classifications, the low grade squamous intraepithelial lesion (Low SIL), for lesions that were previously classified as koilocytic atypia and/ or CIN1, and high grade squamous intraepithelial lesion (High SIL) for lesions that were previously classified as CIN2 or 3. Undefined cases were designated as Atypical Squamous Cell lesion of Undetermined Significance (ASCUS), and they had repeat pap smear 6 months later to classify them into one of the SIL groups.

The study variables of interest were age and parity of the women, age at coitarche, marriage and first childbirth, marital status, number of sexual partners, educational and socioeconomic status, family history of cervical cancer, history of vaginal discharge, abnormal vaginal bleeding, previous genital warts or HIV/AIDS infection, use of hormonal contraceptives, or cigarette smoking, and the

results of the pap smear test, to determine the group of allocation. The socioeconomic status of the women was determined by their educational status and the husband's occupation.

Sample Size Determination

Bukar et al [10],in a study from Maiduguri in Nigeria, found a prevalence rate of 7.8% for dyskaryosis among the women who attended their gynaecological clinic. Using the result obtained in the study above, and accepting a study power of 80%, confidence interval of 95%, and an acceptable dropout rate of 5%.

$$n = \frac{Z^2 P(1-P)}{d^2}$$

where n = sample size,
Z = Z statistic for a level of confidence,
P= expected prevalence or proportion, and
d = precision.

$$= \frac{1.96^2 \times 0.078\ (1- 0.078)}{0.05^2}$$

$$= \frac{3.84 \times 0.0719}{0.0025}$$

= approximately 110 respondents.

Multiply by a factor of 5.0, because of the expected high number of Pap negative cases among the study population.

n = 110 × 5.0 = 550 patients.

The data obtained were recorded on a pre-tested questionnaire that was designed for the study, and were entered into Microsoft excel data base, and statistical analysis was done using EPI INFO version 6.0 software packages. Chi square and Fisher exact tests were used to test associations, and level of significance was set at $P < 0.05$.

RESULTS

During the study period, 550 patients had Pap smear, among them 64 patients had abnormal Pap smear, giving a period incidence of 11.6% for precancerous lesions of the cervix, among the cohort of women who attended the gynaecological oncology clinic.

Dyskaryosis showed significant association with high parity (≥ para 5) ($P < 0.001$), no formal literacy ($P < 0.001$) and socioeconomic status ($P < 0.001$), age at first marriage ($P < 0.001$), coitarche ($P = 0.019$) and first childbirth < 18 years ($P < 0.001$), women ≥ 35 years ($P < 0.001$), high parity ≥ 5 ($P < 0.01$). In the marital status, dyskaryosis was significant among women who were in polygamous marriage ($P = 0.028$), divorced ($P = 0.023$), and in second or more order of marriage ($P = 0.043$), previous history of excessive vaginal discharge ($P < 0.001$), family history of cancer of the cervix ($P < 0.001$), and HIV/AIDS infection ($P < 0.001$). However it did not show significant association with women who had abnormal vaginal bleeding ($P = 940$), used hormonal contraceptives ($P = 0.597$) or had genital warts ($P = 0.055$). There was no case of use of alcohol or cigarette smoking among the women.

DISCUSSION

The period incidence of 11.6% among a cohort of women in this study, is similar to 7.8% from Maiduguri[1], and 9.0% from India,[6] which are resource poor countries, but it is lower than 1.2% from Saudi-Arabia[15] a resource rich country. This may probably be because cervical dysplasia is caused by infection of the cervix with the HPV, and there is a higher prevalence of STDs in developing countries, because of risky sexual behaviours that are common among the poor and illiterates that are more prevalent in these regions[10].

Early girl marriage, early age at coitarche and age at first child birth, which are closely relayed, were found to be significant risk factors in this study, which agrees with the findings of other studies from developing countries[1,2,6]. This may be because early girl' marriage which is common in developing countries for socio-cultural and religious reasons severely increases these young girls' vulnerability to cancer of the cervix, because of the dynamic nature of the transformation zone during this period of life, and the softer vaginal membranes, which are more prone to infections[8].

