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Original Research Article

The Role of HPV Genotype among Colposcopy Diagnosed Cervical Precancerous Lesions

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Abstract: ***Background:*** Cancer is the leading cause of death and a major contributor to reduced life expectancy in every country on Earth [1]. Cervical cancer (CC) is a serious global health concern that is more common in developing countries, especially those on the Indian subcontinent. More and more women are suffering from CC. Cervical cancer is mostly caused by the Human Papillomavirus (HPV), a sexually transmitted virus that is one of the most common illnesses of the reproductive system. ***Objective:*** The aim of this study is to evaluate the role of HPV genotype among colposcopy diagnosed cervical precancerous lesions. ***Methods:*** The cross-sectional observational study was conducted in the Department of Gynecological Oncology of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, from July 2021 to June 2022. A total of 132 subjects were included in the study. Data were collected by face-to-face interview and analyzed by appropriate computer based programmed software Statistical Package for the Social Sciences (SPSS), version 24. ***Results:*** In this study, the mean age was found to be 36.7±6.3 years, with a range from 31 to 60 years, the majority 53 (40.2%) of patients completed SSC and 118 (89.4%) were housewives and 125(94.7%) were Muslims. In this study most of the patients 101 (76.5%) came from middle-income families. About 45 (34.1%) patients were married between the ages of 15-17 years, 45 (34.1%) were between 16-18 years during their first delivery and 56 (42.4%) had 3-4 children. Most of the patients 92(69.7%) had history of received OCP. About 10(7.0%) patients were found HPV 16 positive followed by 1(0.7%) HPV 18, 3(2.1%) other HR-HPV, 3(2.1%) HPV 16 & other HR-HPV and 1(0.7%) HPV 16-HPV 18 & other HR-HPV. Most of the 95 (72.0%) patients had CIN I, 30 (22.7%) had CIN II and 7 (5.3%) had CIN III identification by colposcopy reports. In this study 59 (44.7%) patients had CIN I followed by 13 (9.8%) had CIN II, 9 (6.8%) had CIN III, 5 (3.8%) had CIS and 46 (34.8%) had normal/squamous metaplasia by histopathological reports. ***Conclusion:*** HPV 16 is the most prevalent of the 14- HR HPV genotypes, while HPV 18 was extremely infrequent in cases of cervical precancer detected by colposcopy. Colposcopy-identified cervical precancerous lesions can be efficiently managed using HPV genotyping, avoiding over- or under-treatment.

Keywords: HPV, Colposcopy, Cervical Precancerous Lesions.

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INTRODUCTION

In every nation on Earth, cancer is the primary cause of death and a significant impediment to life expectancy [1]. Women are increasingly suffering from cervical cancer (CC), a major global health concern that is particularly prevalent in developing nations, particularly those on the Indian subcontinent. The Human Papillomavirus (HPV), a sexually transmitted virus that is one of the most prevalent infections of the reproductive system, is the main cause of cervical cancer.

With an expected 5,70,000 new cases in 2018, CC is the fourth most common malignancy in women and accounts for 6.6% of all female cancer cases [2]. According to estimates, cervical cancer claimed 311365 lives globally in 2018; 90% of these deaths were in low- and middle-income nations [3]. On the other hand, the Globocan 2020 study estimates that there were 341,831 new CC deaths and 604,127 new cases globally in 2020 [4]. There have been more deaths and newly diagnosed cases than there were in the 2018 report that came before.

The second most frequent cancer among women in Bangladesh is CC. According to estimates, there are 8068 new cases of CC diagnosed year, 5,214 women pass away from the disease, and CC accounts for almost 12% of all female cancer cases in this nation [2]. The stage at which CC patients are diagnosed has a significant impact on their likelihood of survival. Death rates from cervical cancer are high in Bangladesh because of delayed diagnosis and poor management facilities.

According to Sung *et al.,* (2021), the incidence and mortality rates in transitioning versus transitioned countries are disproportionately high (18.8 vs. 11.3 per 100,000 for incidence and 12.4 vs. 5.2 per 100,000 for mortality) [4]. These deaths most likely resulted from a lack of screening. Because of systematic screening programs, the incidence of CC has declined during the past few decades in developed nations.

