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Does Repeat Large Loop Excision of the Transformation Zone Achieve a Cure for Histologically Proven Persistent High Grade Squamous Intra-epithelial Lesion at Margins?

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Abstract— Background: *Cervical cancer is the second most common malignant neoplasm in women world-wide. Cervical Intra-epithelial Neoplasia (CIN) is a precursor lesion of cervical cancer and effective treatment of this lesion by Large Loop Excision of the Transformation Zone (LLETZ), can prevent progression to cervical cancer.* ***Objectives:*** *The aim of this study was to establish if repeat LLETZ achieves a cure for histologically proven persistent high grade CIN lesions at margins.* ***Methods****: A retrospective quantitative descriptive study, done at the Charlotte Maxeke Johannesburg Academic Hospital colposcopy clinic, South Africa. Data was collected from patient files (1500) over a period of 10 years (2006-2016). Patients who initially had HGSIL, then were treated using LLETZ and the repeat cytology showed persistent HGSIL then subsequently had a second LLETZ done. A total of 71 patients met the inclusion criteria.* ***Results:*** *74,6% of the women had HGSIL (CIN 2, 3 and HGSIL) at the second/repeat LLETZ and 22.1% had LGSIL (CIN1 and LGSIL). Ecto-cervical margins were positive in 5 (8.5%) of the patients who had the initial LLETZ biopsy, negative in 3 (5.1%) and unreported in 1 (1.7%). This was as compared to positive margins in 8 (13.6%), negative margins in 15 (37.3%) and unreported in 3 (5.1%) at the second (repeat) LLETZ. Endo-cervical margins were positive in 17 (28.8%) of patients who had an initial LLETZ biopsy as compared to 11 (18.6%) at the second LLETZ. This showed an improvement of 35.4% from the first to the second biopsy. In 55.9% of patients, there was both ecto-cervical and endo-cervical margin involvement post the initial LLETZ as compared to 37.3% post repeat LLETZ. This was an improvement of about 33.3% post repeat LLETZ. There was no association between previous ecto-margins status (Pearson chi2 (98) = 106.7434 Pr = 0.257), previous endo-margins status (Pearson chi2 (10) = 2.8432 Pr = 0.985), both ecto and endo-margins status (Pearson chi2 (98) = 109.7042 Pr = 0.197) of the initial LLETZ and repeated LLETZ margin status. The cytology results post LLETZ had 22 (37.3%) patients with persistent HGSIL, 1 (1.7%) ASCUS-H, 21 (35.6%) LGSIL, 2 (3.4%) ASCUS and 13 (22.0%) had normal cytology report. There was regression to less severe form of the lesions in 61.0% of women post second LLETZ.* ***Conclusion:*** *Patients above 35 years of age with positive margins are at high risk or persistent CIN lesions as opposed to younger patient and those with negative margins. Repeat LLETZ offers improvement in margins (endo- and ecto - cervical) status, but doesn't offer a complete cure. It reduced the positive margin status and increased negative repeat cytology findings.*

Keywords— *Cervical Dysplasia; Colposcopy; LLETZ; Repeat LLETZ*

I. INTRODUCTION

Cervical cancer is the second most common malignant neoplasm in women worldwide. [1] Cervical intraepithelial neoplasia (CIN) is a precursor lesion of cervical cancer and is classified by histology as CIN 1, CIN 2, or CIN 3. Cervical screening using cytology combined with Human Papilloma virus (HPV) testing has resulted in a considerable increase in the number of women diagnosed with CIN in recent decades. [2]

CIN2 and CIN3 are equivalent to high grade squamous intra-epithelial lesions (HGSIL) as per Bethesda Classification system (2001) used to classify the results of the Papanicolaou smear (Pap smear). The Bethesda system is used to differentiate between the high risk and low risk intra-epithelial lesions. There is significant evidence to support that CIN lesions in conjunction with persistent high-risk HPV (types 16/18/31, etc.) infection that are not treated, progress to cervical cancer. The rate of progression is almost double in immune-compromised women. [3] Therefore, treatment of these lesions is necessary in order to prevent significant morbidity and mortality.

