# CIN in Upper Egypt (LEEP Treatment)

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**Abstract:** The present study was To evaluate the effectiveness and safety of the loop electrosurgical excision procedure (LEEP) in the treatment of cervical intraepithelial neoplasia (CIN), Women participating in a cervical screening study with histologically confirmed cervix were visually inspected with acetic acid, followed by coloposcopy and biopsy taken from abnormal areas, Cure was defined as no clinical or histologic evidence of CIN. Factors influencing cure rates were evaluated by $\chi^2$ tests Out of the 1000 screened women 126 were found to be CIN positive (12.6%), 120 underwent LEEP. Six months follow up of 114 cases showed complete cure of 108 women (94.7%), LEEP Cure rates were 96.7%, 88.9%, and 80% for $CIN_I$, $CIN_{II}$ and $CIN_{III}$ respectively. Single Pass and Multiple Pass cure rates were 97% and 90% respectively. Minor adverse effects were observed in 15 women and complications were seen in 5 women.LEEP was associated with minimal complications and good cure rates especially in those with $CIN_I$ even in cases with large lesions.

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**Keywords:** CIN, LEEP**,** colposcopy.

## 1.Introduction

Cervical cancer is the second most common cancer among women.(1). A woman's risk of developing cervical cancer by age 65 years ranges from 0.8% in developed countries to 1.5% in developing countries(2). Some cervical intraepithelial neoplasia (CIN) lesions progress to cervical cancer. Most of them, particularly CIN 1 and 2 lesions, regress spontaneously without treatment (3). Current consensus guidelines recommend follow up with cytology for up to 2 years for some women with CIN (4).

LEEP, the out-patient surgical procedure to evaluate and treat CIN, is widely used in cervical screening programs in high-income countries. Electrically activated tungsten wire loop electrodes are used to excise the entire transformation zone and provide tissue samples for histologic assessment of the disease and excised margins. The procedure's effectiveness, adverse effects, complications, and long-term morbidity have been widely reported in high-income settings [5-11], and it has been found to be an effective and simple outpatient treatment for women with CIN. Similar cure rates for CIN have been found with LEEP and alternative surgical treatments, such as laser ablation and conization [1]. However, the effectiveness, safety, and acceptability of LEEP have not been widely investigated in low-resource settings [12], and it is unclear whether similar cure rates and safety profile can be achieved.

The aim of the present study was to evaluate the effectiveness of LEEP following confirmation of CIN and any adverse effects or complications associated with the procedure.

## 2.Material and Methods:

In Al–Azhar University Hospital- Assiut 1000 women aged 20-70 years old screened for CIN by pap. Smear. Women with positive pap smears results underwent colposcopy (6x to 12x magnification) guided punch biopsies for further investigation. The biopsy specimens were processed and graded according to CIN nomenclature.

Women diagnosed with CIN based on their punch biopsy results attended for LEEP. A detailed medical history was taken from each patient to exclude uncontrolled hypertension, diabetes mellitus, bleeding disorders, allergic reactions, exposure to diethylstilbestrol, pregnancy, and active genital tract infection. Each patient was counseled about the procedure and provided informed consent. LEEP was carried out as an outpatient procedure under local anesthetic and colposcopic guidance. A speculum was used to expose the cervix, followed by application of 5% acetic acid and Lugol's iodine solutions to assess the lesion. Local anesthesia was given by submucosal infiltration of 2% Xylocatine (AstraZeneca, London, UK). The appropriate loop electrode was used for excision of the transformation zone under colposcopic observation. The excision was initiated peripheral to the nonuptake area of iodine and single or multiple passes or 2-layer excisions were performed depending on the extent of the lesion. Bleeding was stopped by fulguration and application of ferric subsulfate solution. The excised specimens were sent for histopathological examination. As part of internal quality assurance, processing of specimens, laboratory manuals, and reporting procedures were periodically reviewed.

After the procedure the women were advised not to use vaginal douches or tampons, nor to have sexual intercourse for 1 month after treatment, and to return to the clinic if they experienced any of the following within 4 weeks of the procedure: free for more than 2 days; severe lower abdominal pain; foul-smelling greenish-yellow discharge; bleeding with clots; or bleeding for more than 2 days. The women were informed that they may experience mild cramps and blood stained discharge in the following 2 weeks. A routine course of empirical antibiotics comprising doxycycline and metronidazole was prescribed, in addition to analgesics for pain.

The women were advised to attend for follow-up 6 months later to rule out residual or recurrent cervical neoplasia. At follow-up the cervix was assessed with pap. semear colpscopy, and biopsy of abnormal areas observed colposcopically. Women with confirmed CIN underwent repeat LEEP, or simple hysterectomy depending on the lesion and the patient's preference. Women were considered disease free when no colposcopic features of CIN were observed or when no CIN lesions were established histologically if a biopsy sample was taken.

