

Therapeutic Effectiveness of Large Loop Excision of Transformation Zone (LLETZ) in Management of Cervical Lesions

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Abstract

LLETZ is a simple, outpatient means of removing the transformation Zone or morbidity to the patient. The aim of our study was to evaluate the therapeutic effectiveness of LLETZ in management of cervical lesions. This prospective study was conducted at Department obstetrics & Gynecology Zenana Hospital, SMS Medical College, Jaipur from December 2014 to June 2015. The study includes all patients who attended colposcopy clinic with complaints of persistent leucorrhea, postcoital bleeding, intermenstrual bleeding and postmenopausal bleeding. We had 29 cases of chronic endocervicitis, 27 showed an inflammatory smear while 2 showed LGSIL. 3 patients showing HGSIL on pap smear showed CIN – I on histopathology. This was false positive of Pap smear (6%). 1 patient of invasive squamous cell carcinoma showed HGSIL on pap smear. Thus LEEP was useful in diagnosing a case of invasive carcinoma which would have been missed with Pap smear alone. Also 3 patients of CIN – II on biopsy had inflammatory (1) and LGSIL (2) on pap smear. LEEP (Loop Electrosurgical Excision Procedure) is a feasible management strategy for cervical lesions especially in developing countries like India where incidence of cervical carcinoma remains high because of ineffective screening and poor patient compliance for follow up.

Keywords: Cervical lesions, transformation zone, cytology, colposcopy, histopathology.

1. Introduction

Large loop excision of transformation zone (LLETZ) of cervix was introduced by Walter Prendiville in 1989. [1] LLETZ is a simple, outpatient means of removing the transformation Zone or morbidity to the patient. LLETZ is almost identical in terms of therapeutic efficacy to hysterectomy in the treatment of CIN – III. [2]

The indications of LLETZ are mainly cytological / colposcopic suspicion of CIN – II or worse and persistent CIN – I (>12 months duration), Unsatisfactory colposcopic examination in presence of convincing cytologic abnormality or likelihood of glandular intraepithelial abnormality and CIN – I where likelihood of follow – up is low or when patient requests treatment. It can also be used for Recurrent /chronic cervicitis association with ectropion or erosion or polyps and to reduce a hypertrophied cervix.[3]

It has few complications like intra operative & post operative bleeding, pain, cervical stenosis and deformity, electric burns and rarely post operative pelvic cellulitis or adenexal abscess formation.

Aim & Objectives

The study was conducted with the following aims & objectives:

- To determine the therapeutic effectiveness of LLETZ in management of cervical lesions
- To examine the long term efficacy of LLETZ in the treatment of cervical lesions by using colposcopy and cytology in the follow up of these women
- To frame out a better protocol for early detection and management of preinvasive cervical lesions in young patients

2. Material & Methods

This prospective hospital based study was conducted at Department obstetrics & Gynecology Zenana Hospital, SMS Medical College, Jaipur from December 2014 to June 2015.

The study includes all patients who attended colposcopy clinic with complaints of persistent leucorrhea, postcoital bleeding, intermenstrual bleeding and postmenopausal bleeding. After a detailed clinical history all patients were subjected to cytological study by Pap smear followed by a detailed bimanual and colposcopic examination followed by excision of the lesion together with transformation zone upto a depth of 8mm and excised tissue was sent for histopathological examination.

Patient with diagnosed invasive cervical carcinoma on cytology report or on colposcopic assessment, acute cervicitis, pregnant patients, patient with acute pelvic inflammatory disease were excluded. All patients were followed up at 6 weeks, 3 month, than 3 monthly for one year.

3. Observation & Discussion

As shown in Table no.1 maximum number of patients 48% were in 30 – 39 years age group. 70% of the HGSIL lesions were seen in the ≥40 year’s age group. Mean age was 38.6 years.

This correlates with a study carried out by Jatashankar *et al* which concluded that incidence of CIN – II, III showed progressive rise with increasing age.[4]

This table shows that the maximum numbers of high grade lesions were seen in grand – multipara i.e. 6/10 (70%) while 30% were seen in multipara and 10% were seen primiparas.

This correlates with the study carried out by Sapkal RU in which he reported that HGSIL was more common in women with parity 3 – 5. [5]

Jatashankar *et al* also reported that SIL rate was found to be maximum in women of high parity. [4] Majority of cases came from middle socio – economic status (52%). 25% cases of low socio – economic status had HGSIL compared to 15.35% in middle socio – economic group. This could be due to poor genital hygiene in low socio – economic group.

