

A comparative study between results of different modalities of management of cervical intraepithelial neoplasia I

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Abstract

Background: Carcinoma cervix is a preventable disease. It runs a long preinvasive stage, such as Normal - CIN I - CIN II - CIN III - Cancer cervix. It can be prevented at early stage of development with proper diagnosis, treatment & follow up. A major portion of CIN I spontaneously regress but some need treatment.

Objective: The purpose of this study was to determine the frequency of abnormal colposcopic findings during the 1 year follow up period in patients of CIN I treated with cold coagulation, LEEP and expectant management.

Materials and Methods: This retrospective study was conducted in colposcopic centre of Khulna medical college hospital, Khulna, Bangladesh from January 2018 to December 2019. After confirmation of CIN I, ladies were arranged in three groups according to their treatment modalities - Expectant management (group A), Cold coagulation (group B) & LEEP (group C). They were reexamined with colposcopy after 6 months, or after one year of first visit. Persistence or reappearance of CIN was assayed & correlation between colposcopic results during follow up of different groups was analysed.

Results: Total 195 ladies were diagnosed colposcopically as CIN I. Of them 75 women were confirmed by histological examination. Among 75 ladies, 25 ladies received no treatment, grouped as group A. Forty ladies treated with cold coagulation falls in group B, whereas 10 ladies who treated with LEEP were grouped as group C. Distribution of age, parity, monthly income, education, marital age, age at first delivery was similar in different group. During follow up persistence of disease were found in 2(13.3%) ladies who did not receive any form of treatment, 3(10.7%) who were treated with cold coagulation (*p* value 0.333) and 1(12.5%) lady who received treatment with LEEP (*p* value 0.667), were not significant.

Conclusion: Colposcopic surveillance without treatment appears reasonable in treating CIN I because of the high rate of spontaneous regression of CIN I, but adherence to the follow up should be emphasized to the patients during the follow up visits.

Key words: Carcinoma cervix, Cervical intraepithelial neoplasia, Colposcopy

Introduction

Cervical cancer is the most common female cancer in our country and second most common in Asia pacific region. Estimated new cases in 2018 are 569,800 representing 6.6% of all female cancers. Total 311,400 deaths in worldwide approximately 90% of deaths from cervical cancer occurred in low and middle income countries.¹ About 12,931 new cases in Bangladesh and about 6,561 women died due to cervical cancer in every year.² Cervical cancer is one of the few cancers that can be preventable. Cervical Intraepithelial neoplasia,

(CIN) or cervical dysplasia refers to abnormal changes in the cells on the surface of the cervix. CIN I is low grade lesion (LSIL) whereas, CIN II, CIN III & invasive carcinoma comprise high grade lesions (HSIL).

Cervical cancer usually develops gradually and has a long preinvasive state, so screening is very important because we can stop it from developing in the first step (CIN I). There are some screening tests-Pap's smear, VIA test, Colposcopy, HPV testing. Our national project on cervical and breast

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cancer screening has been already running. Those who were VIA positive (+ve) or suspicious then referred to Colposcopy clinic. On colposcopy, if any one diagnosed as CIN, then any of following methods was applied for managing that lady. Methods are expectant management, cryotherapy, cold coagulation (thermal coagulation), electro cauterisation, Loop Electro Surgical Excision Procedure (LEEP), hysterectomy.

Cervical intraepithelial neoplasia I (CIN I) is the most common form of CIN and up to 60% of CIN I & for young patient 91% spontaneously regresses.³ But many clinicians treat CIN I with ablation either cryotherapy or cold coagulation and excision of transformation zone (LEEP) depending upon lesion size & compliance of patient & risk factors. However, any modality of management requires cytologic and /or colposcopic follow up to detect progression, persistence, and recurrence of disease.

Disadvantages of using any form of treatment such as cramping during and after the procedure, vaginal spotting and watery vaginal discharge have been reported. On the other hand, patients treated with expectant management may experience the progression of CIN grading, resulting in a requirement for treatment with more invasive procedures.⁴

The purpose of this study was to determine the frequency of abnormal colposcopic findings during the 1 year follow up period in patients of CIN I treated with cold coagulation, LEEP and expectant management.