The adverse effects of LEEP were defined as mild pain or mild cramps during or after treatment, vasomotor symptoms of fainting and flushing during or immediately after treatment, mild bleeding or spotting immediately after treatment, foul smelling discharge, menorrhagia, and fever or chills after treatment; and these were used as the indicators of acceptability [13]. Anaphylactic reactions during LEEP, vaginal burns, severe pain, cramps or severe bleeding during or after LEEP that required further treatment, severe local cervical infections, unintended surgery within 4 weeks of LEEP, pelvic inflammatory disease, and functional cervical stenosis were assumed to be complications caused by the procedure and were used to assess its safety [14]. Cure rates, adverse effects, and complications were reported as frequency percentages. Cure rates categorized by age, menopausal status, extent of cervical lesion. Involvement of the endocervical canal, type of LEEP, margin involvement, and grade of CIN were compared using $\chi^2$ tests.

**3. Result analysis:**

**Fig.(1)** shows schedule for management and follow-up after 6 months.

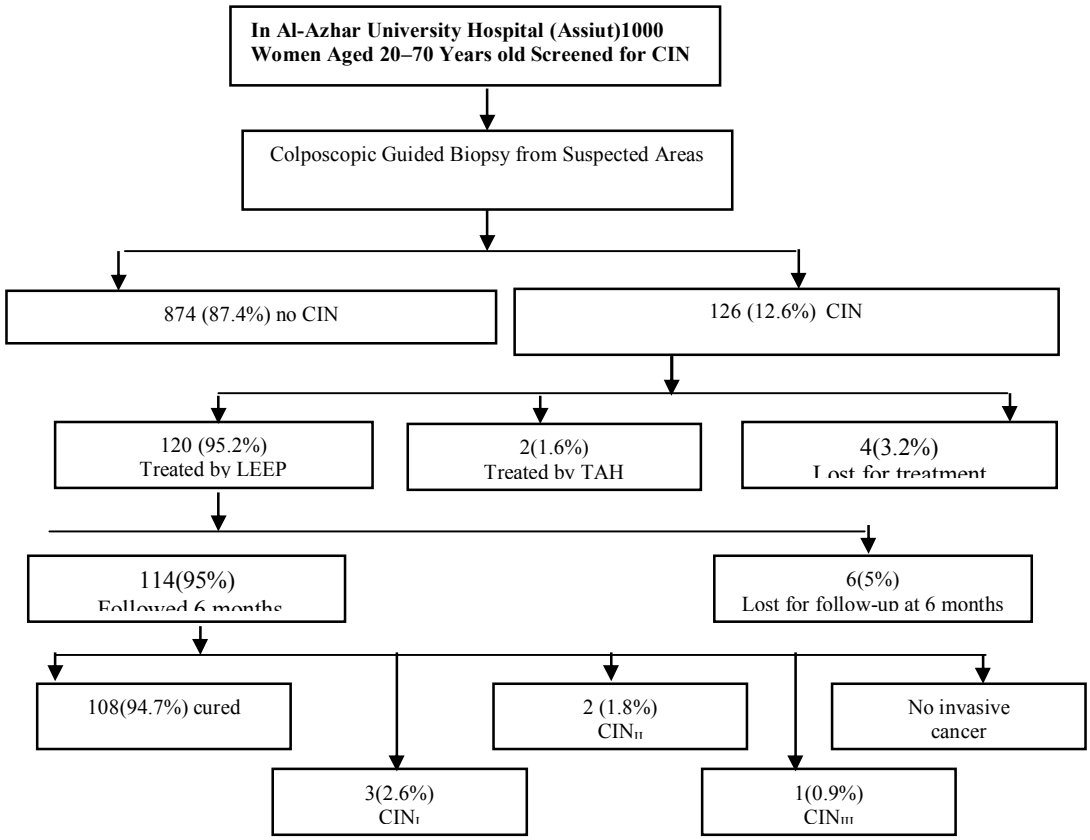


**Fig. (1)** Out of 1000 screened women 126 were found to be CIN positive. LEEP was allowed to 120 women, 114 were followed up for 6 months that resulted in cure rate of 94.7% and $CIN_I$, $CIN_{II}$ and $CIN_{III}$ in2.6%, 1.8% and 0.9% of cases respectively.

