

Research Article

Open Access

Prevalence of Cervical Intraepithelial Neoplasia (CIN) in Bangladesh

Ashrafun Nessa¹, Afroza Khanam², Howa Akhter Jahan³, Karuna Rani Karmakar⁴, Shaila Jesmin⁵, SM Shahida⁶, Mohammad Harun Ur Rashid⁷

¹ Department of Gynaecological-Oncology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbag, Dhaka, Bangladesh

² Department of Obstetrics & Gynaecology, Khulna Medical College Hospital (MCH), Khulna, Bangladesh

³ Department of Obstetrics & Gynaecology, Sher-E-Bangla MCH, Barisal, Bangladesh

⁴ Department of Obstetrics & Gynaecology, Comilla MCH, Comilla, Bangladesh

⁵ Department of Obstetrics & Gynaecology, Rajshahi MCH, Rajshahi, Bangladesh

⁶ Department of Obstetrics & Gynaecology, Dhaka MCH, Dhaka, Bangladesh

⁷ Directorate General of Health Services, Mohakhali, Dhaka, Bangladesh

***Corresponding author:** Ashrafun Nessa, Professor, Department of Gynaecological-Oncology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbag, Dhaka, Bangladesh, Email: ashra58@yahoo.co.uk

Citation: Nessa A, et al (2021) Prevalence of Cervical Intraepithelial Neoplasia (CIN) in Bangladesh. J Gyn ob adv 1(2): 1-8.

Received Date: July 05, 2021; **Accepted Date:** August 27, 2021; **Published Date:** September 01, 2021

Abstract

Introduction: Cervical cancer is the most common genital tract cancer among Bangladeshi women. The government of Bangladesh (GOB) has introduced Visual Inspection of Cervix with Acetic Acid (VIA) method for cervical cancer screening at the all-tier public health facilities. VIA positive cases are being referred to the colposcopy clinics at higher facilities where evaluation and management are carried out. It is important to know the baseline prevalence of cervical cancer and pre-cancer of the unscreened population at the preliminary part of the national screening program.

Objectives: This study was conducted to detect the prevalence of Cervical Intraepithelial Neoplasia (CIN) among Bangladeshi women and the influence of socio-demographic factors on the prevalence.

Methodology: This cross-sectional, population-based study was carried out among selected women of 20 randomly selected sub-districts of 20 randomly selected districts of 5 divisions (Dhaka, Khulna, Chittagong, Rajshahi and Barisal) of Bangladesh by the Department of Obstetrics and Gynaecology of 5 Medical College Hospitals (MCHs) and Bangabandhu Sheikh Mujib Medical University (BSMMU). Almost equal number of married women between 25-55 years of age and who were non-pregnant were randomly recruited from each selected sub-districts and they had colposcopy at health complexes of respected sub-districts through temporary arrangement between August 2014 and July 2015 and a total of 5369 women were participated in this study. Suspected pre-cancer cases had cervical biopsy and all histopathology examinations were done at the Department of Pathology of BSMMU. Diagnosed CIN cases were called at the colposcopy clinic of respective MCHs for necessary managements.

Results: The mean age recruited women were 36.34±7.06 years, mean age of their marriage was 17.0±3.34 years and mean age of their first delivery was 19.34±4.08 years. Among them 100 (1.9 %) had histology diagnosed CIN I, 93 (1.7%) had CIN II, 24(.4%) had CIN III and one women had squamous cell carcinoma. Considering histopathology as gold standard and CIN II /III and cancer as disease, the sensitivity and specificity of colposcopy were 68.6% and 99.4%. Regression analysis revealed that women's age 40 years and above ($p = 0.031$) and women's low level of education ($p = 0.024$) had significant influence on development of cervical pre-cancer.

Conclusions: The prevalence of CIN was comparable to other developing Asian countries. Women's age 40 years and above and women's education less than secondary level had independent influence on development of cervical pre-cancer and they should get priority for rapid detection at shorter duration in the initial part of the screening program.

