ORIGINAL ARTICLE

Clinical effectiveness of VIA and colposcopy based management of cervical intraepithelial neoplasia

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Abstract

Cervical cancer develops from early precancerous lesion known as cervical intraepithelial neoplasia (CIN). Khulna Medical college Hospital provides primary screening for preventing cervical cancer and a secondary referral centre for management of CIN by colposcopy. Primary objective of this study was to do an audit between January 2012 to February 2014 to update clinical efficacy of colposcopy based diagnosis, treatment and follow up of 510 CIN cases and also to document any shortcomings in existing services and suggestion for early rectification. Colposcopic findings in our study group were: 309(60.6%) cases were CIN-1, 124 (24.3%) cases was CIN II, and 49 (9.6%) cases were CIN III. Suspicious of invasive lesion was in 7 (1.4%) abnormal looking cervix and biopsy was done in 21(4.1%). Treatment procedure was done with individualization of cases and options were cold coagulation, Loop electrosurgical excision procedure (LEEP), hysterectomy, biopsy and post treatment follow up. Histopathological diagnosis was documented in 387 cases, where CINI was found in 161 (31.6%), CIN II in 92 (18%), CIN III in 26 (5.1%), non specific Inflammatory cervicitis in 87(17.1%), Squamous cell carcinoma in 15(2.9%), abnormalities consistent with koilocytic atypia in 6 (12%) and reports missed in 123 (24.1%). Cases results showed Positive predictive value (PPV) of 53% and 68% respectively for low grade (CIN I) and high grade lesion (CIN II, III). 481 patient were eligible for post treatment follow up but only 99 (20.5%) patient came and among them 74 (74.7%) were colposcopically negative, 25 (25.2%) had residual CIN and Risk Ratio (RR) was 0.25. Colposcopy is gold standard for diagnosis of CIN but our screening program is opportunistic and far way from population based. Histopathological correlation were often inaccurate with colposcopic diagnosis in practice and about one third case reports were missed. Majority of women did not complete follow up protocol. Residual or recurrent CIN lesion in dropped out cases would be a concern in near future.

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Introduction

Cervical cancer is the second most common cause of cancer related morbidity and mortality among women in developing countries. Worldwide Low and medium income countries (LMIC) account for four-fifths of the estimated 500,000 new cervical cancer cases and 300,000 deaths annually, yet no effective method of screening exist in most of them.[1] Cervical cancer develops from well defined precursor lesion over a varied period of time. The key to reduce morbidity and mortality from cervical cancer is detection of those early pre cancerous lesion known as Cervical intraepilhelial neoplasia (CIN) results from persisted infection with Human papilloma virus (HPV). Women in developing country like Bangladesh are at increased risk of cervical cancer and living with out facility for early cancer screening.

In Bangladesh there are around 13,000 new cases and 6,600 deaths due to cervical cancer each year.[2] In last decade screening for CIN by Visual inspection of cervix with 5% acetic acid (VIA) and referral for colposcopic evaluation and offering curative treatment has been started in our country. Cervical cancer Screening by VIA developed its own essence in low resource settings where no access to HPV-DNA testing or cytology screening.[3] In Bangladesh cancer related death will increase from 7.5% in 2005 and 13% in 2030 if measures are not taken.[4] Developed country not only already achieved population based screening but also have major opportunities for primary prevention by vaccination against common high risk HPV 16,18 between 9-26 yr age.[5] Just as in the U.S., cervical cancer around the world is