High-grade squamous intraepithelial lesion is a common pre-neoplastic condition of the cervix that encompasses moderate (CIN 2) or severe (CIN 3) dysplasia. LLETZ biopsies were introduced in 1989 by Prendiville *et al*, to treat lesions that could be visualized by colposcopy. Type 2 and 3 transformation zone lesions need excision and LLETZ has been proven to be superior compared to cold knife conisation, in terms of post procedure complications. [4]

LLETZ has been proven to be a safe method for treating lesions that involve the endocervix and has several advantages over cold-knife conization, including shorter operating times, less blood loss, and fewer complications overall. [4] Few studies have been conducted that evaluate the rate of persistence of disease after the repeat conisation for persistent or residual high grade CIN lesion 2 and 3.

Several studies have investigated the recurrence rate following LLETZ and it was found to range from 11.3% to 54%. [1, 5-8] The factors associated with recurrence are age (independent predictor), positive margins on previous LLETZ

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specimens [5] and women with persistent high-risk human papilloma virus infection.[7] Zhu M *et al.* (2015), in their study in China, found that the rates of HGSIL persistence/recurrence in patients who had a subsequent LLETZ and hysterectomy were 31.82 % (7/22) and 20.90 % (14/67), respectively, while that in patients who were selected for close follow-up (cytology or cytology combined with colposcopy-guided biopsy) was 4.02% (6/149). The predictive factors for persistence/recurrence in a group of patients with HGSIL and HGSIL-involved margins, were the patients' age and diameter of the tumour (size). The age more than 35 years was the only independent predictive factor. [5]

A study done in Turkey found that the risk factors for residual disease post initial conisation were, multiple sweeps at the initial conisation of the lesion, as well as lesions that cover more that 50% of the cervical circumference.[9]

The purpose of this study was to determine if repeat LLETZ provides a cure for histology proven persistent HGSIL at margins. This was a retrospective study of patients who were followed up at the Charlotte Maxeke Johannesburg Academic hospital (CMJAH) Colposcopy clinic over a period of ten years (2007-2016).

II. Study Design and Methodology

The study was conducted at the CMJAH colposcopy clinic located at area 176 of the Gynaecology unit of the Department of Obstetrics and Gynaecology. Patients seen in this unit were referred by the CMJAH general Gynaecology ward, area 164, level 2 hospitals within the cluster, Community Health Centres as well as Private Gynaecology and Specialized units within the CMJAH such as Transplant (Renal and Hepatic) units and other Surgical Departments. The referral criteria are as per the South African Guidelines. Colposcopy and LLETZ were done by Oncology unit consultants and a consultant doing sessions. The clinic ran 3 days of the week. Patients' records including initial assessment, histology and follow up care, are kept within the unit and were manually retrieved and sorted. A total of 120 patients were seen at the colposcopy clinic on a monthly basis (new and follow up).

The data was collected retrospectively from patient files by the principal investigator at CMJAH Colposcopy clinic. The colposcopy clinic keeps all the patients' records/files separately from the main hospital records store. All files are accessible to healthcare workers within the unit. The files were manually selected from a total of 1500 files based on the inclusion criteria and only 71 were found to meet the criteria.

Patients selected were those who had, within the files, 2 or more histology results of the LLETZ procedure with cervical cytology done between each LLETZ and had a diagnosis of CIN 2/3. Where histology results were not found in the file or where the indication for a repeat LLETZ were not found, patients were excluded. Twelve (12) patients were excluded because of lack of follow up Pap smears (6), no available histology results (2), and no colposcopy findings noted (4). The total number of patient files included were 59.

All the data was collected as per data collection sheet and entered directly into the RedCap® tool and then migrated to the STATA Statistical Software for analysis. The results that were not included in the files were traced back to the NHLS laboratory service via TrakCare Lab Results service. Biographic data and medical conditions were collected as reflected on the initial assessment chart at the colposcopy clinic.

Quantitative techniques and descriptive analysis of the data were carried out. Categorical variables were summarized by frequency and percentage tabulation, and illustrated by means of bar charts. Continuous variables were summarized by the mean, standard deviation, median and interquartile range, and their distribution illustrated by means of histograms. Data analysis was carried out in STATA Software. The 5% significance level was used. Precision was managed by using 95% confidence interval.