Introduction

Cervical cancer is one of the common cancers in women across the globe. In Bangladesh, cervical cancer is the 2nd most common cancer among women, with age-standardized rates (ASRs) for incidence and mortality much higher than the global average statistics (Incidence rates: 19.3 vs. 14.0/100,000 women; Mortality rates: 11.5 vs. 6.8/100,000 women). It is estimated that every year 11,956 new cases of cervical cancer are detected in Bangladesh and 6582 women die of the disease [1]. Survival of cervical cancer patients is strongly determined by stage at diagnosis. The overall 5-year relative survival for early and localized cancers is 73.2%, but can be as low as 7.4% for advanced stage disease [2]. Cervical cancer is a slowly progressing disease and it is widely accepted that detection and treatment of cervical pre-cancer reduces the incidence of frank cancer. Death from cervical cancer is also preventable by vaccination against human papillomavirus (HPV) at younger age. HPV vaccination is not yet introduced at national level in Bangladesh and it is important to identify women with cervical pre-cancer and treat them to reduce the cervical cancer burden in this country. The Government of Bangladesh (GOB) is providing particular emphasis on this secondary prevention of cervical cancer by developing nationwide cervical cancer screening program. Visual Inspection of Cervix with Acetic Acid (VIA) is the accepted method of cervical cancer screening at selected sub-districts, maternal and child welfare centers (MCWCs), Upazila health complexes (UHCs), district hospitals (DHs), medical college hospitals (MCHs) and Bangabandhu Sheikh Mujib Medical University (BSMMU). VIA is performed by trained family welfare visitors (FWVs), senior staff nurses (SSNs) and doctors to detect precancerous conditions or initial stages of cervical cancer for the women of 30 years and above. Screen-positive women have colposcopic evaluation and management at different government MCHs and BSMMU [3-7]. GOB developed about 411 'VIA centers' at different level of health care system and continuing expansion of the programme [7-9]. Most of the districts have at least 4-6 VIA centers and the program is providing opportunistic screening services. A population based organized services should be developed to fulfill the requirement of the country with expectation of reducing cervical cancer prevalence in near future. Therefore, to assess the ultimate impact of the programme, assessment of the baseline prevalence of cervical intraepithelial neoplasia (CIN) at different areas of the country was required. This population-based study aimed to determine the prevalence of CIN among unscreened women of five out of eight divisions of Bangladesh. The socio-demographic variables, reproductive factors relevant to development of CIN and cervical cancer were also explored.

Methodology

This cross-sectional, population-based study was carried out by the Department of Obstetrics and Gynaecology of BSMMU and 5 different MCHs among women of twenty randomly selected sub-districts (UHCs of 20 randomly selected districts) of 5 divisions of

Bangladesh.

Recruitment of women

Colposcopists from the MCHs of selected divisions and BSMMU provided daylong orientation to nurses and female field health workers of the selected UHCs on methodology of the study, counseling, recruitment and referral of women. Married women between 25-55 years of age, mentally able to provide informed consent were recruited through door-to-door visits by the trained female field health workers. Women were selected after face-to-face communication and attempt was taken to recruit almost equal number of women from each ward (functional units of sub-districts). Woman from alternate household was offered to participate in the research and referred to respective UHC at sub-districts on a selected date. If woman from a particular household disagreed to participate, woman was recruited from the next household. Women with chronic illness, pregnancy, and unwilling to participate in the study were excluded in this study.

Data collection

About 25-55 women were invited on specified date set UHC of each selected sub-district from 1st August 2014 to 31st July 2015. At the UHC, the women were further counseled and interviewed using a standardised questionnaire by female doctor or research assistant and written informed consent was taken from each participant. The interview questionnaire collected information on socio-demographic and reproductive health characteristics, examination findings, histopathology report and treatment related information. A temporary colposcopy facility using standard colposcopes (Karl Kaps Som 52 or Leisegang 1DF) was arranged at the selected UHCs for duration of about 15 days and the colposcopists from respective MCH and BSMMU performed colposcopy of the selected women and collected biopsy whenever necessary. Severity of CIN was assessed on intensity of aceto-whitening of epithelium, margins and surface contour of aceto-white areas, vascular features (punctuation, mosaics) and color changes after iodine application. All histopathology examinations were done at the Department of Pathology of BSMMU. Diagnosed cases with high grade lesions were called at colposcopy clinic of respective MCHs for necessary managements. Ethical clearance for the research was obtained from the Institutional Review Board (IRB) of BSMMU.

Data management and analysis plan

The calculated minimum sample size from each sub-district following the standard sample size estimation formula with 03% prevalence of cervical pre-cancer with 95% confidence was 220 and attempt was taken to fulfill it during data collection. The data analysis was performed using Statistical Package for the Social Sciences (SPSS) Version 17.0. The baseline characteristics of the women were summarized using means and frequencies. Rates of CIN I, CIN II, CIN III, Ca-cervix and normal findings, as well as demographic data were calculated. Sensitivity and specificity were calculated using histopathology as a gold-standard. Logistic

regression analysis was performed to find out the influence of socio-demographic and reproductive factors on cervical pre-cancer.

Results

Among 5549 women attending the colposcopy setup of twenty UHCs, 5369 women were finally recruited from selected sub-districts considering the exclusion and inclusion criteria. From each sub-district about 200-300 women participated in this prevalence study (Table 1).