Materials and Methods

This retrospective study was conducted in colposcopic centre of Khulna medical college hospital, Khulna, Bangladesh. Study period was two years from January 2018 to December 2019. All VIA positive and suspected cases (1,113 ladies) were evaluated with colposcopy by expert clinicians. They were categorized into normal findings, chronic cervicitis, CIN I, CIN II, CIN III & carcinoma cervix and registered in register book supplied by national Government project. About 195 ladies were diagnosed as CIN I in that period. Some patients were treated with "see & treat" method without histopathological examination; some received expectant management but no treatment without histopathology. Others were evaluated with histopathological examinations with treatment or expectant management.

Patients after histopathological confirmation were grouped into three groups- who were on expectant

management, who received cold coagulation, who were treated with LEEP. They were reexamined either after 6 months or after one year with colposcopic evaluation in the whole year of 2018 & 2019. Some of them did not come for follow-up in that period. Outcome measure was the colposcopic results at 6 month & at 12 month follow-up visit.

Data were collected, compiled and entered in spreadsheet and analyzed using Microsoft Excel data analysis statistical tool. Correlation between colposcopic results during follow up of different groups was analysed. A p-value was calculated with Microsoft Excel. A p-value of less than 0.05 was considered statistically significant.

Result

A total of 1,113 women were evaluated with colposcopic examination from January to December 2018. Among them 195 were diagnosed CIN I on colposcopy. Seventy five ladies were confirmed CIN I by histopathological examination. These 75 ladies fulfilled the study inclusion criteria. These ladies were divided into three groups regarding their treatment modalities (Table I). In Group A, 25 ladies (33.3%) were included who received no treatment (expectant management), 40 (53.3%) participants were included in group B who were treated with cold coagulation (thermo coagulation) and 10(13.3%) women were grouped as group C, those received treatment with LEEP.

Table I

Treatment modalities among participants (n=75)

Treatment modalities	Groups	Number	Percentage
Expectant management	Group A	25	33.3
Cold coagulation	Group B	40	53.3
LEEP	Group C	10	13.3

Table II shows the socio-demographic profile of study people. Maximum ladies were in age group 30 to 39 years in all groups, where as in age group 20-29 years were minimum numbers. Regarding education among study people, illiterate were in group A about 4%, whereas 22.5% in group B & 20% in group C. Maximum participants had secondary education in all groups. Maximum women were housewife. Regarding monthly income maximum had income of 10,000 taka or less, about 75% in group B. Multipara ladies were found maximum in all groups. About 60% of group C ladies were married before the age of sixteen years, whereas only 20% of group A, B & 10% of group C

were married at the age of 19 years or more. Regarding age of first delivery, maximum ladies delivered their first child before the age of 20 years maximum about 80%, whereas 20% of group C were delivered at the age of 20 years or more.

Table II

Socio-demographic profile of study subjects

Variables		Group A	Group B	Group C
		n-25(%)	n-40(%)	n-10(%)
Age (year)	20 -29	6(24)	8(20)	0
	30-39	13(52)	22(55)	9(90)
	>40	6(24)	10(25)	1(10)
Education	Illiterate	1(4)	9(22.5)	2(20)
	Primary	4(16)	5(12.5)	2(20)
	Secondary	16(64)	16(40)	5(50)
	HSC & more	4(16)	10(25)	1(10)
Occupation	House wife	25(100)	37(92.5)	10(100)
	Service holder	0	3(7.5)	0
Monthly income (taka)	10,000	16(64)	30(75)	5(50)
	20,000	8(32)	2(5)	3(30)
	>20,000	1(4)	8(20)	2(20)
Parity	Nil	1(4)	1(2.5)	0
	Para-1	5(20)	14(35)	0
	multipara	19(76)	25(62.5)	10(100)
Age of marriage (years)	£15	9(36)	15(37.5)	6(60)
	16-18	11(44)	17(42.5)	3(30)
	³19	5(20)	8(20)	1(10)
Age of first delivery (years)	<19	16(64)	27(67.5)	8(80)
	>20	9(36)	13(32.5)	2(20)

Table III shows percentages of ladies came for follow up after six months or after one year of fast visit. About 6(24%) of group A, 30%(12) of group B & 3(30%) ladies of group C came after 6 months, whereas 9(36%) of group A, 40%(16) of group B & 5(50%) women of group C came for follow up after one year. Total 47(62.7%) ladies came for follow up out of 75.