The X^2 test was used to assess the relationships between treatment group and demographic and clinical characteristics. Fisher's exact test was used where the requirements for the X^2 test were not met.

Colposcopy and LLETZ Procedure

At CMJAH, the "see and treat one step approach" has been adopted and is used on patients who undergo colposcopy assessment. The most common procedure done during colposcopy examination of the cervix is the LLETZ.

Before the colposcopy procedure, all the patients were counselled on the indication and possible complications of the procedure (LLETZ) and a history of allergies ascertained. During the procedure, acetic acid was used to paint the cervix to ascertain the abnormal epithelium, which will stain white in almost all the patients. Lugol's iodine was not often used because of the unavailability of the resource most of the time. The areas on the cervix that stain white with the acetic acid were excised using LLETZ. The size of the loop was determined by the surface area that need to be removed. However, the size of the loop used was not recorded on the colposcopy notes. Bleeding areas were cauterized and a betadine-soaked tampon inserted to both stop further bleeding and prevent infection. The patients were then counselled about the findings of the procedure, advised to avoid intercourse and given prophylactic oral antibiotics for 7 days.

The specimen taken was then sent for histology and the patient advised to come back in 6 months for results. Since the results were released earlier than the return date, if results reveal any abnormality or cervical cancer, the patient was called back earlier for possible repeat LLETZ/ hysterectomy. A repeat pap smear was done in 6 months after LLETZ. A repeat colposcopy and LLETZ was done if margins were involved, at the colposcopists' discretion. If the histology showed an invasive cancer, the patient was booked for either CKC, Trachelectomy or a hysterectomy depending on the clinical stage and fertility desires. The Reid colposcopy index that considers four signs namely, lesion margin, colour/density of aceto-whitening, blood vessels, and iodine staining was used.

For the purpose of this study, a cure for HGSIL post LLETZ was defined as any regression from HGSIL (CIN2/CIN3) either to LGSIL, ASCUS or NILM (normal)

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findings on subsequent smear. The appearance of ASCUS-H was considered as persistence of the disease.

III. Results

A total number of 71 out of 1500 patients had repeat colposcopy and LLETZ for the study period at the CMJAH Colposcopy clinic. Of these, 59 patients met the inclusion criteria and 12 patients were excluded. The twelve (12) patients that were excluded had lack of follow up Pap smears (6), histology results (2), no colposcopy findings noted (4).

Patients selected, were those who had, in the files, 2 or more histology results of the LLETZ procedure with cervical cytology done between each LLETZ and had a diagnosis of CIN 2/3. Where histology results were not found or where the indication for a repeat LLETZ were not found, patients were excluded.

These patients were mostly referred from their closest facility with a high-grade intraepithelial lesion on Pap smear and were subsequently treated and followed up at the colposcopy clinic between 2007 and 2016.

A. *Repeat LLETZ and margin status*

Ecto-cervical margins were positive in (5) 8.5% of the patients who had the initial LLETZ biopsy, negative in 3 (5.1%) and unreported in 1 (1.7%). This is in comparison to positive margins in 8 (13.6%), negative margins in 15 (37.3%) and unreported in 3 (5.1%) when the second LLETZ was done.

Endo-cervical margins were positive in 17 (28.8%) of patients who had an initial LLETZ biopsy as compared to 11 (18.6%) at the second LLETZ. This showed an improvement of 35.4% from the first to the second LLETZ biopsy and it is a statistically significant change.

The histology results with both the endo-cervical and ecto-cervical margins status are as illustrated below in Fig. 1.

There was involvement of both endo-cervical and ecto-cervical margins in 33 (55.9%) at the first LLETZ as compared to 22 (37.3%) after the second LLETZ biopsy. There was an improvement of 33.3% from the first to the second LLETZ.