Table 1: Distribution of Study Population from Selected Sub-districts (n= 5369)

Division	District	Sub-district	No. (%)
Barisal	Barisal	Wezirpur	248 (4.6)
	Bhola	Daulat khan	248 (4.6)
	Patuakhali	Patuakhali	250 (4.7)
	Jhalokathi	Razapur	254 (4.7)
Chittagong	Comilla	Daudkandi	245 (4.6)
	Cox's Bazar	Ramu	266 (5.0)
	Chandpur	Faridganj	247 (4.6)
	Feni	Sonagazi	251 (4.7)
Dhaka	Munshiganj	Sirajdikhan	341(6.4)
	Dhaka	Dohar	223 (4.2)
	Rajbari	Goyalondo	330 (6.1)
	Gazipur	Kaliganj	233 (4.3)
Khulna	Jessore	Avaynagor	315 (5.9)
	Khulna	Fultola	264 (4.9)
	Bagerhat	Mongla	307 (5.7)
	Satkhira	Tala	313 (5.8)
Rajshahi	Natore	Lalpur	248 (4.6)
	Rajshahi	Puthia	268 (5.0)
	Chapainawabganj	Shibganj	248 (4.6)
	Pabna	Atgoriya	270 (5.0)
Total			5369 (100.0)

The socio-demographic characteristics of the study population showed mean age of women was 36.34 ± 7.06 years and about one thirds of them were 40 years or older. Though a good number of them 3930 (77.7%) had at least primary education, 1611 (30.0%) had secondary education and only 579 (10.7%) had higher secondary education or above (Table 2).

Women's husband had higher level of higher secondary education or above 920 (17.11%). Majority of the women were housewives 5155 (96.0%). About 4655 (86.7%) women were Muslim and remaining were Hindu, Buddhist and Christian. About two third of the family belonged to the low- and middle-income group (Table 2).

Table 2: Socio-Demographic Characteristics of Women (n=5369)

Characteristics	Categories	No. (%)
Age Group	25-29 years	661 (12.3)
	30-34 years	1606 (29.9)
	35-39 years	1304 (24.3)
	40-44 years	852 (15.9)
	45-49 years	627(11.7)
	50-55 years	319 (5.9)
Education of Women	No formal education	860 (16.00)
	Primary education	2319 (43.20)
	Secondary education	1611 (30.00)
	Higher Secondary education	334 (6.20)
	Graduate & above	245(4.50)
Education of Husband	No formal education	1036 (19.30)
	Primary education	1878 (35.00)
	Secondary education	1535 (28.50)
	Higher Secondary education	445 (8.30)
	Graduate & above	475 (8.81)
Occupation of women	House Wife	5155 (96.0)
	Service holder	159 (3.0)
	Teacher	39 (0.7)
	Business	9 (0.2)
Occupation of Husband	Labour	7 (0.2)
	Farmer	1504 (28.00)
	Business	1448 (27.00)
	Service holder	1410 (26.3)
	Teacher	68 (1.3)
	Labour	541 (10.1)
	Driver	204 (3.8)
	Unemployed	164 (3.1)
Religion	Not alive	30 (0.6)
	Islam	4655 (86.7)
	Hindu	644 (12.0)
	Christian	10 (0.2)
Monthly Income	Buddhist	60 (1.1)
	Very poor (up to taka 3000)	491 (9.1)
	Taka 3001-6000	1618 (30.1)
	Taka 6001-9999	1376 (25.6)
Taka 10000 and above	1884 (35.1)	

Reproductive characteristics of the study population revealed the mean age of marriage was 17.04 ± 3.34 years and more than half of them were married before 18 years of age. Mean age of first delivery was 19.34 ± 4.08 and about one third of them had their first delivery before 20 years of age. The mean parity was 2.73 ± 1.40 and 537 (10%) of them had parity 5 and above (Table 3).

Table 3: Reproductive Characteristics of Women (n=5369)

Characteristics	Categories	No. (%)
Age of marriage	Before 18 years	3056 (56.9)
	18 – 20 years	1831 (34.1)
	21 – 24 years	278 (5.2)
	25 and above	204 (3.8)
Age of 1st delivery	Before 18 years	1540 (28.7)
	18 – 20 years	2395 (44.6)
	21 – 24 years	980 (18.3)
	25 and above	454 (8.5)
Number of Marriage of Women	One	5243 (97.7)
	Two	124 (2.3)
	Three	2 (.0)
Number of Marriage of Husband	One	5081 (94.6)
	Two	255 (4.7)
	Three	33 (0.6)
Parity	0-2	2716 (50.6)
	3-4	2116 (39.4)
	5 and above	537 (10.0)

Colposcopic examination showed that among 5369 women, 221 (4.1%) had CINI, 83 (1.5%) had CINII, 27 (0.5%) had CIN III and one woman had early cervical cancer (Table 4). The histology findings of colposcopy guided specimens showed that 100 (1.9%) had CIN I, 93 (1.7%) had CIN II, 24 (0.4%) had CIN III and one woman had squamous cell carcinoma (Table 4).

The distribution of cervical pre-cancer in the selected areas of the country showed that there was one invasive cancer in Puthia of Rajshahi which was included with CIN III during data analysis. There was no significant difference of prevalence of cervical pre-cancer among different sub-districts or districts (Table 5).

