

RESEARCH PAPER

Efficacy of Loop Electrosurgical Excision Procedure in the Management of Cervical Intraepithelial Neoplasia (CIN) –in A Tertiary Level Hospital

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Abstract

Background: Cervical intraepithelial neoplasia (CIN) is the potentially premalignant transformation and abnormal growth of surface epithelial cells of the cervix. CIN is a precancerous condition and curable. Loop electrosurgical excision procedure (LEEP) is a simple, outpatient procedure of removing the transformation zone of cervix.

Objectives: The aim of our study was to evaluate the efficacy of large loop electrosurgical excision procedure (LEEP) as a treatment procedure for cervical intraepithelial neoplasia.

Methods: This prospective observational study was conducted at Colposcopy clinic of Bangabandhu Sheikh Mujib Medical University (BSMMU) from June, 2017 to May, 2019. All consecutive patients having colposcopically and histopathologically proven high grade lesion by colposcopy directed punch biopsy were included in this study. All eligible patients with high grade lesion were underwent LEEP and followed up on 15 days post-procedure, 6 months, 12 months with colposcopy.

Results: Sixty (60) cases were undergone LEEP, among them 48 (80%) cases were diagnosed as CIN2 and 12 (20%) cases were CIN3 by colposcopy- directed biopsy. One patient (1.7%) needed hospital admission to control intra-operative bleeding and in postoperative period 7 (11.7%) patients had mild to moderate post-operative bleeding which was controlled well after application of morsel's pastes and electro-cautery, one patient (1.7%) had pelvic infection. On 6 months follow-up, in case of CIN2 patients, cure rate was 93.5% (43 of 46) and 1 (2.2%) patient had persistent CIN-2. Patient with persistent CIN2 had re-excision and followed up at 12 month with colposcopy. Among case of CIN-3, the cure rate was 81.8% (9 of 11) and 1 (9.1%) case had CIN2. P-value was 0.244, which was not statistically significant. Overall cure rate on 6 month follow-up was 91.2%. On 12 months follow-up cure rate for CIN2 was 97.8% and for CIN3 was 90.9%. Overall cure rate was 96.5%. P-value was 0.352, which was not statistically significant.

Conclusion: Loop electrosurgical excision procedure (LEEP) has a good outcome as a diagnostic and treatment procedure for cervical intraepithelial neoplasia.

Keyword: Colposcopy, LEEP, CIN.

Introduction

Cervical cancer is the fourth most common cancer in women based on Globocan 2020, with 604,000 new cases were diagnosed and 342,000 deaths worldwide in 2020. But the impact of the disease is not shared equally around the world, cervical cancer is the leading

cause of cancer death among women in Sub-Saharan Africa, Melanesia, South America, and South-Eastern Asia.¹ One woman dies of the disease in every two minutes. So, in 2018, World Health Organization (WHO) Director General has made a call for global action toward the elimination of cervical cancer (d⁴ per 100,000 women worldwide) through the three-action strategy of: 1) vaccinating 90% of all girls by age 15 years, 2) screening 70% of women twice in the age range of 35 to 45 years, and 3) treating at least 90% of all precancerous lesions detected during screening.²

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In Bangladesh, cervical cancer is the 2nd most common cancer diagnosed in women aged 15 to 44 years. About 8,268 new cases were diagnosed and 4,971 lives has passed away of cervical cancer, according to Globocan, 2020.³

Cervical intraepithelial neoplasia is the potentially premalignant transformation and abnormal growth of squamous epithelial cells of the cervix.⁴ According to Bethesda system, a low-grade squamous intraepithelial lesion (LSIL) corresponds to CIN-1 and a high-grade squamous intraepithelial neoplasia (HSIL) encompasses to CIN-2 and CIN-3.⁵

