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Effects of Human Papillomavirus Infection with Pre-invasive Cervical Lesions: Bangladesh Perspectives

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Abstract:

Background: *Cervical cancer remains a major public health problem worldwide – particularly in less developed countries. Around 85% of their new cases and 86% of deaths occur in less development countries (IARC, 2012). In Bangladesh, Cervical cancer is the second most common disease among female with an estimated 11,956 new cases and 6,582 deaths in 2012.*

Objectives: The present study was undertaken to identify the Effects of Human Papillomavirus infection with Pre-invasive cervical lesions in Bangladesh.

Methods: *This cross sectional study was carried out at the colposcopy clinic of Gynaecology and Obstetrics department of Bangabandhu Sheikh Mujib Medical University during the study period January 2015 - December 2015. A total of 65 consecutive women with VIA +ve cases of all three grades of CIN (CIN I, CIN II, CIN III) were enrolled in this study. Women having invasive cervical disease and women who not interested were excluded from this study.*

Results: *More than one third (35.3%) patients were in 3rd decade. More than one third (35.4%) patients had normal colposcopic findings followed by 23(35.4%) was CIN I, 11(16.9%) was CIN II and 8(12.3%) was CIN III. Majority (42.6%) patients was found CIN I, 11(26.1%) was CIN II, 8(19.4%) was CIN III and 5(11.9%) had normal in Histopathology. CIN I histopathological finding was found 18 cases, among them 8(44.4%) in positive HC-2/Viral load/ RLU index. In multivariate analysis CIN III was significantly increased 1.34 times in HC-2/Viral load/RLU index positive (human Papillomavirus) cases (95% CI 0.22 – 8.9%, <0.05). Validity test of benign HPV DNA test of the study women showed that HPV DNA had sensitivity 51.4%, specificity 92.9%, accuracy 69.2%, positive predictive values 90.5% and negative predictive values 59.1%. Benign Colposcopic finding had had sensitivity 86.5%, specificity 64.3%, accuracy 76.9%, positive predictive values 76.2% and negative predictive values 78.3%. CIN III significantly 1.34 times increased HC-2/Viral load/ RLU index positive (human Papillomavirus) in multivariate analysis.*

Conclusion: *From the findings of the study it was observed that colposcopy had a high sensitivity and optimum specificity; HPV DNA test had lower sensitivity and higher specificity. Colposcopic findings were closely associated with Histopathology, where the validity test was high when compared to HPV DNA test. So it can be concluded that the Colposcopy is a useful screening test for detection of cervical lesions and Human Papillomavirus is associated with pre-invasive cervical lessons. So the HPV DNA test can be used as a co-test with Colposcopy for screening of cervical lesions.*

Key words: *Effects Human Papillomavirus, Infection, Pre-invasive, cervical lesions.*

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Introduction:

In Bangladesh, Cervical cancer is the second most common disease among female with an estimated 11,956 new cases and 6,582 deaths in 2012[1]. Hospital based statistics indicated that cervical cancer constitutes 22-35% of the female cancer in different areas of Bangladesh[2]. Majority of the patients diagnosed with this preventable cancer present in clinically advanced inoperable stages. The literature identifies several risk factors for the acquisition and prevalence of HPV infection. Age is a strong predictor. Other factors include number of recent / life time sexual partners, age at onset of sexual activity, socio-economic status, male circumcision, extended use of condom, oral contraceptive use, cigarette smoking.[3-7] High parity will also be identified as a risk factor for HR-HPV infection[8]. Human papilloma virus (HPV) is one of the most commonly acquired sexually transmitted infection and significant source of morbidity and mortality[9]. HPV is recognized as estimated cause of cervical cancer and pre-invasive condition for last few decades[2]. Persistent infection with certain types of HPV is a leading cause of cervical cancer. About 10-15 types of high and intermediate risk HPV (HRHPV) types are responsible for more than 90% of cervical cancer. As persistence of certain risk groups of HRHPV plays very important role in development of cervical cancer and CIN. Identification of prevalence of HPVs among women with CIN and normal cervix play important role in screening, prevention and management of CIN. The cervical cancer rates in the United States have progressively declined because of the widespread application of cervical cancer screening and treatment of precancerous lesions, but in the low income countries the incidence in still high because of lack of well-organized screening programme. The presentence and severity of precancerous changes influences the progress of the diseases. The likelihood of regression of CIN I, CIN II, CIN III is 60%, 40%, 33%, respectively and progression to invasive stage is 1%, 5% and greater than 12% respectively. The time interval between infection and development of cervical cancer varies and is apparently more than 15 year[9]. Apart from the risk factors that are already described, the most important risk factor in low income countries is infrequent cervical screening or lack of accessible cervical screening services. Infections with high-risk strain of Human Papilloma Virus (HPV) are of the root causes of cervical cancer. The virus cancer like works by triggering alterations in the cell of the cervix, which can lead to the development of cervical intraepithelial neoplasia (CIN), which may be turned into invasive cervical cancer (ICC) subsequently.