Considering histopathology as gold standard, the sensitivity and specificity of colposcopy were 68.6% and 99.4% when CIN II /III and cancer identified as disease in both colposcopy and histopathology.

Among different cofactors for development of cervical pre-cancer and cancer, age, education, age of marriage, age of first delivery, parity and socio-economic condition were considered in this study. Considering histopathology as gold standard and high-grade lesions as disease, logistic regression analysis did not show any significant association of parity five or more, age of

marriage less than 18 years, age of 1st delivery 20 years and less and low socio-economic condition on development of cervical pre-cancer. Among all the socio-demographic and reproductive factors considered, women's age 40 years and above ($p = 0.031$) and women's education less than secondary level ($p = 0.024$) had significant influence on development of cervical pre-cancer (Table 6).

Table 4: Colposcopy and Histopathology findings of the study population (n=5369)

Procedure	Findings	No. (%)
Colposcopy	Normal	5037 (93.8)
	CINI	221 (4.1)
	CINII	83 (1.5)
	CINIII	27 (0.5)
	Cervical cancer	1 (0.0)
Histopathology	Normal	108 (2.0)
	CIN I	100 (1.9)
	CIN II	93 (1.7)
	CIN III	24 (.4)
	Squamous Cell Carcinoma	1 (.0)
	Report not available	8 (0.1)
	Not Necessary	5035 (93.8)
Total		5369

Discussions

The information on population-based prevalence of cervical pre-cancer and cancer reflects the burden of the disease in different areas of a country and helps in planning appropriate screening strategies on the basis of regional prevalence. This is the 1st population-based study informing prevalence of cervical pre-cancer in different districts, its regional variation and risk factors of cervical pre-cancer and cancer in Bangladesh. The present study included information principally from rural population of 20 out of 64 districts of the country including hilly areas. So far almost no information was available on baseline prevalence of cervical cancer or pre-cancer in Bangladesh. Therefore, results obtained from this study will be helpful in cervical cancer prevention program in Bangladesh and other developing countries.

In the present population-based study, the overall prevalence of histopathology detected CIN I, CIN II and CIN III were 1.9%, 1.7% and 0.4% respectively. There was only one case of invasive cancer. A demonstration project among 39,740 women in the rural districts of Eastern India showed nearer histology detection rates following colposcopy of VIA positive women. The detection rate of CINI, CINII, CINIII and invasive cancer were 3.72%, 0.2%, 0.18% and 0.10% respectively [10]. Another community-based study in similar population in India among 44,110 women, used HPV test