This correlates with the study by Bhattacharyya SK *et al* which concluded that socio – economic status inversely correlates with cervical CIN. [6]

This table also shows that HGSIL is more common in those women who have 1st coitus at ≤18 years of age. 70% of HGSIL and 63.6% patients with CIN – I occurred in those with age at 1st coitus ≤18 years of age. This correlated with study conducted by Sapkal RU (2002) in which highest percentage of CIN lesions were seen in patients whose age at first coitus was less than 18 years. [5]

According to Green *et al* (2003), risk of cervical cancer increased with early age at first intercourse. [7]

Table No.1: Distribution of cases according to Demographic Profile

S. No	Age (in years)	CEC	CIN – I	CIN – II	CIN – III	SCC
1.	20 – 29	5	1	0	0	0
2.	30 – 39	16	5	2	1	0
3.	≥40	8	5	5	1	1
Parity						
1.	Primipara	2	1	1	–	–
2.	Multipara (≤3)	16	8	1	1	1
3.	Grand Multipara (≥3)	11	1	5	1	–
Socioeconomic status						
1.	Low	12	3	3	2	–
2.	Middle	15	7	3	–	1
3.	High	2	1	1	–	–
Age at 1 st coitus (years)						
1.	>18	13	4	2	1	–
2.	≤18	16	7	5	1	1

As shown in figure 1, maximum number of patients 60% presented with leucorrhoea, 22% with postcoital bleeding, 12% with intermenstrual bleeding and 6% with

postmenopausal bleeding. This correlates with study done by Pathare *et al* in which LEEP was performed as an outdoor procedure in patient with above similar complaints. [8]

Figure 1: Distribution of cases according to Chief Complaints

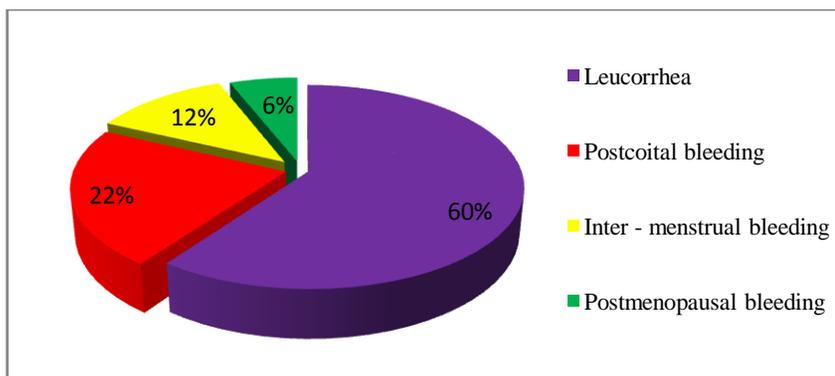


Table No. 2 shows that majority of patients with leucorrhoea present after 6 months duration. This may be because this symptom is not considered alarming by the patient. All of the patients who presented before 6 months duration had chronic endocervicitis on LLETZ biopsy. However 21.4% who presented after 6 months duration had CIN – I on pathology and 7.14% had CIN – II.

Patients with post – coital bleeding presented earlier (within 6 months). 45.4% of patients had CIN – I on histology, 27.2% had CIN – 2. 1 case of CIN – III was seen in a patient who presented between 3 – 6 months of complaint and one case of invasive squamous cell carcinoma was seen at more than 6 months duration. Hence, the degree of dysplasia increased with the duration of complaints.

This correlates with study conducted by Adam N Rosenthal (2001) in which 16% of patients with postcoital bleeding had inflammatory changes / metaplasia, 5% had CIN – I, 12% had CIN – II and 3% had cervical cancer. [9]

Postcoital bleeding should be considered an indication for prompt referral to a colposcopic clinic and a high risk factor for CIN.

50% of patients with complaints of intermenstrual bleeding with duration of less than 3 months had CIN – I on histopathology , 1 patient who presented with duration of complaint 3 – 6 months had CIN – III and 66.6% of those presenting with duration >6 months had CIN – II on histopathology and 33.3% had CIN – I.