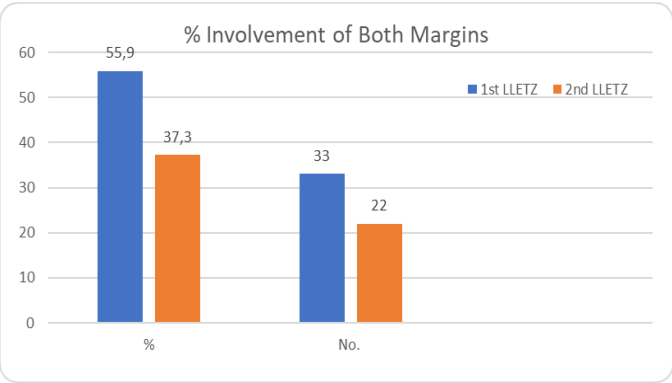

Fig. 1. The involvement of both the endo-cervical and ecto-cervical margins status.

There was no statistical association between previous ecto-margins status (Pearson Chi2 (98) = 106.7434 Pr = 0.257), previous endo-margins status (Pearson chi2 (10) = 2.8432 Pr = 0.985), both ecto and endo-margins status (Pearson chi2 (98) = 109.7042 Pr = 0.197) and repeated LLETZ margin status on second LLETZ.

B. *Demographics*

The mean age of women seen and treated for high grade intraepithelial lesions was 36.9 years (SD±6.54), the youngest being 24 years of age and the oldest patient being 58 years. The mean parity was 2(SD±1.07) with only 5% of these patients being nulliparous at first presentation. There were 54 patients (91.5%) who were of African race and the other 5 (8.47%) patients whose racial status was not recorded in their files. None of the patients were white or of mixed race.

The majority (96.6% vs 3.4%) of the patients were pre-menopausal. Fig. 2 below illustrates the menopausal status. At least half (50.9%) of the patients were not using any form of contraception and information on contraceptive use was not available in 7 (11%) patients. The most commonly used contraceptive method was barrier (condoms) (45.6%). There were 6 (27.3%) who were on injectable contraceptives and 27.3% who were on oral contraceptive pills (the type of oral contraception was not specified in the colposcopy clinic clerking sheet).

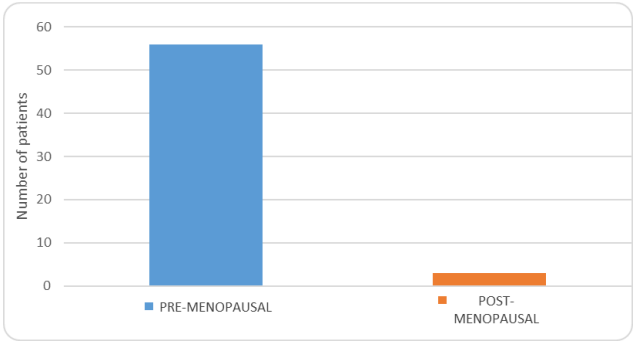

Fig. 2. The distribution of patients according to reproductive age.

C. *Risk Factors*

Smoking history was not recorded on the notes. The HIV status was not known in 5.08% of the patients. There were 44(74.58%) patients who were HIV positive and 12(20.34%) who were HIV negative. Of the patients who were HIV positive, their mean CD4 count was 365 copies/ml (SD±210.38) and 29 (64.4%) were on antiretroviral treatment. The mean duration of months on treatment was 4.7 months for all those on treatment.

D. *Referral Criteria*

Most of the patients were referred from the local clinics and Community Health Centers (CHCs) (78%) and 7 (11.9%) were referred from the private general practitioners. The majority of the patients (98.3%) were referred with a high-grade intraepithelial lesion (HSIL) on Pap smear and only 1 (1.7%) was referred for atypical squamous cells of unknown significance but HSIL could not be excluded (ASCUS-H).

E. *LLETZ Procedure*

The majority of the patients (94.9%) had their first

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colposcopy done by a consultant and acetic acid was used to mark the abnormal areas in 88.1% of the patients. There was an abnormal acetic acid stain in 43 (72.9%) patients and the lesion was resected with a LLETZ.

At the first colposcopy, Lugols' iodine was used for only 1 patient (1.7%) and the reason this was done was because there was no aceto-whitening achieved. There was no iodine used in 52 patients (88.1%), and in 10.2% of the patients, there was no information given on the use of either Lugols' iodine or Acetic acid. This compared to the second colposcopy where Lugols' iodine was only used in 1 patient and none was used in 40 (69.5%) and it was unknown in 18 (30.5%) patients.