Several human malignancies, including CC, are caused by oncogenic human papillomaviruses (HPVs). According to Hausen (1977), HPV is the cause of CC. Out of the over 220 HPV varieties, 12 are deemed carcinogenic (HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, and 59), and HPV 68 is considered likely to cause cancer. HPV 16 has the highest carcinogenic potential, followed by HPV 18 [5]. About thirty different kinds of HPV, out of approximately 200 different genotypes, infect the genital mucosa [6].

HPV has been classified as Low-risk (6,11,42,43,44), Intermediate-risk (31,33,35,51,52), and High-risk (16,18,45,56) [7]. The prevalence of genital HPV infection declines after 30 years, peaking between the ages of 20 and 25 [8]. A tiny percentage of women are unable to overcome the illness, but the majority of women are able to do so through natural immunity. Neoplastic alterations in the transformation zone are brought on by persistent HPV infection [9].

Moreover, high-grade cervical lesions, which have the potential to develop into invasive cervical cancer, are mostly dependent on persistent hr-HPV infection. Furthermore, various co-factors such as multi-parity, the age of the first full-term pregnancy, and the use of the oral contraceptive pill are linked to the progression of HPV infection to invasive malignancy [10]. Certain HPV tests only look for HPV 16 and 18, along with an additional 12 strains that are combined to present as "Other HPV." The carcinogenic potential of the 12 HPV varieties that are included under "Other HPVs" varies significantly. Although a high viral load has been linked to an increased risk of cervical cancer (CC), it is unclear if other HPV strains, such as HPV 16, are also at risk for cervical cancer due to viral loads. Since 2014, HPV-based cervical screening has been advised worldwide and World Health Organization (WHO) has declared the global elimination of cervical cancer as a prioritized goal, with HPV based screening as a major tool to accomplish this (Hortlund *et al.,* 2021). WHO's global strategy for CC eliminationwas endorsed by the World Health Assembly in 2020. As per the strategy, 90% of girls will be fully vaccinated with the HPV vaccine by the age of 15 years, 70% of women are to be screened regularly for cervical disease with a high-performance test, and 90% of cervical disease among those needing it to receive appropriate treatment. WHO recommends HPV DNA as a primary screening test, starting at age 30 and every 5 to 10 years screening interval for CC prevention [11].

METHODOLOGY

The cross-sectional observational study was conducted in the Department of Gynecological Oncology of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, from July 2021 to June 2022. A total of 132 subjects were included in the study. Women with colposcopy diagnosed cervical precancerous lesions and who matched the inclusion and exclusion criteria were approached for participation in the study. Patients who were not willing to give consent were excluded. Purposive sampling was done according to the availability of the patients who fulfilled the selection criteria. Face to face interview was done to collect data with a semi-structured questionnaire. After collection, the data were checked and cleaned, followed by editing, compiling, coding, and categorizing according to the objectives and variable to detect errors and to maintain consistency, relevancy and quality control. Statistical evaluation of the results used to be obtained via the use of a window-based computer software program devised with Statistical Packages for Social Sciences (SPSS-24).

RESULT

Table I: Distribution of the patients according to age (n = 132)

Age group	Frequency	%
31 – 35 years	45	34.1
36 - 40 years	40	30.3
41 - 45 years	22	16.7
46 - 50 years	12	9.1
51 - 55 years	7	5.3
56 - 60 years	6	4.5
Total	**132**	**100.0**
Mean±SD = 36.7±6.3		

Table I shows that, the mean age was found to be 36.7±6.3 years, with a range from 31 to 60 years maximum 45 (34.1%) of the patients were within the age group of 31- 35 years and minimum 6 (4.5%) of the patients were within the age group of 56 - 60 years

Table II: Distribution of the patients according to educational status (n = 132)

Educational status	Frequency	%
No schooling	14	10.6
Up primary	29	22.0
SSC	53	40.2
HSC	21	15.9
Graduate & above	15	11.4
Total	**132**	**100.0**

Table II shows that, the majority 53 (40.2%) of patients completed SSC and 14 (10.6%) patients had no schooling

Table III: Distribution of the patients according to occupational status (n = 132)

Occupational status	Frequency	%
Housewife	118	89.4
Service holder	14	10.6
Total	**132**	**100.0**

Table III shows that most of the patients 118 (89.4%) were housewives and 14 (10.6%) were service holder