Women can develop CIN at any age, however incidence of HSIL reaches peak around the ages of 25-35.⁶ A prerequisite for the development of cervical dysplasia is a persistent infection with high risk human papillomavirus (HPV 16,18,31,33,45,52 and 58) types.⁷ The majority of HPV infections are self-limiting, 70% washes away within 1 year and 90% within 2 years.⁶ Among these high-risk HPV types, particularly HPV 16 and 18, are responsible for the vast majority of cervical cancers.⁸

Different treatment modalities are available for pre-invasive cervical disease. Among them, ablative procedures including cryosurgery, electrocoagulation diathermy, cold or thermal coagulation, CO₂ laser. Excisional procedures, include loop electrosurgical excision procedure (LEEP), conization, CO₂ laser excision and hysterectomy.⁹

Loop electrosurgical excision procedure (LEEP), was introduced by Walter Prendiville in 1989, with a low complication rate and morbidity coupled with a 98% success rate of treatment.¹⁰

According to 2019 American Society for Colposcopy and Cervical Pathology (ASCCP) Risk-Based Management Consensus Guidelines for Abnormal Cervical Cancer Screening Tests and Cancer Precursors, excisional procedure is the preferred treatment modality for the management of CIN-2 and CIN-3 lesion (11). LEEP has similar efficacy to other available therapeutic modalities and general complications such as intraoperative or postoperative bleeding, infection, pain.^{12,13} But cervical stenosis or weakness and a consequent increase in miscarriages and premature birth rates in future pregnancies are not as significant as those associated with other available excisional techniques, namely cold knife conization or laser conization.^{14,15}

So, the effectiveness and safety of LEEP in the treatment of CIN has been widely evaluated in developed countries. LEEP also offers the advantage of obtaining a large specimen for pathological assessment to define disease as well as the completeness of treatment and it is the most shared disadvantage of non-excisional techniques. Due to limited resources, LEEP available in few centers of Bangladesh.

The aim of this study was to evaluate the efficacy of loop electrosurgical excision procedure (LEEP) as a treatment procedure for cervical intraepithelial neoplasia in patients who were diagnosed as high grade lesion (HSIL) on colposcopy and histopathologically proven by colposcopy directed punch biopsy. So that early diagnosis is possible, rendering effective and curative treatment for the pre-invasive disease and reducing the incidence of invasive disease.

Materials and Methods

This prospective study was conducted at Colposcopy clinic of Bangabandhu Sheikh Mujib Medical University (BSMMU) from June, 2017 to May, 2019. Permission of the institutional ethical committee was obtained for conducting the study. The study included all cases, who was referred to Colposcopy clinic of BSMMU with the complaints of post-coital bleeding, intermenstrual bleeding and who came for cervical cancer screening with VIA (visual inspection of acetowhite area) positive and with HSIL (High grade squamous intraepithelial lesion) cytology. Informed consent was taken from all participants prior to their inclusion into the study. Sixty (60) cases were selected purposively according to inclusion and exclusion criteria. Patients with diagnosed as invasive cervical carcinoma, active infection of genital tract, pregnancy and postpartum \leq 6 weeks, bleeding disorder, uncontrolled hypertension and diabetes were excluded. After a detailed history all patients were subjected to VIA (visual inspection of acetowhite area) and colposcopic examination. Those who had CIN2 and CIN3 lesion during colposcopic examination were confirmed by punch biopsy and histopathology. Then LEEP (Loop electrosurgical excision procedure) was performed under local anaesthesia who were diagnosed with CIN2 and CIN3. Lignocaine 1% solution was used in a ring pattern 1-2 mm depth (at 3,6,9,12 o'clock position) at the periphery of the lesion and transformation zone using a 5 ml syringe and 25 to