Table 5: Area wise distribution of cervical pre-cancer

Name of Division	Name of District	Name of Sub-district (Upazila)	Normal	CIN I	CIN II	CIN III	All grades of CIN	Not Necessary	Report not available	Total
Dhaka	Dhaka	Dohar	1 (0.4%)	2 (0.9%)	8 (3.6%)	1 (0.4%)	11 (4.9%)	211 (94.6%)	0 (0%)	223 (100.0%)
	Gazipur	Kaliganj	15 (6.5%)	9 (3.9%)	3 (1.3%)	1 (0.4%)	13 (5.6%)	203 (87.9%)	0 (0%)	233 (100.0%)
	Munshiganj	Sirajdikhan	6 (1.8%)	2 (0.6%)	4 (1.2%)	1 (0.3%)	7 (2.1%)	329 (95.9%)	1 (0.4%)	343 (100.0%)
	Rajbari	Goyalondo	4 (1.2%)	4 (1.2%)	3 (0.9%)	1 (0.3%)	8 (2.4%)	318 (96.4%)	0 (0%)	330 (100.0%)
Chittagong	Comilla	Daudkandi	10 (4.1%)	2 (0.8%)	8 (3.3%)	1 (0.4%)	11 (4.4%)	223 (91.0%)	1 (0.4%)	245 (100.0%)
	Chandpur	Faridgong	5 (2.0%)	4 (1.6%)	3 (1.2%)	1 (0.4%)	8 (3.2%)	234 (94.7%)	0 (0%)	247 (100.0%)
	Cox's Bazar	Ramu	2 (0.8%)	7 (2.6%)	2 (0.8%)	1 (0.4%)	10 (3.8%)	252 (94.7%)	2 (0.8%)	266 (100.0%)
	Feni	Sonagazi	6 (2.4%)	1 (0.4%)	3 (1.2%)	1 (0.4%)	5 (2.0%)	240 (95.6%)	0 (0%)	251 (100.0%)
Khulna	Bagerhat	Mongla	6 (2.0%)	13 (4.2%)	6 (2.0%)	2 (0.7%)	21 (6.9%)	279 (90.9%)	1 (0.3%)	307 (100.0%)
	Jessore	Avaynagor	8 (2.5%)	7 (2.2%)	3 (1.0%)	1 (0.3%)	11 (3.3%)	296 (94.0%)	0 (0%)	315 (100.0%)
	Khulna	Fultola	6 (2.3%)	13 (4.9%)	2 (0.8%)	4 (1.5%)	19 (7.2%)	239 (90.5%)	0 (0%)	264 (100.0%)
	Satkhira	Tala	6 (2.0%)	10 (3.2%)	4 (1.3%)	1 (0.3%)	15 (4.8%)	292 (93.3%)	0 (0%)	313 (100.0%)
Rajshahi	Chapainawabganj	Shibganj	4 (1.6%)	3 (1.2%)	4 (1.6%)	1 (0.4%)	8 (3.2%)	236 (95.2%)	0 (0%)	248 (100.0%)
	Natore	Lalpur	3 (1.2%)	7 (2.8%)	12 (4.8%)	1 (0.4%)	20 (8.1%)	225 (90.7%)	0 (0%)	248 (100.0%)
	Pabna	Atgoriya	7 (2.6%)	3 (1.1%)	7 (2.6%)	1 (0.4%)	11 (4.4%)	252 (93.3%)	0 (0%)	270 (100.0%)
	Rajshahi	Puthia	10 (3.7%)	4 (1.5%)	7 (2.6%)	1 (0.4%)	12 (4.5%)	245 (91.4%)	0 (0%)	268 (100.0%)
Barisal	Barisal	Wezirpur	5 (2.0%)	1 (0.4%)	5 (2.0%)	1 (0.4%)	7 (2.8%)	235 (94.8%)	1 (0.4%)	248 (100.0%)
	Bhola	Daulat Khan	2 (0.8%)	6 (2.4%)	4 (1.6%)	1 (0.4%)	11 (4.4%)	235 (94.8%)	0 (0%)	248 (100.0%)
	Jhalokathi	Razapur	1 (0.4%)	1 (0.4%)	3 (1.2%)	1 (0.4%)	5 (2.0%)	246 (96.9%)	2 (0.8%)	254 (100.0%)
	Patuakhali	Patuakhali	1 (0.4%)	1 (0.4%)	2 (0.8%)	1 (0.4%)	4 (1.6%)	245 (98.0%)	0 (0%)	250 (100.0%)
Total			108 (2.0%)	100 (1.9%)	93 (1.7%)	24 (0.4%)	217 (4.0%)	5035 (93.8%)	8 (0.1%)	5368* (100.0%)

* Excluding 1 invasive cancer, n= 5368

Table 6: Regression analysis of influence of socio-demographic and reproductive factors on Histology diagnosed cervical pre-cancer

Histopathology Result	B	S.E.	Wald	df	Sig.	Exp (B)	Lower Bound	Upper Bound
Intercept	-2.779	0.75	13.71	1	0			
Age 40 years and more	-0.471	0.222	4.482	1	0.034	0.625	0.404	0.966
Less than secondary education	-0.482	0.214	5.056	1	0.025	0.617	0.406	0.94
Parity five and above	0.303	0.284	1.144	1	0.285	1.354	0.777	2.361
Age of Marriage less than 18 years	0.559	0.26	4.61	1	0.032	1.749	1.05	2.914
Age of delivery 20 years and below	-0.238	0.252	0.898	1	0.343	0.788	0.481	1.29
Low socio-economic condition	-0.382	0.208	3.388	1	0.66	0.682	0.454	1.025

a. The reference category is: Non-diseased.

as primary detection method with HPV positivity (HC2) of 4.7% showed the histology proved CIN3+ as 0.39% [11]. Pooled data from three community-based studies in West Bengal, in Eastern India found prevalence of CIN1, CIN2, CIN3 and invasive cancer as 2.9%, 0.6%, 0.4% and 0.2% respectively considering the prevalence analysis by high-risk HPV, colposcopy and histopathology grading as the gold standard for CIN and cancer diagnosis [12]. Study in Andhra Pradesh of India revealed an overall prevalence of CIN 2+ lesion rate as 1.05% by VIA test followed by colposcopy and histopathology confirmation [13]. All these studies showed the prevalence of cervical pre-cancer of Bangladesh is nearer to India. Nepal showed a prevalence of cervical neoplasia as 3.69% among rural women in mid-western region [14-15]. Among 30207 women from 17 population-based studies throughout China, age standardized prevalence of CIN II was 1.5 % and 0.7%, CIN III 1.2% and 0.6% in urban and rural areas respectively [16]. All these findings of Asian countries are similar to the observation of this prevalence study.

There is world wide variation in prevalence and risk factor of cervical pre-cancer among different countries. The most important risk factor of CIN is HPV infection and variation of cervical pre-cancer may be related to variation of HPV prevalence in different countries. The High-Risk HPV (HR-HPV) prevalence among Bangladeshi women is about 7.7% which is quite nearer to the prevalence in Nepal (9%), China (12.9%) and Bhutan (10%) in Delhi of India (12.01%) and India (12.5%) [17-22]. Therefore, the prevalence of HPV infection among Bangladeshi women is almost similar to other regions of Asia and this factor is probably related to almost similar prevalence of cervical pre-cancer and cancer in all these regions.

