

Prevalence of Cervical Intraepithelial Neoplasia (CIN) at Khulna Division of Bangladesh

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Summary:

Back ground: Cervical cancer is the most common genital tract cancer and the important cause of cancer death among Bangladeshi women. Information about actual number of women living with preinvasive phase of cervical cancer and their diagnosis and treatment is limited. For strengthening the programme and policy for cervical cancer prevention, the baseline prevalence of cervical intraepithelial neoplasia (CIN) need to be assessed.

Methods: This population based study aimed to determine the prevalence of CIN among women of Khulna division of Bangladesh. Data has been collected from four upazila of four districts of Khulna division. VIA and colposcopy and histopathology was used for detection of cervical pre-cancers and early cancers among 1232 women of the mentioned population.

Results: Crude prevalence of CIN was 5.84 %, CIN-II 1.1% and CIN- III .73% in colposcopically directed biopsy. Ninety two participants with CIN received treatment at the Colposcopy Clinic of Obstetrics and Gynaecology department of Khulna Medical College Hospital (KMCH).

Conclusion: This population based prevalence study of CIN and socio demography would have conducive effect on future cervical cancer prevention programme.

Key word: CIN, population prevalence, Bangladesh.

Introduction:

Cervical cancer is the fourth most common cancer in women with an estimated 527,624 new cases and 265,653 deaths in 2012. Around 85% of these new cases and 86% of deaths occur in less developed countries. In Bangladesh, cervical cancer is the 2nd most common cancer in 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).¹ Death from cervical cancer is preventable by early detection in precancerous stage by screening for CIN (cervical intraepithelial neoplasia). Between 1988-1994 cytological screening by national call and recall

system reached 85% coverage of target population and had reduced the incidence and mortality from cervical cancer in England.² Coverage of cervical cancer screening in developing countries is low, 19% on average, compared to 63% in developed countries, and reported as low as 1% in Bangladesh. Older and poor women, who are at the highest risk of developing cervical cancer, are least likely to be screened. Challenges in introducing Cytological screening in low and middle –income countries led to alternative screening strategies that must be adapted to meet the specific needs of individual countries.^{3,4} In Bangladesh visual inspection of cervix with acetic acid (VIA) is an accepted method of cervical cancer screening at maternal and child

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welfare centers (MCWC), district hospitals (DH), medical college hospitals (MCH) and Bangabandhu Sheikh Mujib Medical University (BSMMU). VIA is administered by trained family welfare visitors (FWV), senior staff nurses (SSN) and doctors. Screen-positive women are referred to BSMMU and Medical college Hospitals for colposcopic evaluation and management.⁵ Present study was conducted using this infrastructure. Quality assurance body report of cervical cancer screening program in 44 districts of Bangladesh (2004, published in 2008) suggested that coverage of target population was low and screening was opportunistic, the compliance to colposcopy was good.⁶ So prevention of cervical cancer needs wide coverage of target population with budgetary allocation and development of manpower. Population Prevalence of cervical intraepithelial neoplasia(CIN) is an important indicator and help to judge the potential cervical cancer burden in the community. Regular screening by VIA and treating precancerous lesion, even by single visit screen and treat approach is recommended in resource poor settings to prevent cervical cancer.^{7,8} In rural Andhra Pradesh, South India, a total of 18,869 women screened by a single round of VIA, the prevalence of cervical intraepithelial neoplasia (CIN) 2+ lesion rate was 1.05%, with a VIA positive rate of 10.75%.⁹ In China high risk HPV(HR-HPV) positive was 31.4%, age standardized prevalence of CIN II 1.5% and 0.7%, |CIN 3 1.2% and 0.6% respectively in rural and urban location. CIN 3 steadily increased with age peaking in 45-49 years women due to lack of lesion removal through screening¹⁰. In Bangladesh cervical cancer causes death of women when they are raising the family and cases are diagnosed late as they missed the opportunity for cure by screening. For preventive program and designing interventions at national level, it is important to know the baseline prevalence of CIN, but such data is not available. Study on prevalence of CIN in this research was performed to detect the prevalence of CIN in an unscreened population of Khulna division of Bangladesh. Documentation of sociodemography and reproductive history, management relevant to women at risk of cervical cancer was also done. The findings of this study may help implementing population based organized screening services for cervical cancer with

expectation of reducing cervical cancer prevalence in Bangladesh.