Table III

Participants came for follow up

	Group A	Group B	Group C
	n-25(%)	n-40(%)	n-10(%)
No Follow Up	10(40)	12(30)	2(20)
Follow up after 6m	6(24)	12(30)	3(30)
Follow up after 1yr	9(36)	16(40)	5(50)
Total Follow up	15(60)	24(70)	8(80)

Table IV shows CIN I were persistent or reappeared in study groups. Total persistence or reappearance of disease (CIN I) were 2 (13.3%) in group A (Expectant management), 3 (10.7%) in group B (Cold Coagulation) & 1 (12.%) in group C (LEEP). About 13 (86.7%) of group A, 25 (89.3%) of group B & 9 (87.5%) in group C were disease free in screening after 6 months & after one year.

Table IV

Persistence of disease (CIN 1) among follow up participants

CIN I	Group A	Group B	Group C
Follow up	n-15(%)	n-28(%)	n-8(%)
During 6 months	1(6.6)	1(3.5)	0
During 1 year	1 (6.6)	2(7.2)	1(12.5)
Total persistence	2(13.3)	3(10.7)	1(12.5)
Disease free	13 (86.6)	25 (89.2)	9(87.5)

Table V shows comparison of persistence of CIN I between expectant management & Cold coagulation. Total persistence or reappearance of disease during six month & one year follow up was 2 (13.3%) in group A & 3 (10.7%) in group B.

Table V

Comparison between Expectant management & Cold coagulation

CIN I	Group A	Group B	p value
Follow up	n-15(%)	n-28(%)	
During 6 month	1(6.7)	1(3.6)	0.333
During 1 year	1(6.7)	2(7.2)	
Total persistence	2(13.3)	3(10.7)	

Table VI shows comparison of persistence of CIN I between expectant management & LEEP. Total persistence or reappearance of disease during follow up was 2(13.3%) in group A & 1(12.5%) in group C. The p-value > 0.05 means not significant.

Table VI

Comparison between Expectant management & LEEP

CIN I	Group A	Group C	p value
Follow up	n-15(%)	n-8(%)	
During 6 month	1(6.7)	0	0.666
During 1 year	1 (6.7)	1(12.5)	
Total persistence	2(13.3)	1(12.5)	

Discussion

Cervical cancer is a preventable disease but in developing countries it makes 80% of global burdens. Preventable measures are neither uniformly nor vigorously implemented. In 2012 new and generally consistent cervical cancer screening recommendations for the general population, HPV vaccinated and unvaccinated, were released by two separate groups: the U.S preventive services Task force (USPSTF) and the multi disciplinary partnership of the American cancer society, American society for Colposcopy and cervical pathology, and American society of clinical pathology (ACS/ASCCP/ASCP).⁵

Distributions of age, parity, monthly income, education, marital age, age at first delivery were similar in different group in this study. Proper follow up after screening and management is the key for prevention of cervical cancer. But follow up rate is low. In this study, follow up rate were 62.7% in one year period, whereas 54% in another study.⁶ The high rate of loss during follow up (37.3%) was observed in this study. The length of time between colposcopic diagnosis and recommended follow up period may have an impact on compliance of the patients.

According to WHO's manual, if the final diagnosis in a woman is CIN I, the clinical management may take one of the following courses: either to (a) immediately treat the lesion or (b) follow the woman cytologically or colposcopically and then treat if the lesion is persistent or progressive after 18 to 24 months, and if regression occurs, discharge her from the colposcopy clinic. In the context of developing countries, a decision may be made to treat the woman, as many fail return for a follow up visit. If the decision is made to treat the woman with cryotherapy or LEEP, at least one follow up visit should be scheduled at 9 to 12 months from the date of treatment.⁷ In one study, managements were given among CIN I patients expectant management 34.6%, local ablative methods 7.3% & LEEP 56.8% cases, whereas in this study, expectant treatment were received 25(33.3%), 53.3% were treated with either cold coagulation or other ablative method & 13.3% LEEP regarding their size & extent of lesions.⁸ Excision procedure done in this study were in 13.3% cases, where as in other study it was about 26.4%.⁹