27 gauge needle. Prophylactic antibiotics were not routinely prescribed. Then excision of the lesion together with transformation zone upto a depth of 7 mm was done and excised tissue was sent for histopathological examination. Intraoperative bleeding was controlled by fulguration and applying Monsel's paste. Postoperative vaginal bleeding of less than 14 days which did not require any treatment defined as uncomplicated vaginal bleeding, excluding menstrual bleeding. Persistent vaginal bleeding was defined as prolonged postoperative vaginal bleeding of at least 14 days, excluding menstrual bleeding, which did not require any treatment. Intraoperative bleeding was defined as difficult when adequate hemostasis took more than 30 minutes to achieve using ball cauterization, but did not require cervical suturing or vaginal packing, and was considered a complication if cervical suturing or vaginal packing was necessary. Early (within 24 hours) and delayed (after 24 hours) postoperative bleedings were considered mild to moderate post-operative bleeding is defined as bleeding that requires re-cauterization or application of Monsel's solution, while severe post-operative bleeding is defined as bleeding that requires hospital admission, blood transfusion. Postoperative infection was defined

as purulent vaginal discharge, cervicitis, endometritis, and pelvic inflammatory disease. Patients were advised to avoid sexual intercourse and vaginal douching for 4 weeks. All patients were followed up at 15th day post-procedure for complication related to the procedure. At 6 month and 12 month following LEEP all patients were followed up with colposcopy and histopathologic evaluation of colposcopy directed punch biopsy for clearance, persistence or regression and recurrence of the lesion. Data were recorded using a structured questionnaire containing all the variables of interest, which were analyzed by SPSS version 23.

Results

Socio-demographic analysis have shown that, 26 (43.3%) patients fall in age group 36-45 years and a second peak was seen in 26-35 years (40%), mean age (years): 32.13±5.7, minimum age: 25 years and maximum age: 48 years. In this study 44 (73.3%) women were housewife with educational qualification ranges from illiterate to graduate. Most of the women (33.3%) came from lower socioeconomic status with monthly income d"10,000 taka and only 4 (6.7%) women has monthly income e"70,000 taka. Only 9 (15%) women had smoking habit.

Table I: Socio-demographic characteristics of study subjects (N=60)

Characteristics	Number of subjects with CIN-2 & 3		Percentage
Age in years	≤25	8	13.3%
	26-35	24	40%
	36-45	26	43.3%
	46-55	2	3.3%
	>55	0	0%
Mean age (years): 32.13±5.7	Minimum age (years): 25	Maximum age (years): 48	
Educational status	Illiterate	1	1.7%
	Primary	20	33.3%
	Secondary	24	40%
	Higher Secondary	1	1.7%
	Graduate	14	23.3%
	Post-graduate	0	0
Occupation	Housewife	44	73.3%
	Service-holder	16	26.7%
	Day-labourer	0	0%
Monthly income in taka	≤10,000	20	33.3%
	10,001-25,000	15	25%
	25,001-40,000	9	15%
	40,001-55,000	8	13.3%
	55,001-70,000	4	6.7%
	≥70,000	4	6.7%
Smoking Habit	Smoker	9	15%
	Non-smoker	51	85%

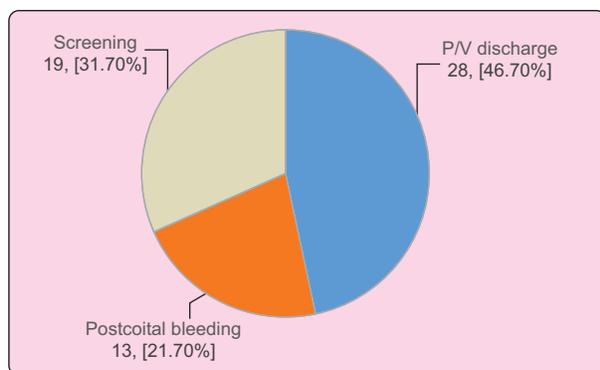


Figure 1: Complaints of study subjects

About 25 (41.7%) women has delivered first child before the age of 17 years and 40 (66.7%) women had three or more children and 35% were using oral contraceptive pill and only 15% cases were smoker.