High parity, low literacy and socioeconomic status, were a triad that were found to be significant risk factors in this study, which was also the findings of other authors [1,6]. This has been attributed to the close association between these factors and early girl marriage[1], because the illiterates and the poor are those that commonly engage in early girl marriages, are averse to modern contraception, with low contraceptive prevalence rates and high parity.[8]

Divorce and multiple marriages, vaginal discharge and HIV/AIDS infections were found to be significantly associated with cervical dysplasia in this study, and other studies from communities where women marry early. [1]This may be because these factors are closely associated with low literacy and socioeconomic status of the women[6]. Low socioeconomic status which is prevalent in developing countries, put strain on the moral virtues that have been acquired by the men and women, with the implications of risky sexual behaviours and other well established risk factors of cervical cancer like divorce and multiple marriages with its implications of multiple sexual partners, poor personal and sexual hygiene and vaginal discharge, and HIV/AIDS infections[8].

Maternal age >35 years, was found to be a significant risk factor in this study, which agrees with other studies[2]. This may be because some HPV infections persist over time rather than resolve, and persistent HPV infection has been shown to play a causal role in the development of precancerous changes (dysplasia) of the uterine cervix, as well as cervical cancer[5,17]. The reason why the infection persists in these women is not fully understood, but advancing age is one of the factors that may influence persistence of the infection[17].

Family history of cancer of the cervix among first degree relatives was found to be a significant risk factor in this study, which agrees with other studies [1,6], and has been attributed to inherited factors that have been implicated in the development of cancer of the cervix[6].

Previous history of vaginal discharge was found to be a significant risk factor in this study, which agrees with the findings of other studies[1,2]. This has been attributed to its being one of the major criteria in the diagnosis of Pelvic Inflammatory Disease, which is commonly associated with STDs, that are implicated in the development of cervical dysplasia and cancer of the cervix [6.8]. Vaidya found a correlation between moniliasis and trichomoniasis, which are associated with vaginal discharge, and development of dysplasia.

The association between HIV/AIDS and cervical dysplasia, may be because it is a sexually transmitted disease like the causative agent HPV, and both are commonly found in women with the risk factors [8]. Immunosuppression that is caused by HIV/AIDS encourages proliferation and growth of HPV, and the resultant effect is development of cervical dysplasia[8].

History of genital warts was not found to be significant risk factors, which agrees with other studies.[6]This may be because HPV infection is common in most populations of the world, and it affects 75% of most of the populations, but in most cases the body's immunity suppresses it and prevents the cutaneous manifestations[8].

Cigarette smoking was not found among any of the women in this study, probably because female cigarette smoking has been found not to be common among our women in our predominantly Islamic community.[7]This did not agree with the findings of other studies from communities where cigarette smoking is common among women[18]. Studies have shown that smoking of more than 20 sticks a day is required to increase the risk of severe dysplasia by 3-4 folds, and dysplasia has been found to be to be about 2-5 times more prevalent among smokers. Also, tobacco related substances have been isolated in the cervical fluid of smokers, and may be a co-factor to an earlier viral infection, in the development of cervical dysplasia[6,18].

Abnormal vaginal bleeding was not found to be a significant risk factor in this study, which

does not agree with other studies[2,6]. This may probably be because injectable contraceptives, which are associated with abnormal vaginal bleeding, are the commonest method of contraception that is used in our hospital[19].

Hormonal contraception did not confer risk of cervical dysplasia in this study, despite hormonal injectable contraceptives being the

Table 1: RELATIONSHIP BETWEEN RISK FACTORS AND DYSKARYOSIS IN AMINU KANO TEACHING HOSPITAL.