All patient with postmenopausal bleeding presented upto 6 months duration of complaints. Patients considered it an alarming symptom. 33.3% of patients each had cervicitis, CIN – I and CIN – II on histopathology. This correlates with the study by Epstein E *et al* in which 2.1% of women with postmenopausal bleeding had cervical cancer. They concluded that diagnostic focus should be directed at excluding cervical pathology. [10]

Table No. 2: Distribution of cases according to duration of presenting complaints

S. No	Complaints	Duration (in months)	CEC	CIN – I	CIN – II	CIN – III	SCC
I.	Leucorrhoea						
1.		<3	1	3	0	0	0
2.		3 – 6	0	2	2	1	0
3.		>6	0	0	1	0	1
II	Post coital bleeding						
1.		<3	1	3	0	0	0
2.		3 – 6	0	2	2	1	0
3.		>6	0	0	1	0	1
III	Intermenstrual Bleeding						
1.		<3	1	1	0	0	0
2.		3 – 6	0	0	0	1	0
3.		>6	0	1	2	0	0
IV	Postmenopausal bleeding						
1.		<3	1	1	0	0	0
2.		3 – 6	0	0	1	0	0
3.		>6	0	0	0	0	0

As shown in Table No 3, maximum number of inflammatory smears (89.68%) were seen in those presenting with leucorrhoea, 45.4% of LGSIL and 50% of HGSIL are seen in patients with post – coital bleeding.

Out of 30 patients with leucorrhoea, only 1/30 had HGSIL compared with (5/11) patients with postcoital bleeding, 3/6 with intermenstrual bleeding and 1/3 with postmenopausal bleeding. Also Sadan O concluded that colposcopically directed LEEP after HGSIL on pap smear may reduce the time interval between diagnosis and treatment.[11]

Out of 50 patients 20 had grade I colposcopy changes and 30 had grade II changes. 80% of those with

grade I changes had leucorrhoea and 46.6% had grade II changes, possibly because they presented after a long duration when their degree of dysplasia had upgraded. 81.8% of patients with postcoital bleeding p/v had grade II colposcopic changes. 83.3% of patients with intermenstrual bleeding and 66.6% of those with postmenopausal bleeding had grade II colposcopic changes. No grade III changes were observed.

This is in accordance with Mridul Gehlot *et al* in which there was correlation in 95.92 % cases between colposcopy and biopsy. [12]

Table No.3: Distribution of cases according to pap smear grading, colposcopy grading and its correlation with presenting complaints

S. No	Pap smear Grade	Leucorrhea	Postcoital Bleeding per vaginum	Intermenstrual bleeding per vaginum	Postmenopausal bleeding per vaginum	Total
1.	Normal	0	0	0	0	0
2.	Inflammatory	26	1	1	1	29
3.	LGSIL	3	5	2	1	11
4.	HGSIL	1	5	3	1	10
	Colposcopic grade					
1.	I	16	2	1	1	20
2.	II	14	9	5	2	30

As seen in Table no.4 most cases of HGSIL (80%) showed erosion on per speculum examination. Hypertrophy of cervix seen in 1 case of postcoital bleeding and old tear in

1 case of intermenstrual bleeding. This correlates with study by Kulkarni *et al* who found that women with cervical erosion form a risk group for dysplasia. [12]

Table No .4: Correlation between per speculum Examination of cervix and presenting complaints in patients with HGSIL

S. No	Presenting Complaints	Erosion	Hypertrophy	Old Tear
1.	Leucorrhea	1	–	–
2.	Postcoital bleeding per vaginum	4	1	–
3.	Intermenstrual bleeding per vaginum	2	–	1
4.	Postmenopausal bleeding per vaginum	1	–	–

As seen in Table no. 5 all patient with Grade I colposcopy changes had an inflammatory smear. Hence there was good correlation between pap smear and colposcopy. All patients with LGSIL and HGSIL on pap smear had Grade II colposcopic changes. This shows that there was 100%

correlation between colposcopy and pap smear for high grade lesions and overall the correlation between colposcopy and pap smear was 82%. This correlates with the study by Sheshadri *et al* in which accuracy rate of satisfactory colposcopy while correlating cytology was 87.6%. [14]

Table No. 5: Correlation between Pap smear and Colposcopy grading

S. No	Colposcopic Grading	Number	Normal	Inflammatory	LGSIL	HGSIL
1.	Grade I	20	0	20	–	–
2.	Grade II	30	0	9	11	10

Table No. 6 shows 29 cases of chronic endocervicitis, 27 showed an inflammatory smear while 2 showed LGSIL. 3 patients showing HGSIL on pap smear showed CIN – I on histopathology. This was false positive of Pap smear (6%). 1 patient of invasive squamous cell carcinoma showed HGSIL on pap smear. Thus LEEP was useful in diagnosing a case of invasive carcinoma which would have been missed with pap smear alone. Also 3 patients of CIN – II on biopsy had inflammatory (1) and LGSIL (2) on pap smear. Hence false negative rate of cytology was 8%.