Methodology:

This cross-sectional and population based study was carried out in four randomly selected sub districts(upazillas) with cervical cancer screening facilities provided for four districts of Khulna division, by the Department of Obstetrics and Gynaecology of Khulna Medical College Hospital (KMCH) and BSMMU from March 2014 to June 2014. The minimum sample size from one upazila was around 220 following the standard sample size estimation formula with 3% prevalence of CIN with 95% confidence interval. As randomly selected four sub districts were considered in this study, the sample size was about 880 (220x4) or more. Resource persons (colposcopists) from KMCH and BSMMU provided daylong orientation to Nurses and Field Staffs of the selected Upazilla health complexes on methodology of the study, counselling, motivation, recruitment of women, and referral system. Married women age between 25-55 years able to understand written and/or oral information, mentally able to provide informed consent were recruited through door to door visits by health workers. Women with chronic illness, women with pregnancy and women already screened were not included in the study. Data collected from selected women of four upazilas after initial recruitment of field staffs on specified dates. Almost equal number of participants were selected from each ward of the selected upazillas. Participants from alternate household were requested to attend UHCs on a selected date. If participants from particular household disagreed to participate, participants were recruited from the next household. After initial recruitment 350 participants were given appointments to have clinical examination, VIA and colposcopy at respective Upazilla Health complex. About 35-40 women were invited each day for examinations. A pretested questionnaire was used as data collection instrument by face to face interview (by Research Assistant/ Doctor /Nurse). Interview was conducted under supervision of investigators. At the UHCs, the women were further counselled regarding examination procedure under privacy. A temporary arrangement for colposcopy were

developed at selected UHCs. All enrolled women underwent VIA and colposcopy. Abnormal colposcopy findings were further evaluated by punch biopsy and endocervical evaluation if needed. After the procedure women had further counselling about possible test results, need for follow up, necessity of biopsy, referral for treatment. All histopathological examinations were done at the Department of Pathology of BSMMU. CIN cases were called at colposcopy clinic of KMCH for necessary managements. Ethical clearance were taken from the Institutional Review Board (IRB) of BSMMU. Interview questionnaire collected information about socio-demographic and reproductive health characteristics, examination results. Completed data were reviewed, edited and processed for computer data entry. The data analysis was performed using Statistical Package for the Social Sciences (SPSS) Version 17.0. The prevalence of CIN was calculated with 95% confidence interval.

Results:

In Khulna division, 1232 women of between 25-55 years age groups participated in the study. Participants from different villages of four upazillas of four districts (Jessore, Khulna, Bagerhat, and Sathkhira Fig 1) were almost equal number about (260-300 women) (Table 1). Socio-demographic data of study population showed majority were between 30-49 years age group (71%). A good number had primary education (44.2%). Majority were housewives (96.3%). More than half of women (61.8%) married before 18 years of age and 1142(92.7%) had their first delivery between 14-25 years. Mean Age at marriage 16.76 ± 3.81 years and mean age at first delivery 19.26 ± 4.475 years. Mean Parity was 233. Ninety seven percent were married one time and majority were living with husband (93.5%). Around 9% of their husband had more than one wives. About two third of the families belonged to low and middle class income groups (monthly income less than Tk 10,000). Seventy five percent of women were Muslim and rest were Hindu (Table 2).

Prevalence of CIN was 5.84%. In colposcopically directed biopsy, CINI 4.0%, CIN-II 1.1% and CIN-III. 73% (Table 3). Colposcopy and histopathology correlation in diagnostic accuracy documented and

Sensitivity and Specificity of colposcopy were 60.9% and 98.65% respectively (Table 4). Prevalence by age showed that CIN II and CIN III were more in 25-44 age group (Table 5). 90% of CIN belongs to low socioeconomic group (Table 6). Treatment received were periodic screening after 5 year 1188(96.9%), LEEP 18(1.8%), Cold coagulation 25(2.1%), and admission in Oncology department 1(.1%)(Table 7)



Fig.-1: Districts of Khulna Division.