Blue light was not used to assess vessels structure in 49 (83.05%) and it was unknown if this was used on the rest of the patients (10). Most of the patients were not assessed using the Reids' Colposcopy index scoring system. They were noted as having aceto-white abnormal changes at colposcopy (71.2%) or not. At least 3 (5.1%) were assessed as having severe dysplasia using the Reids' Colposcopy index score, 3.4% had inflammatory changes and 8.5% with moderate dysplasia. The rest of the patients where not classified as to the type of dysplasia that was found. In 6 (10.17 %) of the patients, the colposcopy findings were not noted and there was no mention of the size of the loop in any of the LLETZ procedure notes. The mean number of specimens collected at Colposcopy and LLETZ was 1.5, which the smallest amount being 1 specimen and the most being 4 pieces.

Only in 1% of the procedures there was a comment on the file regarding the difficulty of achieving haemostasis during the procedure.

The histology results from the first colposcopy and LLETZ procedure were reported in different nomenclature, as CIN 3 in 33 (55.9%), HGSIL in 16 (27.1%) and CIN 2 in 10 (17.0%) patients. All these lesions according to the Bethesda Classification system are considered high grade intraepithelial lesions (HGSIL) and precursors for cervical cancer if not treated. Most of the patients had lesions incompletely excised at first colposcopy and LLETZ evidenced by margins involvement.

The majority of patients, 50 (84.8%), had the lesion involving the endo-cervical margins only and 38 (64.4%) had only the ecto-cervical margins involved. In 55.9% of patients, there was both ecto-cervical and endo-cervical margin involvement post the initial LLETZ as compared to 37.3% post repeat/second LLETZ. This was an improvement of about 18.6% post repeat LLETZ. The second colposcopy and LLETZ were done at 12 months or more from the first procedure in patients who had persistent high-grade lesion diagnosed on a repeat Pap smear results (done 6-months after LLETZ).

The second colposcopy and LLETZ was done by a consultant in 56 (94.9%) of the patients and the other 3 (5.1%) were done by a registrar. The majority of the colposcopic diagnosis and LLETZ procedures were done using acetic acid (69.5%) staining and there were no records of type of staining liquid used on the rest. Most of the patients, 35 (59.3%), had an aceto-whitening abnormality noted at colposcopy with only 2 (3.4%) noted to have severe dysplasia, 2 (3.4%) with inflammatory changes and 3 (5.1%) noted to have mild dysplasia and a normal cervix. The rest did not have comments on dysplasia at colposcopy. Comments about the haemostasis were only made in 4 (6.8%) patients post the second LLETZ.

The mean number of specimens taken at the second LLETZ was 1.5 with the greatest number of specimens being 4. The histology post second LLETZ found that HGSIL lesions (CIN2, 3 HGSIL) were found in 74.6% at the second or repeat LLETZ and 22.1% were LGSIL (CIN1, LGSIL) lesions. HGSIL were reported as CIN 2 in 17%, CIN 3 in 30.5% and HGSIL in 27.1%. LGSIL lesions were reported as LGSIL dysplasia in 11.9%, CIN 1 in 6 (10.2%). It is noted that there is still a different reporting method by different pathologists where an older system is still used and others conforming to the newer reporting system.

F. HPV Status

Only 19 (32.2%) of the histology results had reports that included HPV changes and 40 (67.8%) were not reported. In those who were reported to have HPV changes at the first LLETZ biopsy, there was persistent HPV infection changes at the repeat LLETZ.

G. Papanicolaou Smear Post Second LLETZ

The post second/repeat LLETZ Pap smear was done after 24 weeks (6 months) in 27 (45.8%) patients and in 11 (18.6%) it was done after 28 weeks. Only 8 (13.6%) had a post LLETZ Pap smear within 20 weeks of the procedure. The mean number of weeks post LLETZ was 27.3(SD±). The Pap smear results post LLETZ reported 22 (37.3%) patients with persistent high grade squamous intra-epithelial lesions, 1 (1.7%) with ASCUS-H, 21 (35.6%) had LGSIL, 2(3.4%) had ASCUS and 13 (22.0%) had NILM. There was regression of the lesions in 61.0% of women post second LLETZ.