Table II: Risk factors of study subjects (N=60)

Risk factor	Number of subjects	Percentage
Age at 1 st childbirth (years)		
<17	25	41.7%
≥17	35	58.3%
Parity	Number of subjects	Percentage
1	6	10%
2	14	23.3%
≥3	40	66.7%
Contraception	Number of subjects	Percentage
Oral contraceptive pill	21	35%
Condom	16	26.7%
IUCD	7	11.7%
Implanon	4	6.7%
Inj. DMPA	0	0%
Tubal ligation	0	0%
None	12	20%

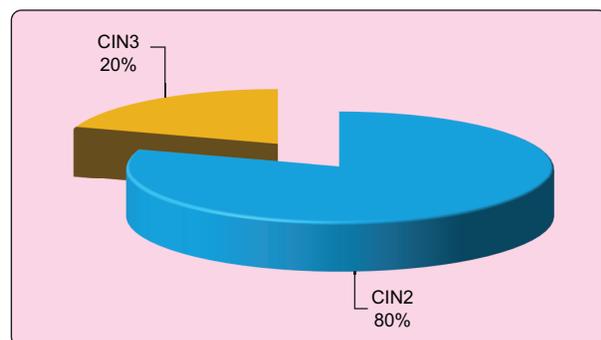


Figure 2: Percentage CIN in study subjects (N = 60)

Per vaginal discharge is the most common (46.7%) complaint, among women who had attended colposcopy clinic and 13 (21.70%) women had h/o post-coital bleeding, 19 (31.70%) women came for cervical cancer screening purpose. Among the participants 80% cases had CIN2 and 20% had CIN3 by colposcopy directed punch biopsy.

Table III: Intraoperative and post-operative complications (N = 60)

Complications	Number of subjects	Percentage
Intraoperative		
Intra-operative bleeding ^a	1	1.7%
Post-operative		
Mild to moderate post-operative bleeding ^b	7	11.7%
Infection	1	1.7%

^a Defined as bleeding that requires suturing or vaginal packing for hemostasis.

^b Defined as bleeding that prompts a return visit to clinic and requires re-cauterization or application of Monsel's solution

During procedure only one patient (1.7%) needed suturing of descending cervical artery to control bleeding and hospital admission for blood transfusion. In postoperative period 7 (11.7%) patients had mild to moderate post-operative bleeding which was controlled well after application of morsel's pastes and electro-cautery. Only one (1.7%) woman had pelvic infection which was well controlled with oral antibiotic on the out-patient treatment.

After procedure patients were followed-up at 6 and 12 months. Colposcopic examination was done on each follow-up and biopsy was taken from abnormal areas for histopathological evaluation.

On 6 months follow-up, 57 (95%) patients came for follow-up. Three patients didn't come for follow-up. Two of them had colposcopy directed biopsy proven CIN2 and one case had CIN3.

In case of CIN2 patients cure rate was 93.5% (43 of 46). Among cases with CIN2 two patients had persisted CIN-1 (4.3%) and 1(2.2%) had persistent CIN-2. Among cases of CIN-3, the cure rate was 81.8% (9 of 11) and 1(9.1%) case had persisted CIN-1, 1(9.1%) case had

Table IV: Follow-up status following LEEP based on histopathology or colposcopy at 6 months (N = 57)

Histology at base line (before Rx)	Total No. of LEEP Performed	Lesion free(%)	Follow-up status at 6 months			P value
			Persistence of CIN (%) According to Grades			
			CIN1	CIN2	CIN3	
CIN2	46	43(93.5%)	2(4.3%)	1(2.2%)	0	0.244
CIN3	11	9(81.8%)	1(9.1%)	1(9.1%)	0	

Table V: Persistent/recurrent cervical intraepithelial neoplasia (CIN) following LEEP (follow-up based on histopathology or colposcopy at 12 months) (N = 57)

Histology at base line (before Rx)	Total No. of LEEP Performed	Lesion free(%)	Follow-up status at 12 months			P value
			Persistence of CIN (%) According to Grades			
			CIN1	CIN2	CIN3	
CIN2	46	45(97.8%)	1(2.2%)	0	0	0.352
CIN3	11	10(90.9%)	1(9.1%)	0	0	

persisted CIN2. Patients with persistent CIN2 had under gone re-excision and patients with CIN1 were followed up at 12month with colposcopy.