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highly preventable through screening tests and vaccination against HPV. FDA approved new HPV vaccine (Gardasil 9) that will prevent 90% of cervical cancer. However, barriers exist in economically developing countries, including access to screening and treatment; the high cost of the vaccines.[6] So emphasis given on Secondary prevention by early detection of CIN. The main rationale of CIN treatment lies in the fact that a significant percentage of untreated CIN lesions will progress to invasive cervical carcinoma if left untreated.[7] Colposcopic technique adherence ensure appropriate treatment and cure. The colposcopic diagnosis of CIN requires an understanding and recognition of four main features color tone intensity of acetowhitening, margins and surface contour of acetowhite area vascular pattern, and iodine staining. Variations in quality and quantity of these atypical appearances help in differentiating CIN from other lesions and between grades of CIN.[8] The algorithm for usual approach for treatment of cervical intraepithelial neoplasia (CIN) offered at colposcopy clinic follows an initial assessment by VIA (at first visit) and VIA positive women has referral for colposcopy and if colposcopically positive biopsy and histology (at visit 2) and performance of local treatment (at visit 3) or in screen and treat policy local treatment done in second visit and follow up.[9] Follow up of CIN is mandatory and recorded up to twenty years to know cure as risk of treatment failure or recurrent CIN described in between 1-20%. The schedule for follow up will be at 6 month to 12 months from the date of treatment. Mordern Techniques for follow-up is double testing include cervical cytology and HPV-DNA typing, adjunct tools are VIA and colposcopy, and endocervical curettage for Adenocarcinoma in situ (AISg) conization and histopathology.[10-11] Primary objective of this study was to do an audit to update clinical efficacy of colposcopy based diagnosis, treatment and follow up of CIN cases, to document any shortcomings in existing services and suggestion for early rectification.

Materials and Methods

This cross sectional observational study was done at VIA and Colposcopy centre in khu1na medical college hospital between January 2012 and February 2014, 510 women with primary diagnosis of CIN on colposcopy or had request for colposcopy and biopsy for abnormal looking cervix were included for study. Populations were screened positive women following visual inspection of cervix with 5% acetic acid (VIA) were referred for or others were adviced for colposcopic examination in outdoor clinic. Then each case evaluated by colposcopy in stepwise fashion starting from low magnified viewing of cervix, study of vascular pattern, VIA test for any acetowhite lesion and lugols iodine application (Schilier test) and then if colposcopically diagnosis of CIN were made biopsy was taken. Individualization of treatment was done either by local excision with Loop electrosurgical excision procedure (LEEP) or local ablative procedure by cold coagulation in same sitting or in another date or need for operative treatment. Obvious cases of cervical carcinoma and normal looking cervix and colposcopically negative cases are excluded from study. Diagnosis treatment and follow up documented in Government registry book and same information supplied to patient with colposcopy card. VIA was done by Nurses and Colposcopists are OBGyn Doctors, the whole team been trained in Bangabandbu Sheikh Mujib Medical University (BSMMU) Dhaka. Punch biopsy and specimen of LEEP biopsy in screen and treat policy were preserved in formol solution and was sent in pathology department of same medical college -Diagnosis established by histopathological report described by CIN nomenclature. Schedule for follow up was documented within at least six month to two year by VIA and Colposcopy. Data were analysed by SPSS version 11.5.

Results

During time period 9800 women underwent cervical cancer screening by VIA and VIA positive were 353 (5.46%), total number of colposcopy including referral cases done in centre was 2306 and CIN detected in 510 (22.1%). Age group of women were between 18 - 60 yrs, most common age group of 25-35 years cases were 302 (59.2%),

Table I

Number and types of cases on colposcopy and histopathology

	Total	%	PPV
Screening by VIA	9800	100	
VIA Positive	353	5.46	
Total colposcopy done	2306	100	
Abnormal on colposcopy	510	22.1	
Low grade CIN-I	309	60.06	
High grade (CIN-11/111)	173	33.92	
Suspicious Invasive lesion	7	1.4	
Abnormal looking cervix	21	4.1	
Histopathology			
CIN-I and cytopathic change	167	32.8	53%
CIN-II	92	18	68%
CIN-III	26	5.1	
Squamous cell ca	15	2.9	
Inflammatory/ cervicitis	87	17.1	
Reports are not available	123	24.1	

mean age was 34.07 yr (SD 8.065), mean parity was 3.1 (SD-2). 1. Colposcopic findings in our study low grade lesion CIN I in 309 (60.6%) followed by high grade lesion (CIN II, HI) in 173 (33.92%). Suspicious of invasive lesion in 7 patient (1.4%), abnormal looking cervix and biopsy in 21(4.1%).

