



(RESEARCH ARTICLE)



## Large loop excision of the transformation zone (LLETZ): experience from sub-Saharan Africa.

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### Abstract

Premalignant cervical lesion, also known as Cervical Intraepithelial Neoplasia (CIN) if left untreated could lead to the development of cervical cancer. Large Loop Excision of the Transformation zone (LLETZ) is effective for treatment of CIN. Experience and equipment for this procedure is not readily and widely available in most health centres in sub-Saharan Africa. The study is aim at reviewing the morbidity and outcome of LLETZ conducted at the Colposcopy Clinic of our Teaching Hospital. A retrospective descriptive review of data obtained from patients who had LLETZ at our Colposcopy clinic from June 2015 to May 2017. LLETZ was performed on 58 patients. Out of these, 52 folders were retrieved and analysed. The mean age of the patients was 35.5 years  $\pm$ 6.2SD while the mean parity was 4.5 $\pm$ 2.3SD. The main indication was CIN2+ in 36(65.2%) patients, followed by persistent postcoital bleeding in 8(15.4%) patients. Perioperative complication was seen in 12(23.1%) patients. The concordance rate for CIN lesions after treatment was 92%. LLETZ is a safe and effective procedure for treatment of CIN lesion. The perioperative complications and the concordance rate for CIN lesion after treatment observed in our centre are within acceptable range.

**Keywords:** Cervical Intraepithelial Neoplasia; LLETZ; Cervical lesion; Treatment; Colposcopy

### 1. Introduction

Cervical cancer is the 4<sup>th</sup> most common cancer in women worldwide with an estimated 528,000 new cases and 266,000 deaths in 2012[1]. It was estimated that about 80% of the global burden of cervical cancer in the world occurs in less developed regions, were almost nine out of ten (87%) cervical cancer death occurs [1]. In Nigeria, cancer of the cervix is the second most common cancer affecting women. In 2012, Nigeria recorded 14,089 new cases of cervical cancer cases and 8240 deaths [2].

Human Papilloma virus (HPV) is the main aetiological agent for the development of cervical cancer, with HPV serotype 16 and 18 accounting for over 70% of cases.

In high-income countries with organized cervical cancer prevention programs, early diagnosis and treatment of precancerous lesions have led to significant reduction in burden of the disease with the incidence of cervical cancer decreases by a remarkable 70-80% [3]. Due to poor access to high quality screening and treatment services, approximately 85% of the global cervical cancer burden is borne by less developed countries of the world. The trend of cervical cancer burden in less developed countries is worsening with estimated 98% by 2050[3]. CIN is a premalignant lesion of the cervix, which if left untreated can progress to cervical cancer [4].

The treatment options for CIN available in low and middle income countries are cryotherapy, Large Loop Excision of the Transformation zone (LLETZ) also known as Loop Electrosurgical Excision Procedure (LEEP) and cold knife conization [4]. Cryotherapy and LLETZ are the most commonly recommended outpatient treatment options for precancerous lesion of the cervix [4]. The objective of LLETZ is the complete excision of the precancerous lesion of the

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cervix and the transformation zone (TZ). In skilled hands, LLETZ is relatively safe, simple and effective procedure than cryotherapy in treating large lesions, lesions that cannot be covered with the cryotip and those that extend into the endocervical canal [5]. LLETZ also has the advantage of obtaining tissue specimen for histological examination. This helps in determining lesion's severity and extent. It is important to excise the entire TZ along with the identified lesion, because the TZ may be harboring HPV even if part of it does not appear to be involved with the lesion. Histological examination of the tissue specimen obtained can then be done for presence and degree of CIN or unsuspected invasive cervical cancer. Histological examination can also confirm if the cervical lesion was removed in its entirety.

Our study was aimed at reviewing the morbidity and outcome of LLETZ done in our health facility. This report also documents our first 24 months' experience with treatment of premalignant cervical lesion using LLETZ.

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## 2. Methodology

This study was a retrospective descriptive review conducted at the Colposcopy unit of the department of Obstetrics and Gynecology of Aminu Kano Teaching Hospital. Medical records, Colposcopy records and pathology reports of patients who had LLETZ from June 2015, when the Colposcopy clinic was established, to May 2017 were examined. Patients with incomplete data and those who had not complete six months follow up after the procedure were excluded from the study. Approval for the study was obtained from the Research and Ethics Committee of our hospital.

