The Influence Of Reproductive Factors On Genital Human Papilloma Virus

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Citation

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Abstract

Aim: To study the association between reproductive factors and human papilloma virus (HPV) of the cervix.Method: The subjects were 450 randomly selected sexually active women attending the antenatal, postnatal, gynaecology and family planning clinics in the Department of Obstetrics and Gynaecology of the University of Maiduguri Teaching Hospital, Nigeria between April 2001 and May 2002. The Pap smears of these patients were examined microscopically for evidence of HPV Infection. Questionnaires assessing various marital characteristics of the patients were administered.Result: Abnormal smears occurred in 245 (54.5%) of the patients screened. Forty eight women (10.7%) had HPV associated changes constituting 19.6% of all abnormal smears. Their ages ranged between 15 and 64 years, with a mean of 26±3 years. There was a statistically significant association between reproductive factors and genital HPV infection.Conclusion: Multiparous women and women on contraceptives are at increased risk of acquiring infection of the cervix and should be the target in a sporadic or an organized cervical cancer screening program without discriminating other sexually active women.

INTRODUCTION

As of 2000, cervical carcinoma was responsible for 466,000 deaths per annum worldwide and is the leading cause of death in middle aged 34-35 years[16]. It was the most common malignancy among women in Nigeria and the rest of the sub-Saharan Africa with a very poor 5-year survival rate. [7,8,18,19]

In Benin, Nigeria, carcinoma of the cervix made up 74.6% of all cases of malignant gynaecological tumors, with stage IIb and above constituting 67.6% of the cases[8]. It accounted for 66.2% of all gynecological malignancies in Zaria Nigeria, with advanced carcinoma of the cervix, stage IIb and above, making up 88.7% of the cases[7]. In Kenya, 55% of women with cancer of the cervix presented with stage III disease and beyond[19].

In 1842, Rigoni- Stern formally hypothesized that cervical cancer had an infective sexually transmitted aetiology[18]. Many studies since then have confirmed the venereal nature of cervical cancer and identified other risk factors. The most exciting development has been the finding that infection with human papilloma virus (HPV) is casually associated with cervical cancer[3,18,].The HPV has been shown to be a determinant of the natural history of cervical intraepithelial neoplasia (CIN). The progression to cervical cancer when HPV co-exists with CIN is about 21% but only 5.6% when CIN lesions occur alone[24].

Many studies have tried to show some kind of association between reproductive factors and the risk of developing HPV and cervical cancer[12]. Such socio-demographic factors may be useful in risk scoring. This is important because risk scoring systems have the potential for assisting the targeting of screening resources, as broad risk targeting of all sexually active women is not a viable option for developing countries due to paucity of both human and financial resources. Even in the industrialized nations of the West, the need for more precise targeting of high risk groups in other to improve the efficiency of cervical cytology programs and conserving funds have become a major issue[15].

The manifestations of HPV infection of the cervix may be clinical or sub-clinical.

Sub-clinical HPV infections of the cervix may be diagnosed by colposcopy, viral and hybridization, polymerase chain reaction (PCR) amplification, histology or by characteristic HPV changes on Papanicolaou smear[12,16].The Papanicolaou smear for cervical cytology fulfils all the criteria for an ideal screening test. Not only is it cost effective, acceptable to most patients and adoptable to wide spread screenings, it is

specific enough to detect HPV changes and subsequent progression to CIN resulting in decreased morbidity and mortality from invasive cervical cancer[11]. DNA hybridization and PCR amplification can detect productive and non- productive infection but appear to be of limited value in predicting the risk of developing CIN or invasive carcinoma[16]. Although cervical cytology, histology and colposcopy are less sensitive, they are capable of detecting significant changes pathological changes associated with productive CIN infection[16].

This study looks at the use of a low cost effective technology such as the Papanicolaou smear to show some kind of association between reproductive factors and human papilloma virus infection of the cervix

SUBJECTS AND METHODS

The subjects were 450 randomly selected sexually active women attending the antenatal clinics in the Department of Obstetrics and Gynaecology of the University of Maiduguri Teaching Hospital, Nigeria, between April 2001 and May 2002. They were recruited after consenting to participate and a formal approval had been given by the institution's Ethics and Research Committee. The recruitment continued until a sample size of 450 was reached. This was calculated using the WHO Epi Info Version 6 program for population or descriptive study using simple random sampling.

It was based on a population of 4,342 patients/clients attending the recruiting clinics from April 2001 and May 2002. The purpose, nature and value of the procedure were explained to each prospective patient and her consent sought. All consenting patients had pap smears taken using a moistened unlubricated Cusco's bivalve speculum and an Ayre's wooden spatula after a questionnaire containing the age and reproductive factors had been filled. The smears were immediately transported to the histopathology laboratory immersed in 95% ethanol for preparation, staining and reading. The smears were examined microscopically by a pathologist at the magnifications of 4, 10 and 100.

The WHO Epi Info statistical programme was used to compute and analyze the results. These included frequency distribution and tests of significance using Chi-square (χ^2).P value of <0.05 was taken to be significant.

