

Risk of cervical cancer associated with HPV infection among the gynae outdoor patients

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Abstract

Human papilloma virus is an oncogenic DNA virus, which is identified in 99.7% case of invasive cancer. It is the most prevalent virus involved in sexually transmitted diseases worldwide and an important public health challenge for the prevention of cervical carcinoma. Cervical cancer is the second cause of malignant neoplasia and death in women. The present study was thus designed to detect the risk factors for HPV infection in normal and unhealthy cervix of women attending tertiary care hospital (BSMMU). HPV DNA was detected among the study population using the Hybrid Capture 2 assay, which determined HPV high risk types. A total of 68 women between 25-70 years of age were included in this cross sectional study. Among them 13 (19.1%) cases were tested positive for HPV DNA. The risk factors for HPV infection identified from this result are early sexual activity, lower level of education, early marriage, multi-parity, total duration of sexual activity in years and long term use of oral contraceptive pill and poor socioeconomic condition. Increased awareness and understanding regarding HPV infection would improve the risk of infection and control in sexually active women. HPV diagnosis at early stages of infection is of fundamental importance. The use of HPV test in routine cervical mass screening may not be possible in developing countries like Bangladesh due to its high cost. Nevertheless, it has been shown to be a useful tool when combined with cytology to diagnose high-risk infection in apparently normal tissues, and may help to reduce the risk of cervical cancers. The results obtained from this study ultimately contribute to cervical cancer prevention among Bangladeshi women.

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Introduction

Worldwide, cervical carcinoma ranks second among the common cancers in women.¹ Human papilloma virus (HPV) is associated with cervical cancer. This virus is predominantly sexually transmitted and is a high-risk factor for development of cervical carcinoma.²⁻³ Persistent infection with certain genotypes of carcinogenic HPV is associated with nearly all cases (99.7%) of cervical cancers.⁴ Among 130 genotypes 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59 and 68 types are "high risk" HPVs. Globally, HPV 16 and 18 contribute to over 70% of all cervical cancers and HPV types 31, 33, 35, 45, 52 and 58 are responsible for an additional 20% of cases.⁵

The global incidence of cervical cancer is estimated as 4,70,600 cases per year with approximately 2,33,400 deaths.⁶⁻⁷ Almost 80% of the cases of cervical cancer occur in the developing countries.⁶ The highest incidence of cervical cancer are observed in Latin America,

Caribbean, sub-Saharan Africa, South and South east Asia.⁷ In the United States, HPV is the most common sexually transmitted infection.⁸ Prevalence of human papilloma virus infection among the general populations varies from 7%-14% in India, Bangladesh, Nepal and Sri Lanka.⁹ Hospital based statistics indicate that cervical cancer constitutes 22%-35% of the female cancers in different areas of Bangladesh and India.¹⁰⁻¹¹ HPV prevalence is related to some risk factors of the patients. Demographic, cultural, socioeconomic variables, multiparity, long term contraceptive use, young age at first coitus, multiple sexual partners, low socioeconomic status, low education level, poor genital hygiene, cigarette smoking, genital tract infections etc, are probable co-factors that increase the risk of cervical cancer with HPV infection.¹²⁻¹⁴

Low socioeconomic status has proven to be a significant risk factor for invasive cervical cancer

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due to its large impact on education and medical resources.¹⁵ In both developed and developing countries, women of low socioeconomic status have a higher risk of cervical cancer. Lower education and higher poverty were found to be associated with increased cervical cancer incidence rates. The increased risk with low socioeconomic status is attributed to a lack of screening, failure to treat precancerous conditions, and lack of knowledge about prevention of HPV infection.¹⁶

In Bangladesh there is no exact type specific HPV infections data causing cervical lesion in sexually active women. So, the present study will design to detect the risk factors that are associated with HPV infection in normal and unhealthy cervix of patients attending tertiary care hospital (BSMMU). The information obtained from this study will give new guide lines for cervical cancer screening.