Table II
Modalities of treatment

Type of procedure	N	%
LEEP	140	27.5
Cold coagulation	211	41.4
Repeat colposcopy or adviced for treatment	29	5.7
Only cervical punch biopsy	98	19.2
Pt refusal for treatment	4	0.8
Admission for Hysterectomy	28	5.5
Total	510	100

patient. Histopathological report were available in 387 (75.9%) cases results showed CIN-I in 161 (31.6%), CIN-II in 92 (18%), CIN-III in 26 (5.1%), inflammatory cervicitis in 87 (17.1%), Squamous, cell carcinoma in 15 (2.9%), cytopathic changes consistent with HPV infection in 6 (1.2%), reports were not available in 123 (24.1%) patients. Colposcopic diagnosis of low grade CIN I and high grade lesion (CIN II, III) had Positive predictive value of 53% and 68% respectively (Table-1) and negative predictive value (NPV) for CIN were 76%. Treatment done were LEEP in 140 (27.5%), Cold coagulation in 211 (41.4%), only punch Biopsy in 98 (19.2%), Advice for biopsy or repeat colposcopy 29 (5.7%), patients refusal for treatment in 4 (.8%) indoor admission for Hysterectomy in 28 (5.5%) (Table-II).

Table-III

Followup colposcopic diagnosis and treatment

	N	%	RR
Colposcopically negative	74	74.7	
Residual CIN	25	25.2	0.25
CIN I	17	17.17	
CIN II	6	6.06	
CIN III	2	2.02	
Treatment			
LEEP	11	44	
Cold coagulation	03	12.24	
Hysterectomy	11	44	

481 patients were eligible for follow up but 99 (20.5%) patient came for follow-up colposcopy and among them 74 (74.7%) were colposcopically negative and 25 (25-21%) had residual lesion showing CIN I in 17 (17.1%), CIN II in 06 (6.06%), CIN III in 02 (2.02%), and treated by LEEP in 11 (44.4), Cold coagulation in 03 (12.3%), and hysterectomy in 11 (44.4%) (Table-III).

Discussion

WHO health bulletin in 2001 suggest VIA may be considered as a suitable early detection test of cervical cancer in the context of early clinical diagnosis in low-income countries. VIA screening provided by trained nurses in a randomized trial in Tamil Nadu in 2004 found that in the presence of good training and sustained quality assurance, it is an effective method to prevent cervical cancer in developing countries.[12]

In centre based study by BSMMU, VIA positive found 4.8% which is at the lower end of positivity and are comparable with screen positive cases of this centre. They mentioned colposcopically positive were 52.3% including cervical cancer.[13] In our study Cervical cancer were excluded and only CIN had included. Similar VIA positive 5.25% observed in one study done in Chittagong medical college hospital.[14] In one population based screening in rural Nigeria in 2013 by VIA, Cytological and HPV typing VIA positive were 0-21% and results were not reproducible in comparison to HPV typing.[15] Similar findings observed in large study in Osmanabad district in the state of Maharashtra, India, where incidence and mortality reduced HPV typing group and they records 8 years of follow-up from 2000.[16]

CIN 1(60.6%) lesions were most common diagnosis on colposcopy in this study as majority were young , total 340 in 18-35yr age group (66.6%) and results had less accuracy with histological diagnosis (Table-1). Screen and treat policy, young age, immature squmaous metaplasia Inflammation and inter observer variation all may be a factors for such a variation Evidence indicates that CIN I and koilocytes are related to the lytic cycle of human papilloma virus (HPV) infection and highly reversible and that CIN II, III are the true cervical cancer precursor, and more emphasis given on treating on high grade lesion in study.[17] Positive predictive value for low grade lesion was 53% and for high grade CIN II/III was 68%. Focusing a comparable study done by Shahida SM Mirza TT where 69.6% were LSIL cases 7.6% were High-grade Lesions and Positive predictive value was 62% for HSIL and 70% for LSIL cases.[18] The suggested accuracy of colposcopic diagnosis for high grade lesion should be at least 65% which were comparable with this study.[19] This study showed that colposcopy is a valid tool for the detection of pre-invasive lesion.

