

## The impact of cervical precancerous lesion by histopathology

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### ABSTRACT

**Background:**A precancerous cervical lesion is a variation in the cervix's cells that has the potential to progress to cervical cancer. One public health issue that adds to women's deaths globally is cervical cancer. Cervical cancer is the leading cause of death in women. Worldwide, cervical cancer is the fourth leading cause of death in women.**Objective:** The aim of this study is to evaluate the impact of cervical precancerous lesion by histopathology.**Methods:** The cross-sectional observational study was conducted in the Department of Colposcopy Clinic of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, from January 2022 to December 2022. A total of 84 subjects were included in the study. The questionnaire was pretested, corrected and finalized. 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 32.8±7.9 years, with a range from 20 to >51 years maximum 32 (38.1%) of the patients were within the age group of 20 - 30 years and minimum 9 (10.7%) of the patients were in the age >51 years. The majority 43 (51.2%) of patients completed primary level and most of the patients 68 (80.9%) were housewives. Most of the patients 80 (95.2%) were Muslims and about 42 (50.0%) came from middle-income families. About 34 (40.5%) patients were married between the ages of 15-17 years and 24 (28.6%) patients were married in the ages of <15 years. About 33 (39.3%) were between 16-18 years during their first delivery and 16 (19.0%) were in ≤15 years during their first delivery. About 34 (40.5%) had 3-4 children and 28 (33.3%) had more than 4 children. Most of the patients 58 (69.4%) had history of received OCP. Regarding colposcopic diagnosis, 16.7% (n=14) were normal, 57.1% (n=48) were CIN I, 14.4% (n=12) were CIN II and 11.9% (n=10) were CIN III and regarding histopathological diagnosis, 32.1% (n=27) chronic cervicitis, 42.9% (n=36) CIN I, 8.3% (n=7) CIN II, 7.1% (n=6) CIN III, 4.8% (n=4) carcinoma in situ and 4.8% (n=4) were invasive squamous cell carcinoma.

**Conclusion:** Precancerous cervical lesions remain a serious public health concern. Women will continue to die from it unless effective screening techniques like VIA and HPV immunization are expanded. This suggests that since most of the determinants may be found early on, clinicians can be crucial in preventing the lesion from progressing to cancer. Therefore, in order to control cervical cancer at the early stages of lesions, effective prevention strategies must take these aspects into account.

**Key words:** Cervical Precancerous Lesions, Histopathology

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## I. INTRODUCTION:

A precancerous cervical lesion, which is also called an intraepithelial lesion, is an abnormality in the cells of the cervix that could eventually develop into cervical cancer [1]. Due to the prevalence of the illness and the potential for successful screening-based prevention, cervical cancer screening is an essential component of any cancer control program [2]. In the past, 99% of women with squamous cervical carcinoma caused by an HPV infection were diagnosed with adenocarcinoma and squamous cell carcinoma [3].

Cervical cancer is the leading cause of death in women. Worldwide, cervical cancer is the fourth leading cause of death in women [4]. By 2020, an estimated 604,000 women have been diagnosed with cervical cancer worldwide and an estimated 342,000 women have died of the disease [3]. Globally, cervical cancer has an occurrence rate of 371,000 cases and a death rate of 190,000 with 80% of the cancer of the cervix death occurring in resource-limited countries. As per the International Agency for Research on Cancer (IARC's) projections for coming decades, deaths from cervical cancer will continue to rise [5].

According to World Health Organization (WHO) estimates, cervical cancer is expected to kill more than 443,000 women by 2030, with a high rate (over 98% of deaths) believed to occur in developing countries (especially in Sub-Saharan Africa (SSA) [6]. Undoubtedly, the most prevalent HPV-related illness is cervical cancer. Seventy percent of precancerous cervical lesions and cervical cancer are caused by HPV 16 and 18. In 2008, Dr. ZurHausen received the Nobel Prize in Physiology or Medicine in recognition of his groundbreaking work identifying the connection between HPV and cervical cancer [7,8].

When precancerous tumors progress to actual cancer and infiltrate the surrounding tissues, symptoms start to appear. Common symptoms include post-coital bleeding, postmenopausal bleeding, intermenstrual bleeding, severe vaginal bleeding, and atypical vaginal discharge that may smell bad and be tinged with blood. One of the main indicators of cervical cancer is thought to be postcoital bleeding [9].