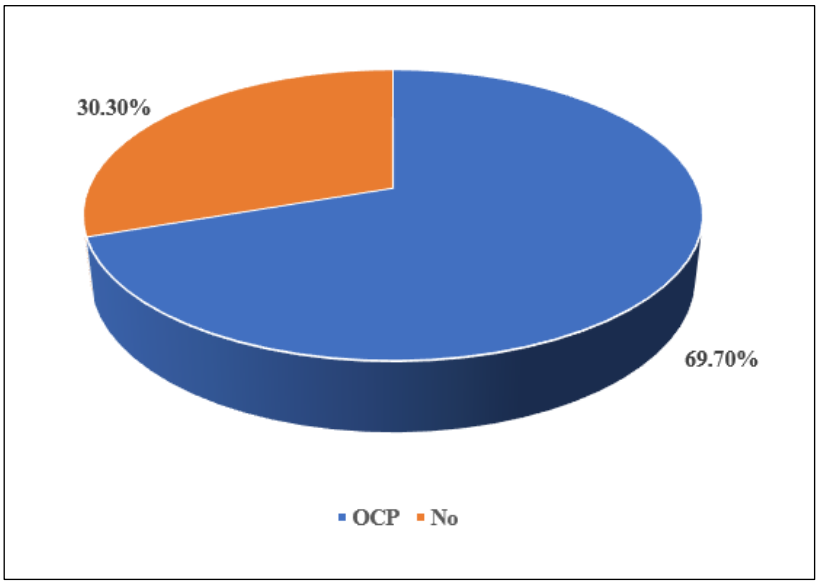

Figure I: Distribution of patients according to religion (n = 132)

Figure I shows that, most of the patients 125(94.7%) were Muslims and 8 (5.3%) were Hindu.

Table IV: Distribution of the patients according to average monthly income (n = 132)

Average monthly income (Taka)	Frequency	%
Low	12	9.1
Meddle	101	76.5
High	19	14.4
Total	132	100.0

Table IV shows that most of the patients 101 (76.5%) came from middle-income families.

Table V: Distribution of the patients according to age at marriage (n = 132)

Age at marriage (years)	Frequency	%
<15	40	30.3
15-17	45	34.1
18-20	33	25.0
>20	14	10.6
Total	**132**	**100.0**

Table V shows that 45 (34.1%) patients were married between the ages of 15-17 years and 40 (30.3%) patients were married in the ages of <15 years

Table VI: Distribution of the patients according to Age at first delivery (n = 132)

Age at first delivery (years)	Frequency	%
≤15	25	18.9
16-18	45	34.1
19-21	38	28.8
>21	24	18.2
Total	**132**	**100.0**

Table VI shows 45 (34.1%) were between 16-18 years during their first delivery and 38 (28.8%) were in ≤15 years during their first delivery

Table VII: Distribution of the patients according to parity (n = 132)

Parity	Frequency	%
No child	1	0.8
1-2 children	24	18.2
3-4 children	56	42.4
>4 children	51	38.6
Total	**132**	**100.0**

Table VII shows that 56 (42.4%) had 3-4 children and 51 (38.6%) had more than 4 children

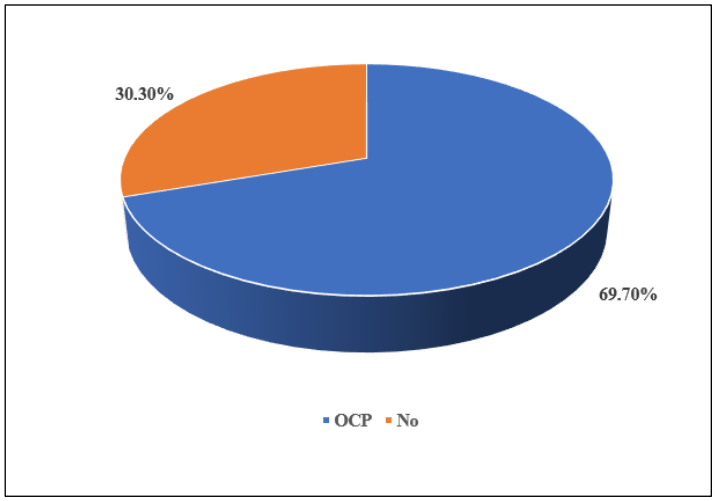

Figure II: Distribution of patients according to contraceptive history (n = 132)

Figure II shows that, most of the patients 92(69.7%) had history of received OCP.