Variable	Dyskaryosis		Test	P-value
	Yes n= 64 (%)	No n= 486 (%)		
Age				
≤ 35	3 (9.1)	252 (10.3)	Fisher exact	0.787
≥ 35	61 (60.9)	234 (63.0)	Chi-square	< 0.001*
Parity				
≤ 4	9 (27.3)	284 (25.5)	Chi-square	0.639
≥ 5	55 (40.9)	202 (40.0)	Chi-square	< 0.001*
Educational Status				
No Formal Education	38 (18.2)	83 (7.0)	Chi-square	< 0.001*
Primary/Secondary	17 (45.5)	248 (43.3)	Chi-square	0.743
Tertiary education	9 (29.0)	155 (31.5)	Chi-square	0.230
Socioeconomic Status				
Low	52 (40.9)	268 (29.7)	Chi-square	< 0.001*
High	12 (47.3)	218 (40.0)		
Age at Coitarche				
< 18	44 (9.1)	254 (10.3)	Chi-square	0.019*
≥ 18	20 (9.1)	232 (10.3)		
Age at First Order Marriage				
< 18	48 (9.1)	226 (10.3)	Chi-square	< 0.001*
≥ 18	16 (9.1)	260 (10.3)		
Age at First Childbirth				
< 18	49 (9.1)	224 (10.3)	Chi-square	< 0.001*
≥ 18	15 (9.1)	262 (10.3)		
Marital Status				
First order marriage Monogamy	4 (9.1)	148 (10.3)	Chi-square	< 0.001**
Multiple marriages /Polygamy	46 (9.1)	275 (10.3)	Chi-square	0.028*
Single	1 (9.1)	2 (10.3)	Fisher exact	0.311
Divorced	8 (9.1)	24 (10.3)	Fisher exact	0.023*
Widowed	5 (9.1)	37 (10.3)	Fisher exact	1.000
Multiple Sexual Partner(s)	8 (9.1)	25 (10.3)	Chi-square	0.043*
Previous history of excessive vaginal Discharge	61 (9.1)	287 (10.3)	Chi-square	< 0.001*
Abnormal vaginal bleeding	13 (9.1)	105 (10.3)	Chi-square	0.940
Use of hormonal contraceptives	38 (9.1)	234 (10.3)	Chi-square	0.597
Family history of cervical cancer	16 (9.1)	1 (10.3)	Chi-square	< 0.001*
History of genital warts	3 (9.1)	5 (10.3)	Chi-square	0.055
History of HIV/AIDS	8 (9.1)	4 (10.3)	Chi-square	< 0.001*

*Statistiacally significant for dyskaryosis.
** Statistiacally significant for normal smear.

commonest method of contraception that is used in our hospital. This did not agree with the findings of some studies [20], which may probably be because the issue of a causal association between injectable contraceptive use and cervical cancer is as yet unresolved, and will require the accumulation of additional data. To date, World Health Organization study found that only a small number of women have used Depomedroxyprogesterone acetate (Depoprovera) for prolonged periods, or have had a long interval since first use[21]. Information on cancer risk in these women can only be gained by initiating additional studies that is focused on these specific topics[21].

CONCLUSION AND RECOMMENDATIONS

The period incidence for abnormal pap smears in this study was 11.6%. The significant risk factors for abnormal pap smear among a cohort of women that attended the gynaecological oncology clinic in Aminu Kano Teaching Hospital are, age ≥ 35years and parity ≥ 5, age at coitarche, first marriage and first childbirth ≤ 18 years, polygamy and multiple sexual partners, low educational and socioeconomic statuses, family history of cervical cancer, history of excessive vaginal discharge, and infections with HIV. These groups of women should have mandatory cervical cancer screening starting from three years from when they become sexually active. Women without risk factors should also have cervical cancer screening from three years from when they become sexually active, and cervical cancer screening should be made mandatory among them from the age of 35 years and above. Female education and empowerment to control male gender dominance, as well as community education about the risky socio-cultural and sexual behaviours, and their repercussions on reproductive health of the women will be necessary, in order to reduce the incidence of abnormal pap smears and cancer of the cervix in the community.

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