**Table (1): Cure rates at 6 month follow-up according to characteristics of women at screening.**

| Characteristics | Cure rate (%) | OR 95% CI | *P-value* |
|---|---|---|---|
| **Age:** | | | |
| 20 → 39 year | (73/76) 96% | 1.0 | < 0.742 |
| 40 → 70 year | (35/38)92% | 0.9 (0.3-2.7) | |
| **Area of lesion involved (%):** | | | |
| < 25 | (58/60)96.7% | 1.0 | < 0.001 |
| 25 – 50 | (37/39)94.8% | 0.2(0.1-0.6) | |
| ≥ 50 | (13/15)86% | 0.1(0.0-0.4) | |
| **endocervical canal involvement:** | | | |
| No | (96/99)96.9% | 1.0 | < 0.058 |
| Yes | (12/15)80% | 0.5(0.2-1.0) | |
| **Menopausal status:** | | | |
| Not attained | (90/94)95.7% | 1.0 | |
| Attained | (18/20)90% | 0.3(0.1-1.0) | < 0.050 |
| **Type of LEEP:** | | | |
| Single Pass | (68/70)97% | 1.0 | < 0.001 |
| Multiple Pass | (40/44)90% | 0.4(0.2-0.9) | |
| **Grade of CIN:** | | | |
| $CIN_I$ | (88/91)96.7%) | 1.0 | < 0.001 |
| $CIN_{II}$ | (16/18)88.8% | 0.4(0.2-1.1) | |
| $CIN_{III}$ | (4/5) 80% | 0.2(0.1-0.5) | 0.001 |

There were significant increase of cure rates with decrease of lesion area, decrease CIN grade, in non menopausal than menopausal women and in single than multiple pass LEEP (P<0.001, 0.001, 0.05 and 0.001 respectively. There were insignificant increase of cure rates wilth decrease of age and in cases without endocervical lesions.

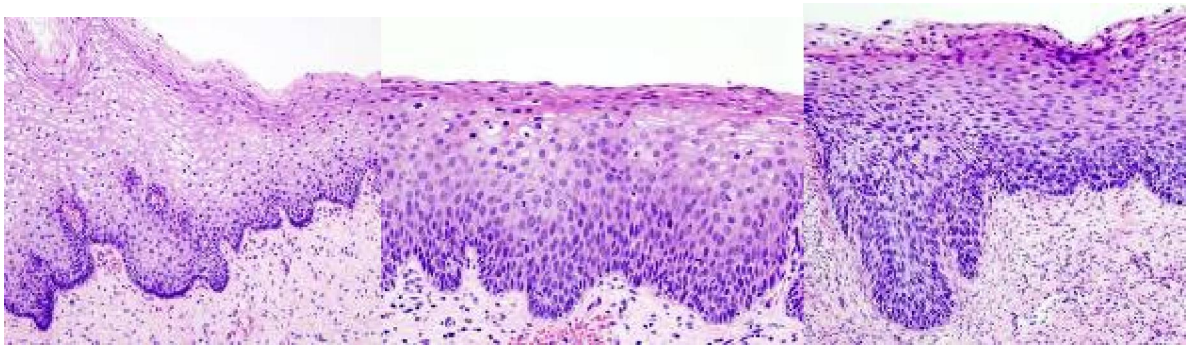

**Figure 1: Cervical Intraepithelial neoplasia (CIN).**
A) CIN grade I showing dysplastic squamous cells in the lower one-third of the epithelium.
B) CIN grade II showing dysplastic squamous cells in the basal two-thirds of the epithelium.
C) CIN grade III showing dysplastic squamous cells marked throughout the full thickness of the epithelium.

**Table (2) Cure rates after 6 months.**

| Punch biopsy histology before LEEP | LEEP Cases | LEEP followed cases | Follow–up after 6 months | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | Cured (%) | $CIN_I$ (%) | $CIN_{II}$ (%) | $CIN_{III}$ (%) | Invasive | Lost cases |
| $CIN_I$ | 96 | 91 | 88(96.7) | 1(1.1) | 2(2.2) | 0(0.0) | 0 | 5(5.2) |
| $CIN_{II}$ | 19 | 18 | 16(88.9) | 1(5.6) | 1(5.6) | 0(0.0) | 0 | 1(5.3) |
| $CIN_{III}$ | 5 | 5 | 4(80) | 0(0) | 0(0.0) | 1(20) | 0 | 0(0.0) |
| Total | 120 | 114 | 108(94.7) | 2(1.8) | 3(2.6) | 1(0.9) | 0 | 6(5.0) |

Total cure rate was 94.7% and that of $CIN_I$, $CIN_{II}$ and $CIN_{III}$ were 96.7%, 88.9% and 80% respectively.