RESULTS

Four hundred and fifty women attending various clinics at the Department of Obstetrics and Gynecology, University of Maiduguri Teaching Hospital had their Pap smears taken and questionnaires on marital factors filled. The cytology results of the Papanicolaou smears are shown in Table 1. Abnormal smears occurred in 245 (54.5%) of the patients screened (Table 1). Forty-eight women (10.7%) had HPV associated changes, constituting 19.6% of all abnormal smears. The ages of the patients screened are shown in Table 2. Their ages ranged between 15 and 64 years with a mean of 26±3 years.

Table 3 shows the association between reproductive factors and human Papilloma virus infection of the cervix. There was a statistically significant association between multiparity, contraceptive use and genital HPV infection (P<0.01).

Figure 1

Table1. Cytology report of Pap smears

Class of Papanicolaou smear	Number	Percentage
Normal	205	45.6
Inflammatory	124	27.6
Cervical dyskaryosis	73	16.2
Human Papilloma virus changes	48	10.7
Total	**450**	**100**

Figure 2

Table 2. Age distribution of the women screened

Age (Years)	Number	Percentage
15-19	60	13.3
20-24	158	35.1
25-29	138	30.7
30-34	53	11.8
≥35	41	9.1
Total	**450**	**100**

- Range =15-64; Mean= 26±3 years

Figure 3

Table 3. Association between reproductive factors and human Papilloma virus infection of the cervix

Variable	Positive	Negative	Total
1 Parity			
Non-parous	7	143	150
Parous	41	259	300
Total	48	402	450
X^2 8.44, df=2, P=0.00			
2 Contraception			
None	8	304	312
Hormones	22	86	108
Intrauterine Contraceptive device	16	10	26
Others	2	2	4
Total	48	402	450
X2 for linear trend=85.14, df=4,P=0.00			

DISCUSSION

The clinical course of HPV infection may be regression, persistence, progression or recurrence [24]. When it progresses, it passes through the precursor lesions of the cervical intraepithelial neoplasia to invasive carcinoma of the cervix[24]. In spite of its high case-fatality rate, cancer of the cervix has up to 100% cure rate if detected early[24].Identifying women with HPV infection of the cervix and following them to monitor their progression to CIN and appropriately managing these precursor lesions will in most cases eliminate invasive disease.

Reproductive factors such as repeated child bearing, especially grandmultiparity [1,9] as well as early age of first pregnancy[5,18] have both been identified to increase the risk of developing cervical cancer. They probably reflect early sexual exposure, although not necessarily so with grand multiparity. Early age of first pregnancy, early marriage, early sexual exposure, marital instability and subsequent multiple partners through remarriages or otherwise are all closely related with synergic effects. They all increase the chances of acquiring sexually transmitted diseases, including HPV.

Contraceptive use, especially the non-barrier methods, have been implicates in cervical cancer[23,24]. This is however by no means universally acknowledged [22,23], except in as much as contraceptive methods promote having multiple sexual partners and genital HPV infection by conferring 'safety' against pregnancy.

There was significant association between contraception, duration of contraception use and cervical HPV infection Hormones and their metabolites have been implicated as co-factors in HPV proliferation and the cervical cancer pathogenesis[14,25]. In their work Von Kenbel Doeberitz et al,(1997), suggested an association between HPV infection and the long term use of oral contraceptives in the genesis of cervical cancer. Progesterone and oestrogen responsive elements were identified in the upstream regulatory region (URR) of HPV 18 of transgenic mice and in other anogenital HPV types, particularly the high risk types, which mediate the response of the enhancer to steroid hormones. Progesterone can also suppress the class 1 human leukocyte antigen (HLA) positive cervical cells.

The effect of contraception might also be secondary to multiple sexual partners due to the 'safety' proffered against pregnancy [22]. Those who had used contraceptives for ≥6 years had ten times a greater risk tan those using contraceptives for less than one year irrespective of the method used, probably buttressing increased sexual promiscuity with contraceptives. There was virtually total absence of use of barrier contraception and hence of any theoretical protection they might provide. Barrier contraceptives such as condoms are less likely to be effective in preventing infections such as genital HPV which can involve skin not covered by a barrier contraceptive.

Studies which have attempted to asses male condom benefit for women have generally found no evidence of protection against infection[2,5,10]. There is data suggesting a benefit of condom use for men although the studies have not adequately assessed consistency and correctness of condom use. Therefore condoms should be used, if only for prevention of other sexually transmitted diseases[24].

Multiparous patients in this study stand a statistically significant risk of acquiring genital HPV infection compared to their non-parous counterparts. Multiparity, probably reflect early sexual exposure. Early age of pregnancy, early marriage, early sexual exposure, marital instability and subsequent multiple sexual partners through remarriages or otherwise are all closely related with synergic effects. They all increase the chance of acquiring sexually transmitted diseases, including HPV[4,18]. This is in agreement with the works of Schiffman et al (1997) and Lorenzato et al (2001), who found multiparity to be a risk factor for cervical HPV

infection. The two major limitations of this study are:

The fact that it was a hospital based study and it was opportunistic. These limitations must be borne in mind when making generalizations to the general population.

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