Developed countries adopted different methods of HPV prevention and cervical pre-cancer prevention. Therefore, the prevalence of cervical pre-cancer and HPV infection in those countries are not comparable to the prevalence in Bangladesh and other developing countries. However, high prevalence of cervical neoplasia was observed among unscreened women population in different African countries. The prevalence of pre-cancer and invasive cervical cancer in Rwanda, a country in Central Africa was 5.9% and 1.7% respectively and higher prevalence of HIV (3-7% of adult population) may be related to this high prevalence of cervical neoplasia [23]. The overall HR HPV prevalence in Rwanda was 34 % and it was also significantly higher among HIV-positive (32%) than in HIV-negative (20 %) women [24]. The findings indicated that high prevalence of HPV and cervical disease is related to HIV co-infection. The present study did not have the opportunity to explore the HIV status of women among the study population. However, HIV prevalence in Bangladesh among general population is low [25].

This study was performed in unscreened population of Bangladesh and found influence of two important demographic factors on high grade cervical pre-cancer. Women's age 40 years

and above ($p = 0.031$) and women's education less than secondary level ($p = 0.024$) showed strong association on high grade cervical pre-cancer. These findings indicate that women of 40 years and above should get priority in the initial part of the screening program to identify more cases of cervical pre-cancers and cancers. Low level of education may lead to lack of awareness about the disease and its prevention and less health care seeking behavior and this can make them vulnerable to acquire cervical pre-cancer and cancer. Several other studies concluded also low education level as an important socio-demographic risk factor for cervical cancer development [23,26,27]. Policy makers should give special emphasis for improving education of women which will further improve their empowerment and health seeking behavior. In the current study, though marriages at or less than 18 years did not have independent influence on development of cervical pre-cancer, but studies in Iraq, Egypt and Rwanda reported marriage at younger age was associated with cervical pre-cancer [23,26,28].

This study found that women of 40 years of age and women with low education level are at higher risk of developing cervical cancer. The current opportunistic national program is continuing at different health care facilities. In order to improve screening coverage specific health interventions should be carried out. The program should give special importance to elderly women, women with low education level during screening to have better detection rate at shorter duration. There are resource limitations to implement cervical cancer screening program and special attention to these women will pick up more pre-cancer and early cancer. Moreover, woman's education and empowerment are important socio-demographic factors and need special attention to improve awareness and health seeking behavior. In addition to this, measures to vaccinate adolescent girls should be carried out.

One of the strong aspects of this study was that women were recruited uniformly with proper design covering 5 out of 8 divisions of the country considering other ethnic groups. Diagnosis was made on histology findings of specimens collected by punch biopsy forceps in colposcopy suspected CIN cases. All Histology examinations were done in the Department of Histopathology of BSMMU and each slide was reviewed by at least two competent histopathologists. Histology report was done by a board of the department in the cases of diagnostic disparity. However, the present prevalence study may cause some under reporting of cervical pre-cancer and cancer related to non-use of HPV test. In a low-resource setting, a single round of HPV testing was associated with a significant reduction in the numbers of advanced cervical cancers and deaths from cervical cancer. Of the 27,192 women screened by the HPV-testing, 2812 (10.3%) had positive results; the proportions of cancers that were detected in stage I were about 60% in the HPV-testing groups, 42% in the VIA group, and 28% in the control group [29-30]. Further prevalence study with larger sample size should be done using HR-HPV test as the primary detection method followed by colposcopy for the HPV positive cases.

In developing countries like Bangladesh, cancer receives less attention and resources than other challenging health and public and environmental requirements such as, tuberculosis, flood, cyclone, refugee problem, poor sanitation, and poverty. Cervical cancer prevention program should be well planned and adequate interventions should be implemented in developing countries as this cancer remains a leading cause of death and morbidity in women.

Conclusion

The prevalence of cervical pre-cancer in Bangladesh is comparable to the prevalence of other Asian countries. Women's age 40 years and above and women's education less than secondary level had independent influence on development of cervical pre-cancer and they should get priority for rapid detection at shorter duration in the initial part of the screening program.

Cervical cancer should be prevented through national screening programmes and the program need to be matched with the country requirement and available resources. The baseline prevalence data obtained from the research should help in successful and sustainable implementation of the prevention programme. The government need to use the obtained information adequately to accelerate the efficacy of the programme. Further research is necessary to find alternatives to VIA-based programmes, specifically molecular testing for HR-HPV.