This correlates with study by Szurkus DC *et al* it was concluded that despite lack of correlation between colposcopic and histologic results, HGSIL in pap smear is an indication for LEEP. [15]

Also in the study carried out by Numnum *et al* which involved LEEP to simultaneously diagnose and treat premalignant cervical lesions in one visit resulted in overtreatment rate of 16% but concluded that such a protocol for patients with HGSIL pap smear, a “see and treat” approach may be acceptable. [16] Hockstead (1992) reported 7.1% false negativity of cytology. [17]

Table No. 6: Correlation between Pap smear findings and Histology

S. No	Grade	Total	CEC	CIN – I	CIN – II	CIN – III	SCC
1.	Normal	0	0	0	0	0	0
2.	Inflammatory	29	27	1	1	0	0
3.	LGSIL	11	2	7	2	0	0
4.	HGSIL	10	0	3	4	2	1

Table No. 7 shows that all patients with grade I and 9 patients of grade II colposcopic changes had chronic endocervicitis on histopathology.

2 patients of CIN – III and one patient of invasive squamous cell carcinoma also grade II colposcopic changes. This represents the false negative rate of colposcopy was 6%.

This correlates with the study by Song X, Wang Q *et al* in which false negative rate of colposcopy was 6% [17] and Hockstead RL reported it to be 5%. [18]

Table No.7: Correlation between Colposcopic findings and histology

S.No	Grade	Total	CEC	CIN – I	CIN – II	CIN – III	SCC
1.	I	20	20	–	–	–	–
2.	II	30	9	11	7	2	1

As seen in Table 8 all patients were given oral antibiotics for 7 days after the procedure. 1 patient had cervical polyp along with erosion which was removed by LLETZ and its biopsy showed an inflammatory polyp.

1 radical hysterectomy was done for squamous cell carcinoma and Ca cervix 1 was diagnosed. Both patients with CIN – 3 also underwent radical hysterectomy by choice after counseling about risks and benefits of both conservative and radical treatment.

2 patient of cervicitis underwent hysterectomy – one as a case of PID and the other, due to associated fibroids.

2 patients of CIN – 2 underwent hysterectomy as they were not willing for follow up. This correlates with study done by Chan *et al* who concluded that use of routine prophylactic antibiotics is not recommended. [19]

However, keeping in mind the low socioeconomic status and poor genital hygiene of patient's prophylactic antibiotic prescribed to all. A study carried out by Das N *et al* that simple hysterectomy appears to be a suitable diagnostic and treatment option for women with recurrent high grade cytological abnormalities where further loop treatment is not possible. [20]

Table No. 8: Treatment advised / Done

S.No	HPR	Antibiotics	TAH	Polypectomy	Radical	Total
1.	CEC	29	2	1	–	29
2.	CIN – I	11	–	–	–	11
3.	CIN – II	7	2	–	–	7
4.	CIN – III	2	–	–	2	2
5.	SCC	1	–	–	1	1

As shown in table No. 9, Patient with leucorrhea complained of discharge p/v during first 6 weeks but experienced complete relief of symptoms thereafter.

Out of 50 patients 42 came for follow up and 34 experienced complete relief. At 3 months 36 of the 38 patients who came experienced relief. At 6 months 34 of 35 patients who came for follow up were relieved of symptoms.

This correlates with study done by Greenspan DL *et al* in which it was found that older patients were more compliant than younger and compared to LEEP, patients

undergoing cold knife biopsy were more likely to come for regular follow up. They concluded that since LEEP is a less – invasive procedure it may convey to the patient that their condition is less severe.[21]

Also in the study done by Pathare SS, LEEP was performed as an outdoor procedure in women who referred with leucorrhea and postcoital bleeding. All the women experienced satisfactory cure from leucorrhea and were left less anxious from fear of cancer without having to undergo any major surgery. [8]

Table No. 9: Number of patients relieved of Symptoms

S.No	Complaints	Before	At 6 weeks		At 3 months		At 6 months	
			Number	Relief	Number	Relief	Number	Relief
1.	Leucorrhea	30	25	18	24	22	24	24
2.	Postcoital bleeding per vaginum (BPV)	11	9	8	8	8	6	5
3.	Intermenstrual BPV	6	5	5	4	4	3	3
4.	Postmenopausal BPV	3	3	3	2	2	2	2

Out of 42 patients reporting for follow – up at 6 weeks, 30 had inflammatory smears and 1 had HSIL on pap smear. On colposcopy 2 had grade II lesions.