H. HIV Status Vs Pap Smear After Repeat LLETZ

Fig. 3. below shows a comparison between HIV positive and HIV negative patients regarding persistence of high-grade dysplasia and regression to lower grades or normal on patients who had a second LLETZ for persistent disease.

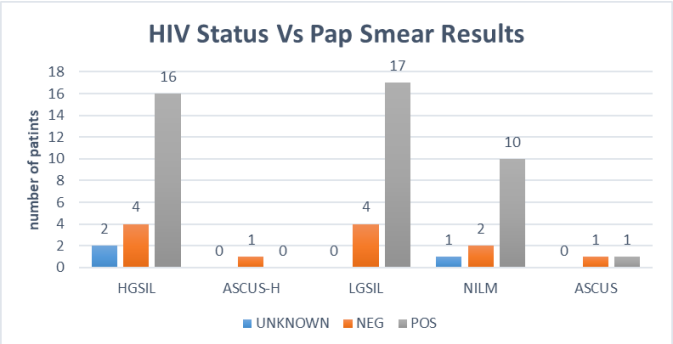

Fig. 3. Comparison between HIV positive and HIV negative patients' cytology results post the repeat LLETZ.

The majority of patients showed regression after second LLETZ amid their HIV positive status.

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The majority of patients (74.6%) who were HIV positive also had a higher incidence of positive endo- cervical margins (25.6%), ecto-cervical margins (7.0%), and both margins (62.8%) reported on first LLETZ with regression to 13.9%, a worsening to 11.6% and regression to 39.5% respectively, after the second LLETZ. However, there was no statistically significant association found (p =0.66).

There was no statistically significant association between the Pap smear results, histology result and the use of contraception (p value=0.8 and 0.4). There was no statistically significant association found between the colposcopist rank and the involvement by HGSIL at the margins (p = 0.3).

IV. Discussion

Our patients' mean age was 36 years with only 2 postmenopausal patients. We presume that this is due to the fact that most of our post-menopausal patients who presented with persistent HGSIL opted for hysterectomy and were excluded in the study. An international study showed that age >35 years alone was independent risk factor for persistent CIN disease, [5] which is in keeping with our study results.

Our study showed that there was regression of disease post the second LLETZ from HGSIL in 61% of patients, to LGSIL, ASCUS, and NILM on cytology. Thirty-nine percent (39%) had persistent HGSIL after the 2nd LLETZ, and some opted for another LLETZ because of desire for future fertility. There were others who were booked or referred for hysterectomy. A study by Zhu, et al, also found that the persistence rate of HGSIL was 31.82% following the subsequent LLETZ.12 The recurrence rate ranged from 11.3% to 54% in several studies. [1, 5-8]

In patients who had both ecto- and endo-cervical margins involved at the first LLETZ histology results, there was a 33.3% reduction after the subsequent LLETZ. Repeat LLETZ was associated with more than 50% reduction in positive margins and minimal change to negative margin status. Therefore, the repeat LLETZ for persistent high-grade cervical lesion proved to be of utmost benefit in our study in terms of margin status, and the subsequent Pap smear results did show a 61% regression to lesser dysplastic state of disease when a repeat LLETZ was done for positive margins. This is in agreement with a study done in Turkey that showed that the risk factors for persistent disease post second conisation include positive margins, which could be seen as inadequate treatment, as well as multiple sweeps of the LLETZ biopsy, especially in lesion that involve more than 50% of the cervix.[9]

Other institutions in South Africa observe patients who are under 35 years, with persistent high-grade lesions (CIN2 and 3) post LLETZ by doing 6 monthly cytology testing for 3 years. If the CIN lesion persists then an intervention is done. At Chris Hani Baragwanath Academic Hospital, a patient who present with persistent HSIL on cytology post LLETZ, gets a repeat LLETZ as long as the cervix still has length (can be done 2-3 times), otherwise a hysterectomy is offered. Therefore, there is no consensus in terms of the treatment of persistent CIN lesion post LLETZ worldwide. Treatment and intervention are institutionalised and individualised according to the patient status and intentions and fertility desires of the patient.