GOB has approved the "National Strategy for Cervical Cancer Prevention and Control Bangladesh (2017-2022)" and this strategy recommends adolescent vaccination. GOB initiated HPV demonstration program at Gazipur in April, 2016 through vaccination to girls of grade V at school and 10 years at community. This is a school-based vaccination program and the HPV vaccine demonstration programme was completed successfully. GOB in now collaborating with development partners to mobilize sufficient resources and awaiting to incorporate it in routine immunization services.

Acknowledgments

This work would not have been possible without the financial support of the Medical Education and family Welfare Division of Ministry of Health and Family Welfare. We are especially indebted to the Department of Obstetrics and Gynecology of Dhaka, Khulna, Chittagong, Rajshahi and Barisal Medical College Hospitals and Bangabandhu Sheikh Mujib Medical University. We are very grateful to all of the women who had participated in this research work. Also thankful to them with whom we had the pleasure to work during this study.

Disclosure

The authors declare that there is no conflict of interest.

References

1. Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, et al. GLOBOCAN 2012: Estimated Cancer Incidence, Mortality and Prevalence Worldwide in 2012 v1.0. Lyon, France: International Agency for Research on Cancer. 2012.
2. Sankaranarayanan R, Swaminathan R, Brenner H, Chen K, Chia KS, Chen JG, et al. Cancer survival in Africa, Asia, and Central America: a population-based study. *Lancet Oncol.* 2010;11(2):165-173.
3. Ahmed T, Ashrafunnessa, Rahman J. Development of a Visual Inspection Programme for Cervical Cancer Prevention in Bangladesh. *Elsevier Reproductive Health Matters.* 2008;16(32):78-85.
4. Basu P, Nessa A, Majid M, et al. Evaluation of the National Cervical Cancer Screening Programme of Bangladesh and the formulation of quality assurance guidelines. *J FamPlannReprodHlth Care.* 2010;36(3):131-134.
5. Nessa A, Hussain MA, Rahman JN, Rashid MH, Muwonge R, Sankaranarayanan R. Screening for cervical neoplasia in Bangladesh using visual inspection with acetic acid. *Int J Gynaecol Obstet.* 2010;111(2):115-118.
6. Nessa A, Rashid MH, Ferdous NE Chowdhury A. Screening for and management of high-grade cervical intraepithelial neoplasia in Bangladesh: A cross-sectional study comparing two protocols. *J Obstet Gynaecol Res.* 2013;39(2):564-571.
7. Holme F, Kapambwe S, Nessa A, Partha B, Murillo R, and Jeronimo J. Scaling up proven innovative cervical cancer screening strategies: Challenges and opportunities in implementation at the population level in low and lower-middle income countries. *Int J Gynecol Obstet.* 2017;138 Suppl 1:63-68.
8. Nessa A, Naud P, Esmey PO, Joshi S, Rema P, Wesley R, Kamal M, Sauvaget C, Muwonge R, Sankaranarayanan R. Efficacy, Safety, and Acceptability of Thermal Coagulation to Treat Cervical Intraepithelial Neoplasia: Pooled Data from Bangladesh, Brazil and India. *Clin Gynecol Obstet.* 2017;6(3-4):58-64.
9. Health Bulletin 2018. Management Information System, Directorate General of Health Services, Ministry of Health and Family Welfare Dhaka, Bangladesh. 2018.
10. Basu P, Mittal S, Banerjee D, Singh P, Panda C, Dutta S, Mandal R, Das P, Biswas J, Muwonge R, and Sankaranarayanan R. Diagnostic accuracy of VIA and HPV detection as primary and sequential screening tests in a cervical cancer screening demonstration project in India. *Int.J.Cancer.* 2015;137(4):859-867.
11. Mittal S, Mandal R, Banerjee D, Das P, Ghosh I, Panda C, Biswas J, Basu P. HPV detection-based cervical cancer screening program in low-resource setting: lessons learnt from a community-based demonstration project in India. *Cancer Causes Control.*