Material and methods

The prospective study was conducted among 68 women with different types of cervical lesions attending the Obstetrics and Gynecology Out-Patients Department (OPD) of Bangabandhu Sheikh Mujib Medical University (BSMMU) Hospital, Dhaka, from January to December, 2008.

Conventional methods are used for diagnosis of cervical lesion of the patients included visible inspection by acetic acid (VIA), colposcopy, histopathology and pap smear tests. Sexually active women above 25 years of age having history of post-coital bleeding, per-vaginal spotting and /or spontaneous bleeding, patients referred for colposcopy due to abnormalities detected on previous pap's smears, VIA test and histopathological examinations, clinically unhealthy looking cervix on per-speculum examination, patients with low-grade squamous intra-epithelial lesions (LSIL) included in this study. Patients were selected after an initial screening using a questionnaire, followed by per-speculum examination by a gynaecologist. After taking informed written consent, cervical specimen for HPV-DNA detection was collected in a cervical sampler consisting of a cervical brush and specimen transport medium (STM), supplied by the manufacturer of HC2 (Digene Corporation, USA). At the Molecular Virology Laboratory of the Dept. of Virology BSMMU, specimens were stored at -20° C until tested. Determination of HPV and estimation of viral load was done by the hybrid capture 2 (HC2) high-risk HPV DNA test kit according to the manufacturer's instructions.¹⁷ It has detected 13 high-risk HPV types. Cytological

and histopathological investigations were conducted at the Department of Pathology, BSMMU by conventional methods. Although serology identifies individuals with current or past infections by HPV, it has limited role in cervical cancer screening purpose. Serological tests are not presently commercialized or standardized.

Results

The present study was carried out among 68 women attending the Gynecology out patients Department (OPD) of BSMMU Hospital. The age range of the study population was 25 to 70 years (mean: 41.4 ± 10.6 years). Out of the 68 women HPV-DNA was positive in 13 (19.1%) and negative in 55 (80.9%) cases.

Table I
General and clinical profile of study population

Characteristics	n(%)
Education level	
No schooling or primary schooling only	17(25.0)
Secondary	28(41.2)
Higher	23(33.8)
History of early marriage (<16yrs)	37(54.4)
Mean age at marriage (SD)	19.8(4.29)
Age of 1st coitus	
<20	19(27.9)
21-25	27(39.7)
>25	20(29.4)
Parity	
1	17(25.0)
2	21(30.8)
3	19(27.9)
4+	11(16.2)
History of contraceptive methods*	
Oral contraceptive pills	39(57.4)
Barrier method/Condoms	43(63.2)
Intrauterine devices	02(2.94)
Clinical manifestation*	
Irregular per vaginal bleeding	23(33.8)
Post coital bleeding	31(45.6)
Dyspareunia	37(54.4)
Excessive vaginal discharge	17(25.0)
Per speculum examination	
Unhealthy cervix	43(63.2)
Enlarged/hard/friable/fixed cervix/others	25(36.8)

Note: *Many patients had more than 1 criteria; thus the total exceeds the total number of patients,

Table-I shows the general and clinical profile of the study patients. The educational level was high in 23 (33.8 %) patients; 28 (41.2 %) patients had secondary education and 17 (25.0%) patients had no schooling or primary schooling only. A total of 37 (54.4%) patients had history of early marriage. Mean age at marriage was 19.8 ± 4.29 years.

Among them, 19 (27.9%) patients had history of early sexual relationship and 11 (16.2%) were multipara (more than 4). History of using contraceptive methods revealed that 39 (57.4%) patients had history of taking oral contraceptive pills (OCP), 43 (63.2 %) patients used condoms and 02 (2.94%) patients used intrauterine devices. Among the clinical manifestations, 23 (33.8%) patients had complaints of irregular per vaginal bleeding, while 31 (45.6%), 37 (54.4%) and 17 (25.0%) had post-coital bleeding, dyspareunia and excessive vaginal discharge respectively. On per speculum examination, unhealthy cervix was observed in 43 (63.2%) patients while 25 (36.8%) patients had other problems e.g. dysuria, urinary incontinence, etc.