Persistence of disease were found in 2(13.3%) ladies those did not receive treatment & came for follow up within 12 months, 3(10.7%) who were treated with cold coagulation & 1(12.5%) lady who

received treatment with LEEP in this study, whereas persistence & progression of disease in case of immediate treatment about 1.7% & 4.4% in non treatment group in another study, which are much lower than this study.¹⁰

There is very little difference in the frequency of colposcopic abnormalities during the follow up period between 3 treatment groups. Expectant management is near to effective as LEEP treatment for patients with CIN I. Patients who had large lesion from colposcopic findings were treated with LEEP. Large lesion may have lower rate of spontaneous regression of the disease and higher rate of colposcopic abnormalities. During follow up majority of cases were colposcopically normal about 86.7% in no treatment group & 89.3% in cold coagulation group & 87.5% in LEEP group. This result confirmed that CIN I can spontaneously remit in a majority of cases without definite treatment.

There are some limitations in this study- sample sizes were small, all patients did not come for follow up and compliance of patients were not satisfactory.

Conclusion

The expectant management of CIN I requires constant follow up which is particularly poor in low resource settings as it requires high quality colposcopy and histopathological examination. Colposcopic surveillance without treatment appears reasonable in treating CIN I because of the high rate of spontaneous regression of CIN I, but adherence to the follow up visit should be emphasized to the patients.

Reference

1. Ferlay J, Colombet M, Soerjomataram I, Mathers C, Parkin DM, Pineros M et al; Estimating global cancer incidence and mortality in 2018. *International Journal of cancer*, 2019; 144: 1767-1774
2. Ferlay J, Bray F, Pisani P, Parkin DM. *Cancer incidence, Mortality and prevalence Worldwide*. Lyon, LARC Press, GLOBOCON 2012: LARC Cancer base no. 5. version 2.0
3. Schlecht NF, Trevisan A, Duarte Franco E, Rohan TE, Ferenczy A, Villa LL, Franco EL. Viral load as a predictor of the risk of cervical intraepithelial neoplasia. *Int J Cancer*. 2003; 103: 519-524
4. Holschneider CH. *Premalignant & malignant disorders of the uterine cervix*, *Current obstetric & Gynaecologic diagnosis & treatment*, 10th edition, Lange, medical publication division, USA, the McGraw Hill companies, 2007; 838-40

5. Holschneider CH. Premalignant & malignant disorders of the uterine cervix, Current Diagnosis & Treatment Obstetrics & Gynecology, eleventh edition, USA, McGraw Hill 2013; 807-809
6. Chase DM, Osann K, Sepina N, Wenzel L, and Tewari KS. The challenge of Follow up in a low income colposcopy clinic: characteristics associated with non compliance in high risk populations. J Low Genit Tract Dis 2012; 16: 345-351
7. Sellors JW and Sankaranarayanan R. Management that provides continuity of care for women; Colposcopy and cervical intraepithelial neoplasia: a beginners manual, WHO: ISBN 13, 2003/4: 92
8. Zeba D, Biswash R, Fatema K. Prevalence and Management of CIN by Colposcopy among VIA Positive Cases in a Tertiary Level Hospital of Bangladesh, Int J Med Res Prof. 2019; 5 ; 184-88
9. Aitken CA, Siebers AG, Matthijsse SM, Jansen EEL, Bekkers RLM, Becker JH, et al. Management and treatment of cervical intraepithelial neoplasia in the Netherlands after referral for colposcopy, Acta Obstet Gynecol Scand 2019; 98: 737-746
10. Elit L, Levine MN, Julian JA, Sellors JW, Lytwyn A, Chong S et al. Expectant Management Versus Immediate Treatment for Low Grade Cervical Intraepithelial Neoplasia A Randomized Trial in Canada and Brazil; J. CANCER 2011; 117; 1438-1445