Table VIII: Distribution of the patients according to HPV genotyping reports (n = 132)

HPV genotype reports	Frequency	%
HPV 16	10	34.1
HPV 18	1	30.3
Other HR-HPV	3	16.7
HPV 16-HPV 18 & other HR-HPV	1	9.1
HPV 16 & other HR-HPV	3	5.3
Negative	114	4.5
Total	**132**	**100.0**

Table VIII shows that, 10(7.0%) patients were found HPV 16 positive followed by 1(0.7%) HPV 18, 3(2.1%) other HR-HPV, 3(2.1%) HPV 16 & other HR-HPV and 1(0.7%) HPV 16-HPV 18 & other HR-HPV.

Table IX: Distribution of the patients according to colposcopy reports (n = 132)

Colposcopy reports	Frequency	%
CIN I	95	72.0
CIN II	30	22.7
CIN III	7	5.3
Total	**132**	**100.0**

Table IX shows that 95 (72.0%) patients had CIN I, 30 (22.7%) had CIN II and 7 (5.3%) had CIN III identification by colposcopy reports.

Table X: Distribution of the patients according to histopathological reports (n = 132)

Histopathological reports	Frequency	%
CIN I	59	44.7
CIN II	13	9.8
CIN III	9	6.8
CIS	5	3.8
Normal/squamous metaplasia	46	34.8
Total	**132**	**100.0**

Table X shows that 59 (44.7%) patients had CIN I followed by 13 (9.8%) had CIN II, 9 (6.8%) had CIN III, 5 (3.8%) had CIS and 46 (34.8%) had normal/squamous metaplasia by histopathological reports.

DISCUSSION

The aberrant proliferation of cells on the surface of the cervix that may eventually result in cervical intraepithelial neoplasia (CIN) is known to cause cervical cancer (CC). The cervix cell's precancerous change is known as CIN. A 1-3 scale is used to grade CIN, with 3 representing the most aberrant. A Human Papilloma Virus (HPV) infection is required for the development of CIN; however, not all HPV infections result in CC. Many women infected with HPV never experience CC or CIN; in these circumstances, the HPV infection goes away on its own. But people who have an HPV infection that lasts longer than a year or two are more likely to get a higher grade of CIN.

The cross-sectional observational study was conducted in the Department of Gynecological Oncology of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, from July 2021 to June 2022 to evaluate the role of HPV genotype among colposcopy diagnosed cervical precancerous lesions. A total of 132 subjects were included in the study.

In this study the mean age was found to be 36.7±6.3 years, with a range from 31 to 60 years maximum 45 (34.1%) of the patients were within the age group of 31- 35 years and minimum 6 (4.5%) of the patients were within the age group of 56 - 60 years and the majority 53 (40.2%) of patients completed SSC and 14 (10.6%) patients had no schooling. Most of the patients 118 (89.4%) were housewives and 14 (10.6%) were service holder. In this study most of the patients 125(94.7%) were Muslims and 8 (5.3%) were Hindu and most of the patients 101 (76.5%) came from middle-income families. About 45 (34.1%) patients were married between the ages of 15-17 years and 40 (30.3%) patients were married in the ages of <15 years and 45 (34.1%) were between 16-18 years during their first delivery and 38 (28.8%) were in ≤15 years during their first delivery. About 56 (42.4%) had 3-4 children and 51 (38.6%) had more than 4 children and most of the patients 92(69.7%) had history of received OCP. About 10(7.0%) patients were found HPV 16 positive followed by 1(0.7%) HPV 18, 3(2.1%) other HR-HPV, 3(2.1%)

HPV 16 & other HR-HPV and 1(0.7%) HPV 16-HPV 18 & other HR-HPV. Most of the 95 (72.0%) patients had CIN I, 30 (22.7%) had CIN II and 7 (5.3%) had CIN III identification by colposcopy reports. In this study 59 (44.7%) patients had CIN I followed by 13 (9.8%) had CIN II, 9 (6.8%) had CIN III, 5 (3.8%) had CIS and 46 (34.8%) had normal/squamous metaplasia by histopathological reports.