All patients recruited for the procedure had initial colposcopic assessment and biopsy. Those with high grade lesion and persistent low grade lesion were offered loop excision. Also women with post coital bleeding and those with colposcopic-pathologic discrepancies were advised to undergo same treatment. Women with invasive cancer and glandular lesions were excluded from the procedure. Women with evidence of Pelvic Inflammatory Disease (PID), cervicitis or bacterial vaginosis were first treated before the procedure was done. Those that recently delivered were at least 3 months post-partum.

Written consent was obtained from the women after being fully informed about the procedure, its effectiveness, complications and possible long term sequel.

**LLETZ Technique:** LLETZ was performed under colposcopic guidance. Colposcopic assessment was carried out immediately before the LLETZ to confirm the location and extent of the lesion. Sometimes, Lugol's iodine was applied to help in outlining the margin of the lesion before the start of the treatment. Insulated vaginal speculum with smoke-evacuator tubing was used to expose the cervix. Insulated vaginal side wall retractor was used in patients with lax vaginal wall. Local anesthesia was achieved using 2% xylocaine. About 5mls or less is injected into the cervical tissue at 3, 6, 9 and 12 o'clock position. The Bovie Electrosurgical Generator (Aaron1250) and ConMed Electrosurgery System 1200 Smoke Evacuator were used for the procedure. The power setting used depend on the size of the Loop electrode being used. The power settings for the 3mm and 5mm ball electrodes are 30 watts and 50 watts respectively. The procedure was aimed at removing the entire TZ with one pass of the loop electrode were feasible. Prophylactic antibiotics were prescribed to all patients after the procedure (Doxycycline 100mg twice daily and metronidazole 400mg three times a day, both for 7 days). After treatment, all women received instruction on self-care and symptoms to expect. Those with persistent vaginal bleeding, offensive vaginal discharge, lower abdominal pain and/or fever were advised to report back. They were also advised not to have sexual intercourse for one month. They were seen 2 weeks after the LLETZ and were enquired about symptoms and complications and were counsel about histology results and follow up. All patients were scheduled for follow up examination at 6 and 12 months after treatment with repeat cytology and Colposcopy.

Postoperative vaginal bleeding/spotting of less than 14 days which did not require any treatment was regarded as uncomplicated vaginal bleeding. Were cervical suturing or vaginal packing was done; such intraoperative vaginal bleeding was regarded as complicated. Persistent vaginal bleeding was defined as prolonged postoperative vaginal bleeding of more than 14 days which did not require any treatment. This was evaluated after excluding menstrual bleeding. Postoperative infection was defined as purulent vaginal discharge, cervicitis, endometritis or pelvic peritonitis.

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## 3. Results

A total of 58 patients were treated in our Colposcopy clinic by LLETZ. We were able to retrieved 52 folders and analysed. Six folders were excluded due to incomplete record or lost to follow up at 6 months.

The ages of the patients range from 23 to 48 years with a mean age of 35.5 years ( $\pm 6.2$ SD). The mean parity was  $4.5 \pm 2.3$ SD. Details were shown in table 1. Table 2 showed that the indication for LLETZ in the majority of the patients, 36(65.2%) was High grade lesion followed by persistent post-coital bleeding in 8(15.4%) patients.

**Table 1** Socio-demographic characteristics

	Frequency	Percentage
Age (years)		
20-29	11	21.2
30-39	32	61.5
40-49	8	15.4
$\geq 50$	1	1.9
Parity		
0	4	7.7
1-2	5	9.6
3-4	17	37.7
$\geq 5$	26	50
Total	52	100

**Table 2** Indication for LLETZ

Indication	Frequency	Percentage
Persistent low grade lesion (CIN 1)	6	11.5
High grade lesion (CIN2+)	36	69.2
Colposcopic-histologic discrepancy	2	3.8
Persistent postcoital bleeding with negative histology	8	15.4
Total	52	100

Table 3 described the perioperative complications experience by the patients. Twelve (23.1%) patients had some form of perioperative complication. Seven patients (13.5%) had intraoperative vaginal bleeding necessitating vaginal packing. One of them who also had cervical suture application was admitted for a day for observation. None had blood transfusion. Other complications were treated on out-patient basis. The total prevalence of post-operative vaginal bleeding was 19.2%