The presence of HGSIL disease on all HPV reported specimens supports the pathogenesis of the majority of cervical dysplasia and these findings were expected. Jian Yan Ming et al, and Thompson V et al, reported that patients with cervical dysplasia and proven HPV positivity, were likely to persist after destructive procedures such as LLETZ, Laser and Cryotherapy. The sensitivity of persistent HPV positive testing was up to 100% in a systematic analysis done by Paraskevaidis E, et al. [2; 7]

Most of our patients (74.6%) were HIV positive and there was poor documentation of their CD4 counts as well as viral loads. The majority of patients (64.4%) were on antiretroviral treatment but others were not despite CD4 counts of less than 350 copies/ml. Perhaps this is because the South African HIV Guidelines regarding initiation of HAART have changed at least 3 times in a space of 10 years regarding when to start patients on anti-retroviral therapy based on their CD4 counts. The current guidelines from 2015 state that every HIV positive patient should be started on antiretroviral therapy regardless of CD4 count. [10]

There was regression of HGSIL lesions after repeat LLETZ in 47.5% of patients who were HIV positive but the results were not significant. It is not known whether this is related to the use and duration of HAART and regaining immunity or just an incidental finding. There are no international studies that have investigated the persistence of HGSIL after LLETZ in patients who are on HAART compared to those who are not. A study done in Soweto, South Africa, showed that there was a higher risk of cytological abnormalities at follow up in patients who were immune-compromised and in those with incomplete excision during treatment. However, the HIV status of the patients was subjective, which could have caused biases. They also emphasised that patients who were negative according to their knowledge could also be in the window period or seroconvert later in the study.[11]

In those patients who were HIV positive and had both endo- and ecto-cervical margin involvement (62.8%), 55.6% of them show persistence of the CIN lesion at both margins post the second LLETZ. Only 14.8% of them had free margins at the subsequent LLETZ biopsy. Most international studies did not include HIV status as one of the measured factors or variables to be observed in patients with persistent disease or recurrent disease.

There is currently no HPV testing done in South African public hospitals, at the time of this research, but we noted that some of the histology results reported the presence of HPV changes which is an important indicator of persistent disease especially in patients where HPV is persistent at histology. In our study, those who were reported to have HPV at the first LLETZ biopsy had persistent HPV infection even at the repeat LLETZ. The inclusion of HPV or HPV changes is currently not a standardised protocol and hence few had such reported. We expected the HPV positivity to be higher that what was found if the testing was standard due to prevalence of HIV in our population.

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A well-functioning Colposcopy clinic is expected to have a checklist, adopt a diagnostic method (Reid's or Swede), and use both Acetic acid and Lugols' iodine to identify dysplastic tissues and to accurately identify areas requiring resection. In our study, the colposcopy clinic had poor recording, no standard protocols were followed towards formulation of a colposcopy diagnosis and there was almost no use of Lugols' iodine.

Colposcopy findings were not recorded using the Reid's Colposcopy Index score in more than half of the patients. Therefore, it was difficult to correlate the clinical findings with the histology results. The histology results mostly reported the presence of a high- grade or low- grade intraepithelial lesion or squamous cell carcinoma and some of the colposcopy findings ranged from moderate to severe dysplasia and others inflammatory changed were noted.

V. Conclusion

Our study showed that patients who are above 35 years of age, and have positive margins on histology of the first LLETZ specimen were at higher risk of persistent CIN lesions as opposed to younger patient and those with negative margin involvement which was in keeping with previous studies.

Repeat LLETZ offers improvement in margins (endo- and ecto - cervical) status, even though it doesn't offer a complete cure. It has reduced the positive margin status and increased the rate of negative repeat Pap smear findings.

In HIV positive patients, there is higher persistence of disease post the initial LLETZ but more studies need to be conducted to ascertain whether persistence of the disease in these patients is due to poor immunity as well as investigate if their chances or persistence are less with improving immunity due to antiretroviral treatment.

The practice of repeat LLETZ however, on these patients with persistent HSIL lesions should be balanced against obstetric risks such as cervical incompetence, stenosis and preterm labour. Although this was not demonstrated in our study, it should be noted that a repeat LLETZ increases risk of injury to the bladder, rectum and vaginal mucosa.

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