Methodology:

This cross-sectional study was conducted in colposcopy clinic of BSMMU during January 2015 to December 2015. For each of every subject separate data collection sheet were prepared. The subjects were 65 women with VIA + ve cases attending the colposcopy clinic of BSMMU. The purpose and procedure of the study were discussed with the patients. Written informed consent was obtained from those who agreed to participate in the study. On receipt of the informed consent, cervical sample was taken with a special cytobrush and transport media used for collection and transport of cervical specimen. The specimens were stored at -20^{o}C upon receipt, until processing. Detection of HPV DNA from cervical samples was performed by hybrid capture 2 (HC-2) tests. HC-2 test was used to examine the existence of HPV DNA in each specimen. Data was collected from the study population on variables of interest using structured design by interview, observation, clinical exam, HPV DNA test, Colposcopic findings and histopathological examination.

Results: Table I shows demographic variable of the study subjects. It was observed that more than one third (35.3%) patients belonged to age 31-40 years. The mean age was found 35.5±9.6 years with range from 21 to 58 years. Age of marriage was found 17.0±3.6 years with range from 12 to 26 years. Majority (89.2%) patients were Muslim. Most of the (84.6%) patients were housewives. Twenty (30.8%) patients had completed primary education. More than a half (54.4%) of the patients came from 10,000-20,000 taka monthly income family. The mean age at 1st child was found 19.3±3.7 years with range from 13 to 29 years.

Table-I

Distribution of the study population by demography variable (n=65)

Demography variable	Number of	Percentage population
Age (in years)		
21-30	21	32.3
31-40	23	35.3
41-50	17	26.2
51-60	4	6.2
Mean± SD	35.5	±9.6
Range (min, max)	21	, 60
Age of marriage		
≤18	43	66.2
>18	22	33.8
Mean± SD	17.0	±3.6
Range (min, max)	13	, 26
Religion		
Islam	58	89.2
Hindu	7	10.8
Occupational status		
House wife	55	84.6
Service holder	8	12.3
Other work	2	3.1
Educational status		
No education	7	10.8
Primary	20	30.8
Secondary	17	26.2
Higher secondary	11	16.9
Graduate	10	15.4
Monthly income (taka)		
10,000-20,000	36	55.4
21,000-30,000	12	18.5
>30,000	17	26.2
Age at 1st child		
<18	26	40.0
18-20	17	26.2
>20	22	33.8
Mean± SD	19.3	±3.7
Range (min, max)	13	±29

Table II shows colposcopic finding of the study population, it were observed that majority (35.4%) patients had normal colposcopic findings followed by 23(35.4%) were CIN I, 11(16.9%) were CIN II and 8(12.3%) were CIN III.

Table-II

Distribution of the study population (CIN I by VIA test) based on colposcopic findings (n=65)

Colposcopic findings	Number of population	Percentage
Normal	23	35.4
CIN I	23	35.4
CIN II	11	16.9
CIN III	8	12.3

Table III shows histopathological findings among study population, it was observed that 28(43.1%) women were found colposcopically normal followed by 18(42.6%) were CIN I, 11(26.1%) were CIN II and 8(19.4%) were CIN III.

Table-III

Distribution of the histopathological findings among study population (n=65)

Histopathological findings	Number of population	Percentage
Normal	28	43.1
CIN I	18	27.7
CIN II	11	16.9
CIN III	8	12.3

Table IV shows Positive HC-2/Viral load/ RLU index were found 65 cases, among them more than two third 67.7% had negative and 21(32.3%) had positive. The mean viral load was found 23.0±82.0 with range in 0.1 to 461.0. The threshold of 1 pg of HPV DNA/ ml of test solution was used for a positive result.

Table-IV

Distribution of the study population by HPV DNA test (n=65)

HPV DNA test	Number of population	Percentage
<1 (Negative)	44	67.7
≥1 (Positive)	21	32.3
Mean± SD	23.0	±82.0
Range (min, max)	0.1	, 461.0

Table V shows comparison between HC-2/Viral load/ RLU index with age of marriagefinding, it were observed that 13(61.9%) patients belonged to ≤18 years in HC-2/Viral load/ RLU index positive and 27(61.4%) in HC-2/Viral load/ RLU index negative.