Table II
The correlation of socioeconomic class with HPV-DNA test

Socioeconomic Class	Total (n=68)	HPV DNA positive (%)
High	48	6(12.5)
Middle	14	3(21.4)
Low	6	4(66.6)

The correlation of socioeconomic class with HPV DNA status among the cases is shown in Table-II. Among the 48 cases of high socioeconomic status, 6 (12.5%) were HPV DNA positive, 3 (21.4%) out of 14 middle class cases were HPV DNA positive, while 4 (66.67%) women from low status were HPV DNA positive.

Discussion:

Human papilloma virus (HPV) is the most prevalent virus involved in sexually transmitted diseases worldwide, and an important public health challenge for the prevention of cervical carcinoma.¹⁸ It is considered as the main cause of most cervical cancers and cervical intraepithelial neoplasia (CIN).¹⁹ Thus, diagnosis of HPV at early stage of the infection is of fundamental importance in order to prevent progression of lesions and thereby decrease the number of cervical cancer related mortality.

The prevalence of HPV is related to some risk factors. In this study, 54.4% of the total study population had history of early marriage. Previous epidemiologic studies observed that the risk of cervical cancer was especially high among women marrying at young ages. In our study, a total of 57.4% patients had history of taking oral contraceptive pills; while 63.2% patients used condoms for contraception. A majority of studies indicate that long-term oral contraceptive pill users are at risk of cervical cancers.^{21,22} Oral

contraceptive pills, Parity and perhaps other variables play important roles in the progression of low grade to high grades of neoplasia.²³ Most of the time, early cervical cancer has no symptoms. Most of the patients come with abnormal vaginal bleeding or discharge, dyspareunia, postcoital bleeding. Preventing all these risk factors for HPV infection is a primary focus programs aimed at reducing cervical cancer incidence and morality. Modifiable and non modifiable risk factors for HPV infection include demographic, socioeconomic factors, sexual activity and life style.

In our study, only 13(19.1%) is HPV DNA positive, out of 68 cases of suspected cervical carcinoma. This result reflects a low prevalence of HPV in the study population in comparison to other studies.^{16,19,22} This low rate may be related to the sociocultural background, low incidence of extramarital sex and custom, family bonding & deep rooted religion etc. which exist in this country. The overall and age-specific prevalence of HPV among women appears to vary by countries, region within countries and population subgroups. In Latin America, the frequency range was between 15% and 16% in Mexico, Costa Rica and Colombia.²⁴⁻²⁶ Large studies have found 16.7 per cent of all screened women to be HPV DNA positive.²⁷ These geographical variations may be due to the prevalence of different subtypes of HPV and host related factors. Moreover, demographic, cultural, socioeconomic variables, multiparity, long term contraceptive use, young age at first coitus, multiple sexual partners, low socioeconomic status, low education level, poor genital hygiene, cigarette smoking, genital tract infections etc, are probable co-factors that increase the risk of cervical cancer in women with HPV infection.^{23,24}

Another important finding in the present study was the low socioeconomic condition which is highly associated with HPV infection (Table-II). Descriptive and analytic studies have demonstrated that cervical cancer predominantly affects women with low socioeconomic classes.²³⁻²⁵ This is most probably due to mal-nutrition, multiparity, multiple-sexual partners, early sexual exposure, concurrent genital infections, and lack of education. Sample size of this study is small due to its high cost and lack of awareness of HPV infection in suspected cervical carcinoma patients. However, further extensive studies with larger sample size should be carried out for confirmation of these findings.

Conclusion:

There is close association between HPV infection and invasive cancer. Therefore identification of high risk type could be an important tool for screening of carcinoma cervix. Primary screening

procedure if not reliable and feasible for developing country, HPV-DNA test can strengthen the result.

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