Zhao *et al.,* (2019) determined the genotype distribution of HPV and attribution to cervical precancerous lesions among women from rural North China. A total of 9,526 women participated in rural China's cervical cancer screening project. The samples of women who tested positive for HPV were retested with a polymerase chain reaction (PCR)-based HPV genotyping test. A total of 22.2% (2,112/9,526) of women were HR-HPV positive and HPV 52 (21.7%) was the most common hr-HPV genotype, followed by HPV 58 (18.2%), HPV 53 (18.2%) and HPV 16 (16.2%). The top three genotypes detected in HR-HPV-positive cervical intraepithelial neoplasia (CIN)1 were HPV16 (36.7%), HPV58 (20.4%), and HPV56 (15.3%). Among CIN2+, the most frequent genotypes were HPV16 (75.6%), HPV52 (17.8%), HPV58 (16.7%). HPV16, 56, 58, 53, 52, 59, 68, and 18 combined were attributed to 84.17% of all CIN1 lesions, and HPV16, 58, and 52 combined were attributed to 86.98% of all CIN2+ lesions. The prevalence of hr-HPV infection among women from rural areas in North China was high, and HPV16, HPV58, and HPV52 had a paramount attributable fraction in CIN2+. Type-specific HPV prevalence and attribution proportion to cervical precancerous lesions should be considered in the development of vaccines and strategies for screening in this population [12].

A cross-sectional and comparative study conducted by Nessa *et al.,* (2013) evaluated the feasibility of the 'see and treat' protocol for the management of high-grade cervical intraepithelial neoplasia (CIN) at a colposcopy clinic in Bangladesh. During the first and second periods, 48 of 87 and 55 of 73 histology-proven high-grade CIN cases, respectively, received treatment. Among the study population, 37.3% of women who had normal or CIN-I in histology were treated unnecessarily in the second period. The compliance to treatment improved by 20% and failure to receive treatment fell by 20%; these changes were statistically significant [13].

Nessa *et al.,* (2019) observed that cervical cancer is the second-most common cancer among women in Bangladesh. The Government of Bangladesh (GOB) has introduced a cervical cancer screening program through Visual Inspection of Cervix with Acetic Acid (VIA). Screen positive cases are referred to the colposcopy clinics of tertiary level health-care facilities (BSMMU/15 Medical College Hospitals) for evaluation and management. From January 2005 to June 2018, 2012752 VIA tests were performed at different facilities throughout the country; among the tested women, 92037 (4.5%) were found VIA-positive. Among the women with VIA-positive reports, 26773(29.1%) attended the colposcopy clinic of BSMMU, of which 11501(44.0%) had precancerous and 1897 (7.0%) had cancerous conditions of the cervix.3563 (13.30%) were treated by local excision (LEEP, Loop Electrosurgical Excision Procedure), 2781 (10.40%) by local ablative method (thermal ablation) and1646 (6.15%) women with cervical cancer were referred to oncology [14].

This retrospective cross-sectional study by Nessa *et al.,* (2020) evaluated the colposcopy outcomes and the association of different demographic and reproductive risk factors with cervical pre-cancer and cancer. A total of 16147 women attended the colposcopy clinic of BSMMU with VIA positive reports. Among them, 65.73% of women were referred from different VIA centers in the Dhaka district. The mean age of marriage of the subjects was 16. 93 (± 1) and the mean age of 1st delivery was 18.45 years (± 4.10). Almost three-fourths of them were married before 18 years and had their 1st delivery by 20 years. Colposcopy examination of the VIA positive women revealed that 36.7% had CINI, 10.6% had CINII/ III, and 7.1% had carcinoma of cervix. Considering CIN as a disease,the Sensitivity, Specificity, PPV and NPV of colposcopy were found at 99.7%, 75.3%, 70.3% and 99.8%, respectively. On the other hand, considering CIN2+ as a disease, the sensitivity, specificity, PPV and NPV of colposcopy were found at 73.8%, 92.7%, 64.4% and 95.2%, respectively. Statistical analysis revealed that higher age (p=0.000), lower level of education (p=0.007), lower socio-economic status (p=0.014), and higher parity (p=0.001) had an individual influence on cervical pre-cancer and cancer. This study indicated higher age, low level of education, lower socio-economic condition and higher parity as the most critical socio-demographic factors for developing cervical pre-cancer and cancer in Bangladesh [15].

CONCLUSION

Of all the 14- HR HPV genotypes, HPV 16 is the most common, whereas HPV 18 was incredibly rare in cases of cervical precancer identified by colposcopy. The study found that high grade lesions had a higher prevalence of HPV16. HPV genotyping can be used to manage cervical precancerous lesions identified by colposcopy effectively, preventing over- or under-treatment.

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