ABSTRACT

Objective: To evaluate the follow-up smear of incompletely excised high grade cervical intraepithelial neoplasia (CIN) at large loop excision of transformation zone. Material and Methods: The data collection was from the computer database maintained at the colposcopy clinic, the patient pathway manager and the result server in the hospital. Data was collected for all women who underwent loop excision for CIN 2 or CIN 3 between January 2009 to December 2009 and the histology was reported with positive excisional margins. All women had at least one follow-up smear after the treatment. Results: 249 women had incomplete excision of high grade CIN. 53/249 did not have a follow-up smear, hence excluded from analysis. Ectocervical margin was involved in 91(44%) women of whom 95% had negative smear and 5% had positive smear at follow-up. Endocervical margin was involved in 25 (14%) of whom 88% had negative smear and 12% had positive smear at follow-up . Lateral margin was involved in 27 (12%) of whom 96% and 4% had negative and positive smear respectively . 46 (26%) women had more than one margin involved, 94% had negative and 6% had positive smear at follow-up . In 7 (4%) women the margin was unspecified, 5/7 (72%) had negative smear and 2/7 (14%) had positive smear. Overall 182/196 (90.8%) had negative smear at follow-up following incomplete excision of CIN at various margins and 14/196 (9.2%) women had positive smear. Conclusion: Women with incomplete excision of high grade CIN at LLETZ can be followed up by smear only at first visit and need not require colposcopy at their first follow-up.

KEYWORDS: Pap smear, colposcopy, follow-up, incomplete excision.
INTRODUCTION
Cervical intraepithelial neoplasia (CIN) is a cytologic and histologic classification of preinvasive cervical neoplastic changes. Treatment of high grade CIN which includes CIN 2 and CIN 3 is usually recommended using either ablative or excisional technique because they have a significant chance of progression to carcinoma if left untreated. Progression to invasive cancer occurs in approximately 5% in CIN 2 and 12% in CIN 3 (Bradshaw et al). Large Loop Excision of Transformation Zone (LLETZ) or Loop Electrical Excision procedure (LEEP) is one of the common method of treatment for CIN. The procedure is usually performed at the colposcopy clinic on out patient basis.

Follow-up of women treated for CIN at six month interval following treatment is an essential part of the management. The need of follow-up at six month is emphasised when the excision is incomplete and the excisional margins are positive. Residual high grade CIN is an independent risk factor for cervical cancer and hence requires prompt regular follow-up.

The present study was a retrospective study to find out the follow-up smear outcome of incomplete excision of high grade CIN following LLETZ procedure at the colposcopy clinic. The study was also aimed to find out the necessity of follow-up at the colposcopy clinic.

MATERIALS AND METHODS
The data collection was from the computer database at the colposcopy clinic, the patient pathway manager and the result server maintained by the Gynaecology oncology unit at St James University Hospital. Data was collected for all women who underwent LLETZ for CIN 2 or CIN 3 (CIN confirmed by histology) between January 2009 to December 2009 and in whom the histology was reported with positive excisional margins.

Data was collected from database for all 797 women who underwent LLETZ between Jan 2009 to Dec 2009.

Inclusion criteria
- women undergoing LLETZ for the first time
- have HGCIN (CIN2/3)
- histology reported as incomplete excision of CIN at various margins/borders
- have had at least one follow-up Pap smear after treatment

Exclusion criteria:
women with CIN1
Cervical glandular intraepithelial neoplasia (CGIN)
Stromal invasion

In the year 2009, total 797 women underwent LLETZ at the colposcopy clinic in St James University Hospital, UK. Out of 797 women 534 had high grade CIN. 285/534 had complete excision and 249 with CIN2/CIN3 were reported to have incomplete excision of CIN at different margins. Fifty three women had no follow-up Pap smear, hence were excluded from the study. Total of 196 women who satisfied the inclusion criteria were considered for the study.

Collected data included the age, complete histology report stating margin positivity ( various margins included were ectocervical, endocervical and lateral margin ), follow-up Pap smear report, time interval from the treatment to first follow-up smear, any further management done for women in whom the follow-up showed abnormal smear.

**RESULTS**

Total 196 women who had incomplete excision of high grade CIN were considered for the study. Mean age was 41 yrs(21 – 61). Four women were aged above 50 yrs.

Table 1. shows the incomplete excision at different margins. Ectocervical margin involvement was seen in majority of the women 91 (44%). In 4% of them, the involvement of margin was uncertain.