P-value was 0.244, which was not statistically significant. Overall cure rate at 6month follow-up was 91.2%.

On 12months follow-up cure rate for CIN2 cases was 97.8% and for CIN3 was 90.9%. One patient with CIN2 persisted as CIN1 (2.1%) and one patient with CIN3 persisted as CIN1 (9.1%) both of them was followed up colposcopically. P-value was 0.352, which was not statistically significant.

Discussion

Cervical intraepithelial neoplasia (CIN) is the pre-malignant changes of the squamous epithelial cells in the transformation zone of cervix. Mild, moderate or severe changes are described by their depth (CIN 1, 2 or 3) of involvement of cervical epithelium. If CIN progresses it develops into squamous cancer.¹² Usually CIN peaks at 25 to 30 years or 20 to 24 years in some population.^{16,17} The relative risk of invasive cervical cancer is 1.77 for first full-term pregnancy before the age of 17 years compared with 25 years or older and the relative risk is 1.76 for women having seven or more full term pregnancies.¹⁸ The International Collaboration of Epidemiological Studies of Cervical Cancer has identified an increase in the relative risk of cervical cancer in current users of oral contraceptives.¹⁹ Smokers with high-risk HPV

(Human papilloma virus) positive women have increased risk of developing an HSIL.²⁰ Depending on the nature and extent of disease the treatment for cervical intraepithelial neoplasia (CIN) is by local ablative therapy or by excisional methods. Excisional treatment is mandatory for a patient with an unsatisfactory colposcopy, suspicion of invasion or glandular abnormality. Loop electrosurgical excision of the transformation zone (LEEP) is an excisional method that offers advantages to define the exact nature of disease as well as completeness of excision of the transformation zone. The most common peri-operative complications following LEEP is bleeding and infection in this study were comparable to those previously reported.^{21,22} A study of Kietpeerakool et al. showed that, 3.4% intraoperative bleeding, 0.6% early post-operative bleeding, 4.9% late postoperative bleeding and 4.3% infection. In this study 11.7% subjects had mild bleeding following 2 weeks post-LEEP. Pelvic infection following LEEP is very less common complaints, only (0.0% to 10.0%) (median, 1.2%) of women had reported pelvic infection following LEEP.²³⁻²⁶ In our study only one case (1.7%) had pelvic infection, and treated effectively at out-patient basis. At 6 months follow-up cure rate was 93.5% (43 of 46) for CIN2 cases and 1 (2.2%) had persistent CIN2. Patient with persistent CIN2 had under gone re-excision and one patient with CIN1 was followed up at 12month with colposcopy. Among cases of CIN3, the cure rate was 81.8% (9 of 11) and 1 (9.1%) case

had CIN1, 1 (9.1%) case had CIN2. P-value was 0.244, which was not statistically significant. Overall cure rate at 6 month follow-up was 91.2%. At 12 months follow-up cure rate for CIN2 cases was 97.8% and for CIN3 was 90.9%. Overall cure rate was 96.5%. P-value was 0.352, which was not statistically significant. All of these results were consisted with other studies. A study of Sankaranarayanan et al. conducted in rural India found 93.3% cure rate at one year follow-up, 93.6% for CIN 2, and 85.0% for CIN 3.²⁴ Another study of Rema et al. showed cure rate of 87.6%, for CIN 2 cure rate was 85.5%, and 72.7% for CIN 3.²⁵

Conclusion

Cervical cancer is the commonest genital tract cancer of female in Bangladesh. It is preventable and almost curable when diagnosed early in a pre-invasive stage. Women with atypical squamous cells on cytology should, if possible be assessed colposcopically and followed-up cytologically. Loop electrosurgical excision procedure is a cheap, effective, easy to perform and enables the diagnosis and treatment of patients with abnormal cervical smears in a single visit. Furthermore by providing an adequate amount of tissue for accurate diagnosis, it also improves the quality of care.

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