Table-V
Findings of HPV DNA test according to age of marriage (n=65)

Age of marriage (in years)		Viral load			
		Positive (n=21)		Negative (n=44)	
	N	n	(%)	n	(%)
≤18	40	13	61.9	27	61.4
>18	25	8	38.1	17	38.6

Table VI shows HC-2/Viral load/ RLU index positive were found 8(44.4%) cases in CIN I, 6(54.5%) in CIN II and 5(62.5%) in CIN III evaluated by histopathology.

Table-VI
Relationship between HPV DNA test with histopathological finding (n=65)

Histopathological finding		HPV DNA test			
		Positive (n=21)		Negative (n=44)	
	n	n	(%)	n	(%)
Negative					
Normal	28	2	9.6	26	100.0
Positive					
CIN I	18	8	38.1	10	55.5
CIN II	11	6	28.6	5	45.4
CIN III	8	5	23.8	3	37.5

Discussion:

In this present study it was observed that 35.3% women belonged to age 21-30 years. The mean age was found 35.5±9.6 years with ranged from 21 to 60 years. Nahar et al. (2014)[10] reported that HPV infection to be most common in younger women with the peak prevalence occurring in women younger than 25 years of age; prevalence started to decline after 30 years of age[11]. The girls of Bangladesh marry at an early age and the study was conducted among married women which may explain high HPV infection in the younger age group. From the present study we get HPV infection 35.3% in the age 20-30 years and 32.3% in age 31-40 years. In another study Franceschi et al. had showed that age at first marriage and numbers of pregnancies among women were unrelated to HPV positivity[12]. In this study, 66.2% women had age of marriage ≤18 years & HPV infection were 61.9% among them 33.8% woman had age of marriage >18 years & had HPV infection 38.1%. High parity was also identified as a risk factor for HR-HPV infection[12]. In this series, it was observed that more than three fourth (73.8%) patients were multi para[13]. In present study, it was observed that almost two third (66.2%) patients were asymptomatic and the remains had symptoms like-vaginal discharge 20.0%, dyspareunia 9.2% and post coital bleeding 4.6%. Similar presentations were revealed by Khatun et al.[14] In the present study, the histopathological finding of the study population were observed that (43.1%) population were found normal histopathological followed by 18(42.6%) were CIN I, 11(26.1%) were CIN II and 8(19.4%) were CIN III. Santos et al. (2003)[16] reported that (19%) were found to have a normal cervix via colposcopy, (76%) presented with minor abnormalities and (4.0%) with major abnormalities. Of the women with colposcopically guided biopsy (5.0%) presented with cervicitis in the histological analysis, 66.0% showed CIN1 and 13(11.0%) had either CIN2 or CIN3[15]. In our country Rahman et al. found a distinct upward trend of high-risk HPV DNA viral load, which had correlated with the histologic grade of the lesion, being highest for invasive carcinoma followed by CIN III, CIN II, CIN I and lowest for chronic cervicitis[16]. Santos et al. mentioned that 85% of the women with CIN2 or CIN3 had a positive HPV DNA test. In this study 62.5% HPV infection in CIN III. 54.5% HPV infection in CIN II, 34.8% HPV infection present in CIN I & 8.7% HPV infection present in normal subjects detected colposcopycally. There were a strong correlation between CIN2 or CIN3 and positivity for HPV DNA when this group was compared with women with only CIN1 or women with normal cervix[15]. In the present study 8 subjects HPV+ve DNA test was 44.4% found in CIN I, 6(54.5%) in CIN II and 5(62.5%) found in CIN III evaluated by histopathology. Sun et al. described women with viral load, were found to be at significantly greater risk squamous intraepithelial lesion. Hubbard had speculated that there may be a relationship

between high-risk HPV DNA viral load with persistent infection and the subsequent development of pre-invasive cervical cancer[17].

Conclusion:

From the findings of the study it was observed that colposcopy had a high sensitivity and optimum specificity; HPV DNA test had lower sensitivity and higher specificity. Colposcopic findings were greatly associated with Histopathology, where the validity test was high with compared to HPV DNA test. So it can be concluded that the Colposcopy is a useful screening test for detection of cervical lesions and Human Papillomavirus is associated with pre-invasive cervical lessons. So the HPV DNA test can be used as a co-test with Colposcopy for screening of cervical lesions.

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