Histopathology has defined historically the concepts of development and progression of cervical precancer to cancer. The idea of carcinoma-in-situ as a cancer precursor dates back to the early cellular pathology of Rudolf Virchow during the nineteenth century. The concept of cervical precancer has been refined over more than a century to include less severe, dysplastic, changes, and then unified into cervical intraepithelial neoplasia of three grades by Richart [4–6]. Histopathology continues to drive key decisions on treatment of precancer and invasive cancer; and for this reason has been used to define clinical endpoints for research into cervical screening, HPV vaccines and biomarkers. As per USPSTF (United States Preventive Services Task Force) recommendation for cervical cancer screening: women aged 21 to 65 years are recommended to undergo screening with Papanicolaou smear every 3 years or, for those women between 30 to 65 years who want to lengthen their screening interval are recommended to screen with a combination of cytology and HPV testing every 5 years [10].

Bangladesh's national cervical cancer screening program was started as a pilot project in 2004 and expanded to a nationwide initiative in 2005. The government screening test program in Bangladesh is called VIA. Women 30 years of age and older are subjected to screening tests. Colposcopy compliance was high; however, therapy was not given to almost half of the patients with high-grade precancerous lesions. The practice of "see and treat" was seldom followed, and cryotherapy was not used frequently. One of the first nations in the world to implement VIA as the screening test for its national program to detect cervical cancer is Bangladesh [11].

If the test is negative, the woman must attend at least two appointments; if the test is positive, she must attend frequently. This is the requirement of conventional cervical cancer screening and prevention programs. In low resource areas, however, the repeated visit-based screening programs have not been able to lower cancer rates. The novel "Screen and Treat" or "See and Treat" single-visit strategy has been created to enhance the results. A "see and treat" approach reduces the possibility of losing follow-up, even though overtreatment is still possible [12]. Studies have shown the advantages of "see and treat," particularly in nations with limited resources [13–15]. VIA and cryotherapy were implemented for screening and treatment by the government partners at demonstration sites in Peru, Uganda and Vietnam. Evaluations in these three countries to explore barriers and facilitating factors showed that use of VIA and cryotherapy is a feasible approach in these settings for cervical cancer prevention services [13]. The most important role of cervical cancer screening tests is to identify the woman with high grade squamous intra-epithelial lesions (HSIL) because the LSIL are frequently regressive [16].

"Screen and treat" methods were suggested by a WHO expert group for patients with cervical intraepithelial lesions. The suggested screening techniques are HPV test only, HPV test plus VIA, HPV test plus cytology. The recommended course of treatment is LEEP or cryotherapy. The application of cold knife cauterization (CKC) as a treatment in a screen-and-treat approach was not advised by the expert panel [17]. In Bangladesh, there are no official guidelines endorsing the "see and treat" or "screen and treat" strategies. Nevertheless, Nessa et al. [5] came to the conclusion that rather than waiting for biopsy confirmation before starting treatment,

cryotherapy or LEEP should be administered as soon as possible after the initial colposcopy. Due to increased treatment compliance, this strategy might help more women, but it also runs the risk of leading to overtreatment.

## II. METHODOLOGY:

The cross-sectional observational study was conducted in the Department of Gynecological Oncology of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, from January 2022 to December 2022. A total of 84 subjects were included in the study. Women with 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).

## III. RESULT:

**Table I: Distribution of the patients according to age (n = 84)**

Table I shows that, the mean age was found to be 36.8±11.9 years, with a range from 20 to >51 years maximum 32 (38.1%) of the patients were within the age group of 20 - 30 years and minimum 9 (10.7%) of the patients were in the age >51 years

Age group	Frequency	%
20 – 30 years	32	38.1
31 - 40 years	28	33.3
41 - 50 years	15	17.9
> 51 years	9	10.7
<b>Total</b>	<b>84</b>	<b>100.0</b>
Mean±SD= 32.8±7.9 years		

**Table II: Distribution of the patients according to educational status (n = 84)**

Table II shows that, the majority 43 (51.2%) of patients completed primary level and 11 (13.1%) patients were illiterate

Educational status	Frequency	%
Illiterate	11	13.1
primary	43	51.2
SSC	13	15.5
HSC	8	9.5
Graduate & above	9	10.7
<b>Total</b>	<b>84</b>	<b>100.0</b>

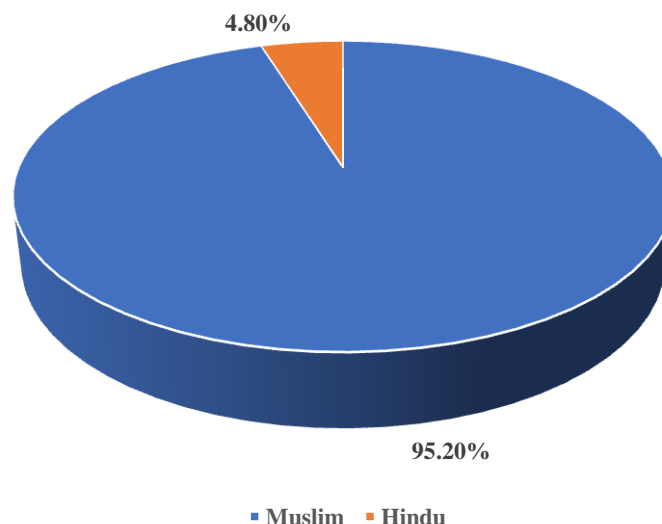
**Table III: Distribution of the patients according to occupational status (n = 84)**