Conservative local treatment done by LEEP or Cold coagulation with biopsy, which are equally effective for CIN lesion with satisfactory colposcopy and complication of these procedure were mild.[20]

Hysterectomy has done in older patient without evidence for invasive cancer[21] in older or non compliant women, and cervical cancer cases managed accordingly.

Patients refusal for treating CIN lesion in 4 (0.8%) women though negligible was observed, and follow up colposcopy done only in one fourth, indicating needs of program for community awareness. In one awareness creating questionnaire in Nigeria about cervical cancer respondents mention were its preventable nature (31.9%), about cervical screening (25%) and screening centers (20.8%) generally low, and screening uptake (0.6%) was abnormally low. Lack of awareness, non-availability of screening centers locally, cost and time were the main reasons not coming for screening in Nigeria and we can count it in our situations.[22]

In this study 99 women came for follow up and 74 (74.7%) were colposcopically negative. In one study done in same centre by S Nahar et al 27 patient out of 61 having treated for high grade lesion were lost from follow up.[23] Post treatment lesion observed in 25 women (25.2%). Different study showed pooled rates of resolution for low-grade, high-grade, or combined squamous intraepithelial lesions were similar across the different treatment modalities (range 85.2-94.7%), which were comparable.[24] In one observational studies, which show rates of residual disease within one year of between 3% and 8%.[25] Here follow up colposcopy were recorded between 6 month and 2 yrs. Residual lesion detected in 25 (24.2%), which was higher than other study may be due to small recruitment for surveillance. Fate of others were not known as their likely risk of having persistent HPV infection which is the limitation of existing services. Women with persistent lesion were often treated by LEEP, cold coagulation and by hysterectomy.

In one study on Finnish women the differences in cancer risk between treatment modalities were minor. They showed women previously treated for CIN have an increased long-term risk of cancers related to Human papilloma virus (HPV) infection with habit of smoking.[26] In another study 6 of the 72 treated women (8%) residual or recurrent CIN occurred. Women with recurrence were significantly older, all six women with recurrence were hr-HPV positive, four had a positive follow-up smear. In similar study, twenty-two cases of invasive cervical cancer (ICC) and 57 cases of CIN III after treatment of CIN were observed . We did not have any ICC in small follow up group. Other study showed there were no statistically significant differences in ICC free survival between different treatment methods or initial grade of CIN.[27] In this study VIA and colposcopy used to detect recurrent lesion in follow up and HPV DNA typing was not feasible in current protocol. The absence of hr-HPV DNA has a 100% negative predictive value in different study.[28] Until then we have to ensure follow up by colposcoy. Fear of cancer and practice of Hysterectomy observed in women with recurrent lesion.

Confirm diagnosis by histopathology was not done in all patients which was a limitation of this study. Majority of women did not complete post treatment surveillance. Residual or recurrent CIN lesion in dropped out cases might create a threat in future. Community awareness, facility of HPV DNA typing with treatment procedure, feedback with histopathologist, and women motivation for continuing follow up is mandatory for success of mission strategy that is screen, treat and prevent cervical cancer.

Conclusions

Colposcopy is the gold standard for diagnosis of CIN and colposcopy based management eradicate CIN in 75% of cases. As our screening program is opportunistic, it should be population based for effective screening. Histopathological correlation were often inaccurate with colposcopic diagnosis in practice and needs further attention before interpretation specially in see and treat policy.

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