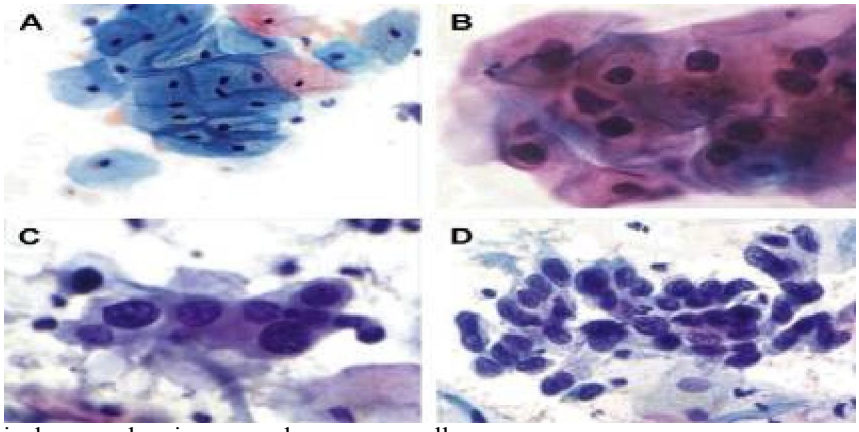


Figure 2: A) Cervical smear showing normal squamous cells.
B) Cervical smear with CIN grade I showing dysplastic cells with mild degree of cellular and nuclear pleomorphism and enlargement.
C) Cervical smear showing CIN grade II with dysplastic cells with moderate degree of cellular and nuclear pleomorhism and enlargement.
D) Cervical smear showing CIN grade III showing dysplastic cells with marked cellular and nuclear pleomorphism and enlargement and increased nucleocytoplasmic ratio and scanty cytoplasm.

The adverse effects observed were mild pain or mild cramps during or after treatment (3.3%), malodorous vaginal discharge following treatment (2.5%), mild bleeding (2.8%), menorrhagia (1.7%), and fever (1.7%). The complications recorded were PID (1.7%), severe bleeding that required suturing and blood transfusion (0.8%), severe pain (0.8%), and vaginal burns (0.8%).

**4. Discussion:**

Cervical cancer is the second most common cancer among women.(1). A woman's risk of developing cervical cancer by age 65 years ranges from 0.8% in developed countries to 1.5% in developing countries (2).

Adequate treatment of CIN is vital for the success of cervical screening to prevent invasive cervical cancer. Cervical screening programs in low- and medium-resource countries have been less successful in reducing cervical cancer, partly because of the inadequate treatment coverage of women with CIN [15,16]; in addition, the lack of well-trained medical staff to perform colposcopy and treatment of the disease is a major resource constraint in many low-income countries [16]. LEEP has emerged as the most widely used CIN excision method in high-income countries and results from well-conducted randomized clinical trials suggest that there is no difference in residual disease following LEEP, laser ablation, laser or cold knife conization [5]. From a practical perspective, LEEP is a superior excision treatment approach given the cheaper equipment and shorter duration of operative training.

The present study showed that LEEP is an effective and safe procedure in a low-resource setting and also reflect the treatment outcomes reported by investigators in high-income countries. The discrepancy between colposcopically-directed biopsy and LEEP histology has been widely reported, and the agreement in the present study is in the higher range (46%-90%) of concordance reported in other studies [10, 17-18]. Clearance of small lesions by punch biopsy and the resulting inflammatory reaction followed by application of ferric subsulfate solution may partly explain this discrepancy.

Treating women with low-grade disease has been a policy priority in this setting because women are likely to receive only one treatment in their lifetime and there are considerable difficulties in ensuring follow-up. A possible limitation of the present study is that only colposcopy and directed biopsies some women with residual disease because the transformation zone may not have been fully visible after LEEP. However, this figure is likely to be small. The overall cure rate of 95% found in the present study is in the lower range of the 90%-95% cure rates reported in nonrandomized studies in the literature [5-11, 21-24], but comparison of treatment results from nonrandomized case series can be limited by biases arising from case treatment failures following LEEP in both randomized and nonrandomized case series are similar and, in most settings, LEEP has around a 90% cure rate for CIN.

A cure rate of 95.3% was reported for 149 patients with CIN treatment by LEEP in a study from Lima, Peru [8]; and the variables that correlated with failure included the grade of lesion and operator's

expertise, in the present study, adverse effects and complications following LEEP were observed in a negligible proportion of women and none were major or life threatening. The frequency of adverse effects and complications favorably compares with those reported from other studies in both high- and low-income countries [5-11, 24, 25].

The findings of the present study and those from other low-income country settings [12, 24, 25] reinforce that LEEP can be performed effectively in these settings with a low frequency of complications and high rates of disease control. The widespread use of LEEP to treat CIN that requires excision should be an important integral component of screening programs in low-income countries. It is vital that adequate resources are available and doctors and nursing personnel are trained to perform LEEP as part of screening programs.

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