**Table 3** Final histology (post LLETZ)

Histological diagnoses	Frequency	Percentage
CIN 1	10	19.2
CIN 2	24	46.2
CIN 3	5	9.6
Carcinoma in-situ	1	1.9
Chronic cervicitis	12	23.1
Total	52	100

The final histological diagnosis was shown in table 4. CIN 2+ was diagnosed in 29(55.8%) patients while CIN 1 was reported in 10(19.2%) patients. Histology report of 12 patients shows chronic cervicitis. One patient with high grade

lesion had final histological diagnosis of carcinoma in-situ and underwent simple hysterectomy. The concordance rate for CIN lesion after treatment was 92%.

**Table 4** Peri-operative complications

Complication	Frequency	Percentage
Persistent vaginal bleeding	2	3.8
Intraoperative bleeding	7	13.5
Late post-operative bleeding	1	1.9
Infection	2	3.8
No complication	40	76.9
Total	52	100

#### 4. Discussion

Screening and treatment of premalignant lesion of the cervix is paramount in prevention of cervical cancer. LLETZ is relatively simple, safe and effective outpatient method for the treatment of cervical precancer [6]. The mean ages of the patients that were treated in our clinic was 35.5 years. This corresponds to the peak incidence for diagnosing high grade lesion. Though CIN 1 has a low potential for progression to cancer and higher prevalence among young women [7,8] 11.5% of the patients treated in our centre had persistent CIN 1. Women with persistent lesion are more likely going to progress to higher lesion. Also in developing countries, women with low grade lesion may be offered treatment to maximize treatment coverage and reduce lost to follow up. Moreover, a study conducted by Efraim Siegler et al discovered that in one-fifth of the women for whom CIN 1 was the indication for LLETZ, CIN 2+ was the final diagnosis [9]. Post coital bleeding with negative histology was the indication for LLETZ in 8(15.4%) patients. Patients with post coital bleeding have a statistically significant higher incidence of CIN [10]. Though these patients had negative histology on initial biopsy, they were offered loop excision (LLETZ) to treat their symptoms and have a more representative tissue sample for repeat histology.

The prevalence of 13.5% for post-operative vaginal bleeding necessitating additional haemostatic technique observed in our study group was higher than what was recommended by regulatory bodies like the UK National Health Service Cervical Cancer Screening Program [11]. Base on their recommendation, the proportion of treatment associated with primary haemorrhage that requires a haemostatic technique in addition to the treatment method applied must be less than 5% [11]. The higher prevalence we observed may be attributed to the fact that haemostatic paste such as Monsel solution is not available in our centre. It helps in haemostasis when applied to the cervix after treatment. Bleeding in our patients were controlled by diathermy ablation with or without vaginal packing. However, despite the higher prevalence of post-operative vaginal bleeding, only 1(1.9%) patient was admitted for observation after suture application. This correspond to the less than 2% recommended [11]. Lack of standardized definition of perioperative complication following LLETZ make it difficult for comparison with other studies.

Table 4 shows the final post LLETZ histology reports. The increase in the number of patients with CIN 1 compare to pre-treatment may be due to over diagnosis of CIN 2+ on colposcopic biopsy. Similar studies also reported either absence of residual lesion or lower grade dysplasia for LLETZ specimen with 14-18% prevalence [13,14,15,16]. Chronic cervicitis was reported in 12(23%) of the patients. The absence of residual dysplasia in LLETZ specimen may be as a result of the fact that dysplastic lesion is usually focal and small and may have been removed by the punch biopsy. More so, 6-50% of CIN 2-3 lesions may spontaneously regress with CIN 2 lesions more likely to regress than CIN 3 lesions [17,18]. Other reported reason for the discrepancy is when pathologist failed to identify areas containing CIN [16].

#### 5. Conclusion

LLETZ is a safe and effective procedure for treatment of CIN and prevention of cervical cancer. The perioperative complications and the concordance rate for CIN lesion after treatment observed in our centre are within acceptable range.

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## Compliance with ethical standards

### *Acknowledgments*

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### *Disclosure of conflict of interest*

The authors have no conflict of interest to declare.

### *Statement of informed consent*

Approval for the study was granted by the hospital Research and Ethics committee

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