Out of 38 patients who came for follow – up at 3 months, 2 had inflammatory and 1 had HSIL smear. On colposcopy 2 had grade II changes.

At 6 months, out of 38 patients, 3 had inflammatory smears and 1 had persistent grade II colposcopy change. This correlates with study by Hulman *et al* in which follow up was for 1.5 – 3.5 years and it was concluded that patients with

incomplete or equivocal of all grades of CIN merit careful, preferably colposcopic follow – up. Patients with completely excised high grade require careful cervical cytologic surveillance. [22]

Hallam *et al* followed up patients for 24 months and found 91% of patients were free of dyskaryosis with complete excision. No cases of invasive carcinoma developed following treatment. [23]

Also in study by Mathevet *et al* follow up was done for 3 years and 2 recurrences were seen in cases of LEEP. [24]

Table No. 10: Follow up after LEEP

S. No		Pap Smear					Colposcopy		
		Total	Normal	Inflammatory	LGSIL	HGSIL	Total	I	II
1.	Before	50	–	29	11	10	50	20	30
2.	6 weeks	42	7	30	4	1	42	40	2
3.	3 months	38	35	2	–	1	38	36	2
4.	6 months	35	32	3	–	–	35	34	1

In this study, 10 patients complaint of intra – operative pain and 6 of immediate post – op bleeding per vaginum. All were treated by ball cautery and none required haemostats or vaginal packing.

In late post – operative complications 5 patients complained of discharge per vaginum and were relieved by vaginal symptoms. 1 patient underwent hysterectomy for

pelvic inflammatory disease. In a study by Dunn TS *et al* minor complications included abdominal pain (14 cases) and vaginal bleeding in 26. Major complication included 1 patient with bowel injury and 1 with haemorrhage.[25]

In study done by Mathevet *et al* cervical stenosis was observed in 1 patient who underwent LEEP. [24]

Table No.11: Complications of LEEP

S. No	Complications	Number
	Intra – operative	
1.	Pain	10
2.	Bleeding	8
3.	Burn	1
	Immediate Post – op	
4.	Pain	6
5.	Bleeding	4
6.	Nausea / Giddiness	2
	Late Post – op	
7.	Discharge PV	5
8.	Stenosis	Nil

4. Conclusion

From this study we can conclude that LEEP (Loop Electrosurgical Excision Procedure) is a feasible management strategy for cervical lesions especially in developing countries like India where incidence of cervical carcinoma remains high because of ineffective screening and poor patient compliance for follow up. Pap smear and colposcopy are complementary to each other and LEEP is a check on them for low grade lesions and treatment option for high grade lesions. Although over treatment rate is high but all women can experience satisfactory cure from complaints and are less anxious due to removal of the fear of cancer without having to undergo any major surgery. Also its morbidity is less and it is a suitable option for younger women who have yet to complete their families.

References

- [1] Prendiville W, Cullimore J, Norman S. LLETZ: A new method of management for women with cervical intraepithelial neoplasia. *British Journal of Obstetrics and Gynaecology*. 1989; 96:111.
- [2] Kang SB, Roh JW, Kim JW *et al*. A comparison of the therapeutic efficacies of LLETZ and hysterectomy for the treatment of cervical intraepithelial neoplasia III. *Int J Gynecol Cancer*. 2001; 11(5): 387 – 91.
- [3] Mc Indole WA, Mc Lean MR, Jones RW, Mullins PR. *Obst Gynecol*. 1984; 64: 451.