Table III shows that most of the patients 68 (80.9%) were housewives and 16 (19.1%) were service holder

Occupational status	Frequency	%
Housewife	68	80.9
Service holder	16	19.1
<b>Total</b>	<b>84</b>	<b>100.0</b>

**Figure I: Distribution of patients according to religion (n = 84)**

Figure I shows that, most of the patients 80 (95.2%) were Muslims and 4 (4.8%) were Hindu.



**Table IV: Distribution of the patients according to average monthly income (n = 84)**

Table IV shows that most of the patients 42 (50.0%) came from middle-income families.

Average monthly income (Taka)	Frequency	%
Low	19	22.6
Meddle	42	50.0
High	23	27.4
<b>Total</b>	<b>84</b>	<b>100.0</b>

**Table V: Distribution of the patients according to age at marriage (n = 84)**

Table V shows that 34 (40.5%) patients were married between the ages of 15-17 years and 24 (28.6%) patients were married in the ages of <15 years

Age at marriage (years)	Frequency	%
<15	24	28.6
15-17	34	40.5
18-20	17	20.2
>20	9	10.7
<b>Total</b>	<b>84</b>	<b>100.0</b>

**Table VI: Distribution of the patients according to Age at first delivery (n = 84)**

Table VI shows 33 (39.3%) were between 16-18 years during their first delivery and 16 (19.0%) were in ≤15 years during their first delivery

Age at first delivery (years)	Frequency	%
≤15	16	19.0
16-18	33	39.3
19-21	21	25.0
>21	14	16.7
<b>Total</b>	<b>84</b>	<b>100.0</b>

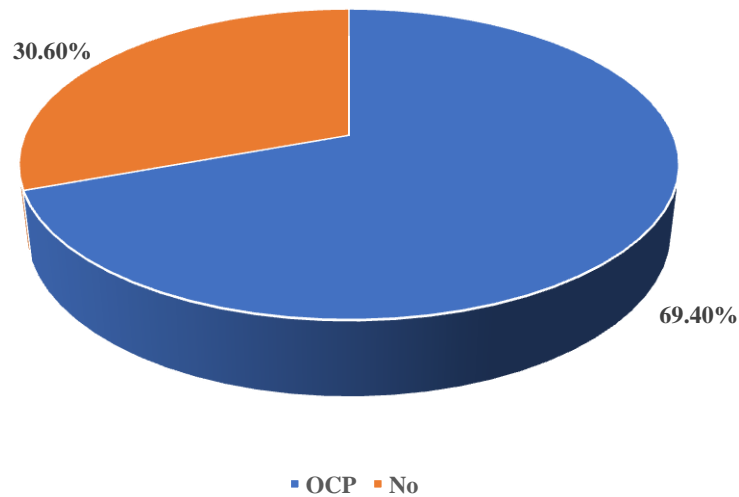
**Table VII: Distribution of the patients according to parity (n = 84)**

Table VII shows that 34 (40.5%) had 3-4 children and 28 (33.3%) had more than 4 children

Parity	Frequency	%
No child	1	1.2
1-2 children	21	25.0
3-4 children	34	40.5
>4 children	28	33.3
<b>Total</b>	<b>84</b>	<b>100.0</b>

**Figure II: Distribution of patients according to contraceptive history (n = 84)**

Figure II shows that, most of the patients 58(69.4%) had history of received OCP.



**Table VIII: Distribution of the patients according to colposcopy diagnosis (n = 84)**

Table VIII shows that regarding colposcopic diagnosis, 16.7% (n=14) were normal, 57.1% (n=48) were CIN I, 14.4% (n=12) were CIN II and 11.9% (n=10) were CIN III.

Colposcopy parameters	Frequency	%
Normal	14	16.7
CIN I	48	57.1
CIN II	12	14.3
CIN III	10	11.9
<b>Total</b>	<b>84</b>	<b>100.0</b>

**Table IX: Distribution of the patients according to histopathologic diagnosis (n = 84)**

Table IX shows that regarding histopathological diagnosis, 32.1% (n=27) chronic cervicitis, 42.9% (n=36) CIN I, 8.3% (n=7) CIN II, 7.1% (n=6) CIN III, 4.8% (n=4) carcinoma in situ and 4.8% (n=4) were invasive squamous cell carcinoma.