- 2016;27(3):351-358. doi: 10.1007/s10552-015-0708-z
12. Basu P, Mittal S, Bhaumik S, Mandal S S, Samaddar A, Ray C, Siddiqi M, Biswas J, Sankaranarayanan R. Prevalence of high-risk human papillomavirus and cervical intraepithelial neoplasias in a previously unscreened population - A pooled analysis from three studies. *Int. J. Cancer*; 2013;132(7):1693-1699.
 13. Poli U R, Bidinger P D, Gowrishankar S. Visual Inspection with Acetic Acid (VIA) Screening Program: 7 Years' Experience in Early Detection of Cervical Cancer and Pre-Cancers in Rural South India. *Indian J Community Med*. 2015;40(3):203-207.
 14. Thapa N, Shrestha G, Maharjan M, Lindell D, Maskey N, Shah R, et al. Burden of cervical neoplasia in mid-western rural Nepal: a population-based study. *J Gynaecol Oncol*. 2018;29:e64.
 15. Tshomo U, Franceschi S, Tshokey T, Tobgay T, Baussano L, Tanet V, et al. Evaluation of cytology versus human papillomavirus-based cervical cancer screening algorithms in Bhutan. *Oncotarget*. 2017;8(42):72438-72446.
 16. Zhao FH, Lewkowitz AK, Hu SY, Chen F, Li LY, Zhang QM, Wu R F, Li C Q, Wei L H, Xu AD, Zhang WH, Pan QJ, Zhang X, Belinson JL, Sellors JW, Smith JS, Qiao YL and Franceschi S. Prevalence of Human Papillomavirus and Cervical Intraepithelial Neoplasia in China; A pooled analysis of 17 population-based studies. *Int J cancer*. 2012; 131(12):2929-2938.
 17. Nahar Q, Sultana F, Alam A, Islam JY, Rahman M, Khatun F, Alam N, Dasgupta SK, Marions L, Ashrafunnessa, Kamal M, Cravioto A, Reichenbach L. Genital human papillomavirus infection among women in Bangladesh: findings from a population-based survey. *PLoS One*, 2014;9(10):e107675. doi: 10.1371/journal.pone.0107675
 18. Sherpa AT L, Clifford GM, Vaccarella S, Shrestha S, Nygard M, Karki B S, Snijders PJF, Meijer CJLM, Franceschi S. Human papillomavirus infection in women with and without cervical cancer in Nepal. *Cancer causes control*. 2010;21(3):323-30. doi: 10.1007/s10552-009-9467-z
 19. Li Z, Liu F, Cheng S, Shi L, Yan Z, Yang J, et al. Prevalence of HPV infection among 28, 457 Chinese women in Yunnan province, southwest china. *SCIENTIFIC REPORTS*. 2016;6:21039. Doi: 10.1038/srep21039
 20. Baussano I, Tshering S, Choden T, Lazzarato F, Tenet V, Plummer M, Franceschi S, Clifford GM, Tshomo U. Cervical cancer screening in rural Bhutan with the care HPV test on self-collected samples: an ongoing cross-sectional, population-based study (REACH-Bhutan). *BMJ Open* 2017;7(7):e016309. doi: 10.1136/bmjopen-2017-016309
 21. Veena S, Premraj S, Narotam S, Pracheta, Ritu P. Study of epidemiology of HPV infection in the Uterine Cervix of Women's in Delhi/NCR regions, India. *Int. J. Drug Dev. & Res*. 2012;4:311-315.
 22. Franceschi S, Rajkumar R, Snijders PJF, Arslan A, Mahe C, Plummer M, et al. Papillomavirus infection in rural women in southern India. *British Journal of Cancer*. 2005;92(3):601-606.
 23. Makuza JD, Nsanzimana S, Muhimpundu MA, Pace LE, Ntaganira J, Riedel DJ. Prevalence and risk factors for cervical cancer and pre-cancerous lesions in Rwanda. *The Pan African Medical Journal*. 2015;11:22-26.
 24. Ngabo F, Franceschi S, Baussano I, Umulisa MC, Snijders PJF, Uytterlinde A M, et al. Human papillomavirus infection in Rwanda at the moment of implementation of a national HPV vaccination programme. *BMC Infectious Diseases*. 2016;16:225. doi: 10.1186/s12879-016-1539-6
 25. National AIDS/STD programme (NASP). Assessment of impact of harm reduction interventions among people who inject drugs (PWID) in Dhaka city. Dhaka, Bangladesh: Ministry of Health and Family Welfare, Directorate General of Health Services. 2014.
 26. El-Moselhy EA, Borg HM, Atlam SA. Cervical Cancer: Sociodemographic and Clinical Risk Factors among Adult Egyptian Females. *Adv Oncol Res Treat*. 2016;1(2):1-7.
 27. Ganesan S, Subbiah VN, Michael JJ. Associated factors with cervical pre-malignant lesions among the married fisher women community at Sadras, Tamil Nadu. *Asia Pac J Oncol Nurs*. 2015;2(1):42-50. doi: 10.4103/2347-5625.146223
 28. Hussain Saad, Khalaf May, Rasheed Faris. Association between Early Marriage and Other Sociomedical Characteristics with the Cervical Pap smear Results in Iraqi Women. *Advances in Sexual Medicine*. 2015;5(4):73. 10.4236/asm.2015.54009
 29. Jensen KE, Schmiedel S, Norrild B, Frederiksen K, Iftner T, Kjaer S K. Parity as a cofactor for high-grade cervical disease among women with persistent human papillomavirus infection: a 13-year follow-up. *Br J Cancer*. 2013;108(1):234-239.
 30. Sankaranarayanan R, Nene BM, Shastri SS, Jayant K, Muwonge R, Budukh A M, et al. HPV Screening for Cervical Cancer in Rural India. *N Engl J Med*. 2009;360(14):1385-1394. doi: 10.1056/NEJMoa0808516