Table-I
Geographical distribution of Study population

District	Upazilla	Frequency	Percent
Jessore	Avaynagar	327	26.5
Khulna	Fultola	267	21.7
Bagerhat	Mongla	319	25.9
Sathkhira	Tala	319	25.9
Total	1232	100.0	

Table-II*Socio-Demographic and Reproductive Characteristics of Women (n=1232)*

Characteristics	No. (%)
Age Group	
25-29 years	224 (18.2)
30-34 years	270 (21.9)
35-39 years	283 (23.0)
40-44 years	193 (15.7)
45-49 years	135(11.0)
50-55 years	127 (10.4)
Religion	
Islam	933 (75.7)
Hindu	299 (24.3)
Education of women	
Illiterate	184 (14.9)
Primary	545(44.2)
Secondary	368(29.9)
Higher Secondary	85(6.9)
Graduate & above	50(4.1)
Occupation of women	
House Wife	1187 (96.3)
Labour	3(.2)
Service	28(2.3)
Business	7(.6)
Teacher	7(.6)
Occupation of Husband	
Unemployed	11(0.9)
Labour	195(15.8)
Farmer	451(36.6)
Business	327(26.5)
Driver	19(1.5)
Service holder	194(15.7)
Teacher	18(1.5)
Not alive	17(1.4)
Age at marriage	
17 years and below	761(61.8%)
18-25 years	439 (35.6%)
26-35 years	25(2 %)
36 and above	7(0.6%)

Table-III*Histopathology Finding in colposcopy guided biopsy*

Histopathology	Frequency	Percent
Normal	21	1.7
CIN-I	49	4.0
CIN-II	13	1.1
CIN-III	9	0.7
Squamous Cell Carcinoma	1	0.1
Total	1232	100.0

Table-IV*Colposcopy - Histopathology Co relation*

Colposcopy	Histopathology					
	Normal	CIN-I	CIN-II	CIN-III	Sq. cell Ca	No
Normal	0	0	0	0	0	1139
CIN-I	17	36	7	2	0	62
CIN-II	3	12	2	2	0	19
CIN-III	1	1	4	5	0	11
Squamous Cell Ca	0	0	0	0	1	1
Total	21	49	13	9	1	1232

Table-V*Types of CIN in different age groups*

Age group	Histopathology Finding				
	Normal	CIN-I	CIN-II	CIN-III	Sq. Cell Ca.
25-29 Years	6	15	3	2	0
30-34 Years	3	12	6	1	0
35-39 Years	5	12	3	5	1
40-44 Years	5	7	0	1	0
45-49 Years	1	2	0	0	0
50-55 Years	1	1	1	0	0
Total	21	49	13	9	1

Table-VI
Socioeconomic Status and CIN

Monthly Family Income	Histopathology Finding					Total
	Normal	CIN-I	CIN-II	CIN-III	Not Necessary	
Taka 3000 or less	4	5	0	2	0	121
Taka 3001-6000	6	19	5	3	0	411
Taka 6001-10000	8	18	5	3	1	319
Taka >10000	3	7	3	1	0	288
Total	21	49	13	9	1	1139

Table-VII
Advice and Treatment of participants

Valid	Frequency	Percent
Follow-up after 3 years	1188	96.9
LEEP Biopsy	18	1.8
Cold Coagulation	25	2.1
Admission in Oncology	1	0.1
Total	1232	100.0

Discussion:

Data on the prevalence on cervical intraepithelial neoplasia in this country is not known. It is very time needed to initiate community screening and educational awareness for screening for prevention and control of cervical cancer. CIN is a premalignant lesion that may exist at any one of three stages CIN 1, CIN 2 and CIN3. If left untreated CIN 2 and CIN 3 (collectively referred to as CIN2+) can progress to cervical cancer. It is estimated that approximately 1-2% of women have CIN2+ lesion each year.¹¹ IARC estimated about one third of global cervical cancer burden in south east Asia and every year 11,956 new cases of cervical cancer are detected in Bangladesh and 6582 women die of the disease. There are multiple modalities of cervical cancer prevention covering the targeted population. Epidemiological study suggested a causal relation with sexual activity and Human papilloma viruses. High risk types of HPV (Mostly 16 and 18) found in 50-80% of CIN2 and CIN 3 lesions and 90% of cervical cancer.¹² HPV geno type distribution showed considerable variation globally.¹³ However PCR based HPV typing is not feasible in mass screening¹⁴. Many researches have focused on HPV types, scope of prophylactic and therapeutic vaccines, improve effectiveness of screening that

was found in ATHENA trail, even then periodic screening needs to be continued.^{15,16}