- [4] Jatashankar M *et al*. Study of high risk factors for cervical carcinogenesis. *J of obstet and Gyn of India*. 2007 Sep/Oct; 57(5): 422-25.
- [5] Sapakal RU. Treatment of cervical intraepithelial neoplasia by loop electrical excisional procedures (LEEP). *Indian J of Gynae Oncology* 2002; 2 (1):5-11.
- [6] Bhattacharya SK, Basu S, Banerjee S. An epidemiological survey of carcinoma cervix in North Bengal Zone. *J Indian Med Assoc*. 2000 Feb; 98(2): 60-61, 66.
- [7] Green J, Berrington de GA, Sweetland *et al*. Risk factors for adenocarcinoma and Squamous cell carcinoma of the cervix in women aged 20 – 44 years: the UK national case control study of cervical cancer. *Br J Cancer*. 2003; 89:2078-86.
- [8] Pathare SS. Success with LLETZ – Time to initiate Universal screening for Ca Cervix in India. *J of Obstet and Gyn of India*. 2001; 51(5): 172-174.
- [9] Rosenthal A N, Panoskalis T, Smith T. The frequency of significant pathology in women attending general gynaecological clinics for postcoital bleeding. *BJOG*. Jan 2001; 108: 103-106.
- [10] Epstein E, Jamei B, Lindquist PG. High risk of cervical pathology among women with postmenopausal bleeding and endometrium \leq 4.4 mm. *Acta Obstet Gynecol Scand*. 2006; 85 (11) : 1368-74.

- [11]Sadan O, Yarden H, Schefter E. Bilevsky E. Treatment of HGSIL: a “see and treat” versus a three step approach. *Eur J Obstet Gynecol. Reprod Biol.* 2007 Mar; 131 (1) 73 – 5.
- [12]Gehlot M, Hooja N. Correlation between colposcopy, cytology and histology in cervical lesions. *J of Obst and Gynae of India.* 2001; 51(5):180-3.
- [13]Kulkarni RN, Durge PM. Role of socio – economic factors and cytology in cervical erosion in reproductive age group women. *Indian J Med Sci.* 2002; 56: 598-601.
- [14]Sheshadri L et al. *Indian J Cancer.* 1990 Sep; 27 (3): 180-6.
- [15]Szurkus DC, Harrison TA. Loop excision foe high grade squamous intraepithelial lesion on cytology: correlation with colposcopic and histologic findings. *Am J Obstet Gynecol.* 2003 May; 188(5): 1180-2.
- [16]Numnum TM, Kirby TO, Leath CA. A prospective evaluation of “see and treat” in women with HSIL pap smear results: Is this an appropriate strategy ? *J Low Genit Tract Dis.* 2005 Jan; 9(1): 2-6.
- [17]Song X, Wang Q. Video colposcopy in diagnosis of cervical squamous intraepithelial lesions. *Zhonghua Fu Chan Ke Za Zhi.* 2001; 36(5):278-81.
- [18]Hockstead RL. A comparison of simultaneous cervical cytology, HPV testing and colposcopy. *Fam Pract Res J.* 1992; 12(1); 53 – 60.
- [19]Chan KK, Tam KF, Tse Ky. The use of vaginal antimicrobials after LLETZ: a prospective randomisd trial. *BJOG.* 2007 Aug; 114(8): 970-6.
- [20]Das N, Naik R, Jackson S. recurrent smear abnormalities where repeat loop treatment is not possible: Is Hysterectomy the answer? *Gynecol Oncol.* 2005 Jun; 97 (3): 751-4.
- [21]Greenspan DL, Fakhion M, Coonrod DV. Compliance after LEEP or cold Knife Biopsy. *Obstet Gynecol.* 2007 Sep; 110 (3): 675-80.
- [22]Hulman G, Pickles CJ, Gie CA. Frequency of CIN following LLETZ. *J Clin Pathol.* 1998 May; 51 (5): 375-377.
- [23]Hallam NF, West J, Harper C. LLETZ is an alternative to both local ablative and cone biopsy treatment: a series of 1000 patients. *J Gynecol Surg.* 1993; 9(2):77 – 82.
- [24]Mathevet P, Chemali E, Roy M. Long term outcome of a randomized study comparing three techniques of colonization: Cold Knife, laser and LEEP. *Eur J Obstet Gynecol Reprod Biol.* 2003 Feb 10; 106 (2): 214- 218.
- [25]Dunn TS, Killoran K, Wolf D. Complications of outpatient LLETZ procedures. *J Reprod Med.* 2004 Feb; 49(2) 76-8.
- [26]Kalogirou D, Antoniou G. Predictive factors used to justify hysterectomy after loop conization: increasing age and severity of disease. *Eur J Gynaecol Oncol.* 1997; 18(2): 113-6.