Histopathological parameters	Frequency	%
Chronic cervicitis	27	32.1
CIN I	36	42.9
CIN II	7	8.3
CIN III	6	7.1
CIS	4	4.8
Cancer	4	4.8
<b>Total</b>	<b>84</b>	<b>100.0</b>

#### IV. DISCUSSION:

The present scientific and therapeutic foundation for cervical cancer prevention and treatment is provided by histopathology and cytopathology. Histopathology classifies the microscopic cell organization patterns in tissue slices from biopsy or surgical specimens into a diagnosis that guides the treatment of cancer and precancer. While viral and molecular knowledge is replacing morphological concepts of cervical cancer and precancer evolution, histopathology is still significant because it is the most commonly used clinical endpoint for evaluating the effectiveness of novel approaches to cervical cancer prevention. The primary technique of cervical screening in effective cervical cancer prevention programs is cervical cytopathology, which examines exfoliated cells removed from the cervix's surface.

The cross-sectional observational study was conducted in the Department of Colposcopy Clinic of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, from January 2022 to December 2022. A total of 84 subjects were included in the study.

In this study, the mean age was found to be  $32.8 \pm 7.9$  years, with a range from 20 to  $>51$  years maximum 32 (38.1%) of the patients were within the age group of 20 - 30 years and minimum 9 (10.7%) of the patients were in the age  $>51$  years. In a study conducted by Parvin et al. 2016, the mean age of the study population was  $37.57 \pm 9.41$  years, range from 20 to 60 years. The mean age of marriage of the study population was  $16.33 \pm 3.35$  years, range 10-30 years and mean age of delivery was  $19.24 \pm 3.91$  years, range 13- 38 years [18]. the majority 43 (51.2%) of patients completed primary level and 11 (13.1%) patients were illiterate and most of the patients 68 (80.9%) were housewives and 16 (19.1%) were service holder. Most of the patients 80 (95.2%) were Muslims and 4 (4.8%) were Hindu and about 42 (50.0%) came from middle-income families. About 34 (40.5%) patients were married between the ages of 15-17 years and 24 (28.6%) patients were married in the ages of  $<15$  years. About 33 (39.3%) were between 16-18 years during their first delivery and 16 (19.0%) were in  $\leq 15$  years during their first delivery. About 34 (40.5%) had 3-4 children and 28 (33.3%) had more than 4 children. Most of the patients 58 (69.4%) had history of received OCP. Regarding colposcopic diagnosis, 16.7% (n=14) were normal, 57.1% (n=48) were CIN I, 14.4% (n=12) were CIN II and 11.9% (n=10) were CIN III and regarding histopathological diagnosis, 32.1% (n=27) chronic cervicitis, 42.9% (n=36) CIN I, 8.3% (n=7) CIN II, 7.1% (n=6) CIN III, 4.8% (n=4) carcinoma in situ and 4.8% (n=4) were invasive squamous cell carcinoma. In a study conducted by Rosenthal et al. 2001 in 314 women presenting with postcoital bleeding, 3% (n=9) had cervical cancer, 5% (n=17) had CIN I, 12% (n=37) had CIN II-III and rest of them having others disease. In the same study, the authors reported cervical cancer in 0.6% of women with postcoital bleeding who had normal looking cervixes and normal smear [9]. Study by Boicea et al, 245 patients who presented with malignant findings at colposcopy and biopsy. Colposcopic findings in their study group: 11.4% (n=28) cases were CIN I, 20.4% (n=50) CIN II, 61.2% (n=150) CIN III, 5.3% (n=13) microinvasive carcinoma and 1.6% (n=4) CIS. Histopathological results were: 1.6% (n=4) cases normal, 10.6% (n=26) CIN I, 22.4% (n=55) CIN II, 56.3% (n=138) CIN III, 6.1% (n=15) microinvasive carcinoma and 2.8% (n=7) CIS.

A cross-sectional and comparative study conducted by Nessa et al. (2019) 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 [20].

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) and 1646 (6.15%) women with cervical cancer were referred to oncology [20].

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  $16.93 (\pm 1)$  and the mean age of 1st delivery was 18.45 years ( $\pm 4.10$ ). 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 [21].

## V. CONCLUSION:

Precancerous cervical lesions remain a serious public health concern. Women will continue to die from it unless effective screening techniques like VIA and HPV immunization are expanded. Precancerous lesion occurrence is also substantially correlated with a history of monthly abnormalities, STIs, bleeding after coitus, parity larger than  $\geq 4$ , steroid use, and an unfavorable attitude toward screening variables. This suggests that since most of the determinants may be found early on, clinicians can be crucial in preventing the lesion from progressing to cancer. Therefore, in order to control cervical cancer at the early stages of lesions, effective prevention strategies must take these aspects into account.

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