Our knowledge in pathogenesis of cervical cancer opened a window of cure.¹⁷ CIN are evident on cytology, histology, and aided visual examination. Screening on high-risk women once or twice in their lifetime using a highly sensitive test, with an emphasis on high coverage (>80%) of the targeted population for developing countries will have to find adequate financial resources, infrastructure and elaborate surveillance mechanisms for screening¹⁸. There is also suggestion that cancer screening should be a component of public health programme in developing country.¹⁹ Population prevalence of CIN is an important indicator to judge the disease burden in the community. Information about prevalence of CIN in Bangladesh was not available. Among 1232 women in 25-55 age group, we reported normal colposcopy 1139/92.5% and biopsy proven CIN I 49/4%, CIN II 13/1.1%, CIN III 9/.73%. A study in Egypt prevalence found 3.3, 0.84 and 0.27 % for CIN I, CIN II and CIN III, respectively by VIA. Prevalence of CIN II or higher was 1.11 %.²⁰

Our study revealed CIN 1 was more prevalent in young age group 25-30 year and CIN 2 and CIN3 more common in older age group of 35- 39 years though statistically were not significant. Factors affecting prevalence of HPV infection and CIN are many. Age trends of high grade lesion peak at 25-40 years in Europe, Middle East, Africa and Asia and at relatively younger age in North America (<30 years). We documented between 25-44 years. Variation in age pattern likely to attributable to difference in age at screening, frequency, coverage and rate of follow up, histological evaluation, processing, referral rate and diagnostic interpretation and HPV typing co testing and status of vaccination.²¹ A pooled analysis

of data from India documented crude prevalence of CIN-1, CIN-2, CIN-3 reported were 2.9%, .6%, and .4% and that of invasive cancer .2% among women between 30-65 years. CIN3 peaks at 35- 39 years and mean age 40.0 ± 8.4 years and decline in sixth decade, were found comparable to our study. In our study CIN 3 could not be detected in 55 years group.²² In this study population sexual life started at younger age after marriage and mean age of marriage 16.76 ± 3.81 years, low literacy, high parity and low income population and land less family were other contributory cofactors.²³ Prevalence of CIN in HIV-infected women found to be two to five times more than HIV-uninfected women.²⁴ Our study did not include any known case of HIV positive woman. All CIN were detected by Colposcopy and histopathology. Study group provide follow up and local treatment of biopsy proven CIN including CIN1 for protocol and ethical reason, though there is a low risk of progression of CIN 1 or less (1.6%).²⁵ Even younger women with low grade cytological lesion and with a single HPV test may not be useful in determining which one worthy - follow up or treatment. In our population HPV status is unknown.²⁶ Most of the time cases of CIN can be treated which are effective for more than 90% of cases, with 10% chances of recurrence.²⁷ *Treatments* available are cryotherapy, large loop excision of the transformation zone (LLETZ, or LEEP), and cold knife conization (CKC).²⁸ Management of participants were advice for periodic screening, LEEP procedure, ablation by thermo coagulator. Outpatient therapy, employing such methods combined with proper follow-up, is appropriate for dealing with visible lesions on the ectocervix. Depending on the method used and the severity of lesion cure rates range from 80% to 95%, with free margin and adequate depth in histopathology.²⁹ Follow up following CIN treatment needs to be focus and found less than 50% in colposcopy clinic of Bangladesh, which is not satisfactory without HPV typing co testing³⁰. We diagnosed one case with invasive lesion. The clinical staging of cervical cancer is the single most important prognostic factor and should be carefully evaluated in choosing optimal treatment between surgery and radiotherapy, with or without chemotherapy.³¹ Strength of this study were many, sample was population based covering different villages, large sample size with proper design, similar demography, rural habitat, homogenous ethnic group, repeated

scrutiny by team throughout study period, diagnosis by colposcopy and histology. This research conducted by master trainer colposcopist from university and medical college.^{32, 33} Other observation was this study has created interest and awareness for cervical screening in community³⁴. This might have conducive effect of future VIA, HPV based screening and vaccination. Limitation of study we did punch biopsy and blinded review of histological report were not done in cases of diagnostic disparity with colposcopy. Other challenges were women's shyness and low awareness about risks and screening for cervical cancer and age group data of population. Health education on cervical cancer for both man and women would make such type of study more fruitful.³⁵

Conclusion:

Prevalence of cervical intraepithelial neoplasia was 5.8% and CIN2+ lesion were common in 25-44 aged multipara women with low income. There was almost no information on baseline prevalence of cervical pre-cancer in Bangladesh. Population prevalence study of CIN in Khulna Division of Bangladesh would not only help in planning appropriate national screening strategies but also provides key inputs for resource allocation for this global health problem with priority. Results obtained from this study would be helpful for implementation of cervical cancer prevention strategy in Bangladesh and provide useful information to other developing countries.

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