**Table 1: Incomplete excision at various margin**

<table>
<thead>
<tr>
<th>Excision margin</th>
<th>No. of patient (n)</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ectocervix</td>
<td>91</td>
<td>44</td>
</tr>
<tr>
<td>Endocervix</td>
<td>25</td>
<td>14</td>
</tr>
<tr>
<td>Lateral</td>
<td>27</td>
<td>12</td>
</tr>
<tr>
<td>&gt;1 margin</td>
<td>46</td>
<td>26</td>
</tr>
<tr>
<td>Unspecified</td>
<td>07</td>
<td>04</td>
</tr>
</tbody>
</table>

Table 2 shows the follow-up smear report for all incompletely excised high grade CIN at LLETZ. Positive ectocervical margin was observed in 91 women. 95% of them had a normal smear at their follow-up at six month interval. Abnormal smear was observed in only 5% of the cases. Women showing borderline nuclear changes had cervical biopsy later which was normal. Women with severe dysksryosis had repeat LLETZ. Twenty five women had positive
endocervical margin following LLETZ. Among them 88% had a normal smear at their follow-up. Though 12% had an abnormal smear at follow-up, women with smear showing borderline nuclear changes had normal histology at cervical biopsy. One women with severe dyskaryosis underwent repeat LLETZ. Out of 27 women who had incomplete excision of lateral margin CIN, 96% showed normal smear at their follow-up. Only 2/27 had abnormal follow-up smear. Both had smear showing borderline nuclear changes and their subsequent cervical biopsy was normal. The follow-up smear report of 46 women in whom the excision of CIN was incomplete at two or more margins, 94% of them had a normal follow-up smear. Women with severe dyskaryosis and moderate dyskaryosis underwent repeat excision which showed residual CIN3.

**Table 2: Follow-up smear after incomplete excision of high grade CIN**

<table>
<thead>
<tr>
<th>Margin</th>
<th>No. of Patient (n)</th>
<th>Smear report (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Normal</td>
</tr>
<tr>
<td>Ectocervix</td>
<td>91</td>
<td>95</td>
</tr>
<tr>
<td>Endocervix</td>
<td>25</td>
<td>88</td>
</tr>
<tr>
<td>Lateral</td>
<td>27</td>
<td>96</td>
</tr>
<tr>
<td>&gt;1 margin</td>
<td>46</td>
<td>94</td>
</tr>
<tr>
<td>Unspecified</td>
<td>07</td>
<td>72</td>
</tr>
</tbody>
</table>

*BORDERLINE NUCLEAR CHANGES

Fig 1: summarises the follow-up smear results of incompletely excised high grade CIN at different margins.

Overall 90.8% had a normal smear at their first follow-up following LLETZ for high grade CIN irrespective of the type of margin being involved and 9.2% had abnormal smear. 65% of women had their first follow-up smear at six month interval and 75% at eight month interval.
DISCUSSION
A balance needs to be maintained while performing LLETZ between sparing healthy cervix and excising the diseased tissue completely. Incomplete excision is significantly more common in high grade CIN.[2] This is probably because high grade CIN tends to be more extensive than low grade CIN and excision at the craters is difficult.

Of the women with incomplete excision, 14% had positive endocervical margin and 44% were positive for ectocervical margin. In this study endocervical margin positivity was less compared to other study with 49% positive margin. They found that women in this group were at high risk for recurrent disease.[3,4] In our study among those 14% with positive endocervical margin though 12% had abnormal smear only one women had severe dyskaryosis. A repeat LLETZ was performed and histology confirmed CIN 3. One meta analysis revealed 18% high grade post-treatment disease in group who had incomplete excision.[4] Many studies emphasise on colposcopic follow-up when excision is incomplete at endocervical margin. In one study 1000 women were followed up after laser ablation for CIN and concluded that routine colposcopic assessment is not required but they can be followed up by cytology only. When ablative procedure is performed, margin status cannot be assessed precisely. Long term follow up is required to compare outcome of CIN treated by ablative and excisional technique.[5]

The standard practice at the institute where the present study was undertaken is that women with incomplete excision to be followed up at the colposcopy clinic irrespective of type of margin involved. The study result show that more than 90% women with incomplete excision have normal smear following LLETZ for high grade CIN and hence can be followed up by smear only.[6]

In our study 65% had their first follow-up smear at six months following LLETZ. National Health Service Cervical Cancer Screening Programme (NHSCSP) guidelines state that women following LLETZ should have their follow-up at six months. Atleast 90% should have their smear done no later than eight months. The need of follow-up has to be emphasised and steps need to be taken to follow the guidelines.

CONCLUSION
More than 90% of all LLETZ with incomplete excision at various margins have negative smear at follow-up hence incompletely excised high grade CIN may be followed up by smear
only and do not essentially require colposcopy at first follow-up. This will also reduce the overload of patients at the colposcopy clinic as follow-up smear can be performed by general practitioners. Factors like age, parity, menopausal state need to be considered in women who have incomplete CIN excision. There is need to ensure that the first follow-up smear is done at six month interval following LLETZ.

Acknowledgements: sincere thanks to Mr Richard Hudson, consultant, Gynecology oncology department for permitting and guiding to do the present study at the institute.

REFERENCES