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RESEARCH ARTICLE

EFFICACY OF SEE AND TREAT IN A CERVICAL SCREENING PROGRAM WITH VISUAL INSPECTION WITH ACETIC ACID (VIA)

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Abstract

SEE and TREAT at Colposcopy has been described in cytology based screening when a high-grade lesion in association with a high grade abnormality in the Pap smear is treated by Large Loop Excision of the Transformation Zone (LLETZ) to minimize loss to follow-up in the multiple step management protocol for CIN. With a vast burden of cervical cancerin developing countries, our aim was to study the efficacy of this approach in patients coming to colposcopy clinic after a positive VIA test. Women in the age group of 25-50years and coming to the general gynecology clinichad opportunistic screening with VIA; those who were found VIA+ underwent Colposcopy. Ifcolposcopy suggested a high-grade lesion, SEE and TREAT using LLETZ was performed.Colposcopy was carried out for 688VIA positive women;of whom 101 had a high-grade lesion and underwent LLETZ. All of them had CIN on histopathology. Thirty-five (34.6%) had CIN 1, 55 (54.5%) had CIN 2 and 11 (10.9%) has CIN 3. Treatment was described as effective if there was CIN of any grade in the LLETZ specimen; overtreatment if there was no CIN. The SEE and TREAT approach was effective in all with no overtreatment. Complete excision was achieved in 96.04%women, 3.96% had positive resection margin.There were no major complications. Thus we conclude that a SEE AND TREAT approach in a low-resource setting with VIA followed by Colposcopy and treatment can help in reducing the number of visits and loss to follow-up.

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Introduction:-

Cervical cancer is the fourth most frequently diagnosed cancer and the fourth leading cause of cancer death in women, with an estimated 604,000 new cases and 342,000 deaths worldwide as per GLOBOCON 2020.[1] It is also the leading cause of cancer death in 36 countries, with the vast majority of these countries found in sub-Saharan Africa, Melanesia, South America, and South-Eastern Asia.[2] Though cervical cancer is a preventable disease, it continues to be the leading cause of mortality among women in South East Asia region. About 3,39,789 new cases and 1,93,395 deaths occurred in South East and South Eastern Asia region as per GLOBOCON 2020.[1] Out of which 1,23,907 new cases and 77,348 deaths occurred in the Indian subcontinent alone.[1]

Multiple visits involving screening and treatment are required which may result in loss to follow up of these women and untreated CIN which may progress. The WHO recommends VIA as a screening test till a low cost HPV test

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becomes available in low income countries as the results are immediate and decision for treatment can be made instantly.[3] If a VIA test is positive, WHO recommends direct treatment with ablation or referral for LLETZ. LLETZ needs to be performed after visualizing the lesion at colposcopy, which may be biopsied or treated right away.

A SEE AND TREAT approachby LLETZ has been described in women screened by cytology, with high grade abnormalities on the Pap smear.[4,5,6] There is a paucity of literature of applying SEE AND TREAT approach in VIA based screening. Our study was aimed to assess the efficacy and overtreatment rate of this approach at Colposcopy in women screened by a VIA test.

Material and Methods:-

Study design:

The present study was a Prospective Interventional study carried out after Ethics Committee approval. All women attending the Gynecology OPD and in the reproductive age group (25-50years) had a detailed medical and gynecological history and examination and opportunistic VIA screening after informed consent following the standard procedure of VIA as described in the VIA reference manual on IARC website.[7]Women who were pregnant, had active vaginitis or cervicitis, were post-hysterectomy, or with frank cancer were excluded. VIA positivity was defined as the appearance of acetowhite areas in the transformation zone close to squamocolumnar junction one minute after application of 5% acetic acid.

All VIA positive women underwent Colposcopy with a digital video Colposcope in our Colposcopy clinic situated in the outpatient department by designated OBGYN trainees supervised by experienced Colposcopists. Any acetowhite area on ectocervix was visualised and further details regarding degree of acetowhiteness, margins and size of lesion were noted. Lugol's Iodine was then applied and a corresponding Iodine negative area was visualised and graded accordingly. Colposcopic findings were documented as per IFCPC 2011 nomenclature and if any abnormal lesion was noted they were scored by Swede score on Colposcopy.[8,9]

If the Colpsocopic Swede score was <5, biopsy was taken and further management was planned based on HPE report. If the Colposcopic Swede score was ≥5, the woman was given an option for either a biopsy followed by treatment based on the HPE report or immediate treatment with LLETZ as per 'See And Treat' approach and the LLETZ specimen was sent for HPE. Those who consented for the latter were included in the study after informed consent.Two of the women had TZ type 3 and underwent cold knife conization. They required more visits and need for the procedure to be done in an OT setting and so were excluded from the analysis. LLETZ was carried out as a day-care procedure after ruling out high risk factors.

The outcome measures of our present study were to see the efficacy of SEE and TREAT approach, evaluate the number of HPE reports with CIN and the complications observed. The woman was explained the procedure, made to lie in a lithotomy position and given intravenous sedation to allay her anxiety. Vulva and vagina were cleaned and draped. An insulated Graves speculum with an outlet for smoke, with a sterile glove finger sleeve to retract the vaginal wallsif lax was inserted; the largest tolerable speculum was used for maximum exposure. A prefilled vial containing a combination of lignocaine 1% and adrenaline 1:80,000 was injected intracervically using a dental syringe for analgesia and to decrease the blood loss. We then applied 5% acetic acid and Lugol's iodine sequentially to visualize the lesion with a good light and then chose the size of the loop according to the size of the lesion. Tungsten loops made of 0.2mm tungsten wire were used. A QL/LEEP II High Frequency Gynecologic Therapy Equipment – LEEP KNIFE was used. A power setting between 20-30 watts of Blend Cut II(combination of cutting and coagulation) current was used for excision. The loop was activated before it came in contact with the cervix. A left to right or right to left pass was made encompassing the os. If the lesion size was bigger, then 2-3 passes were taken but the first pass always included the cervical os. Haemostasis was achieved with ball cautery or chemical cautery using Monsel's paste. If needed, Vicryl 1-0 sutures or vaginal packing was done. Bleeding was assessed on the basis of amount of blood in suction bottle and number of swabs soaked.

Post LLETZ, all women were explained about the precautions to be taken, symptoms needing hospital visit and were sent home after 1-2 hours of observation. They were asked to visit after two weeks or earlier if they had any problem. Histopathological examination of biopsies was performed in our pathology lab by trained pathologists. At the follow-up visit, they were asked about any complaints post procedure; the histopathology report and the resection margin on HPE were noted.

Statistical Analysis:
The data was entered in MS EXCEL spreadsheet and analysis was done using Statistical Package for Social Sciences (SPSS) version 21.0.

Using the European Quality Standards for the Treatment of Cervical Intraepithelial Neoplasia (CIN), we defined the treatment as effective if there was CIN in the excised specimen; and overtreatment if there was no CIN.

Categorical variables were presented in number and percentage (%) and continuous variables were presented as mean ± SD and median. Normality of data was tested by Kolmogorov-Smirnov test. If the normality was rejected then non parametric test was used. A p value of <0.05 was considered statistically significant.

Results:-

There were 688 women who were VIA positive in that period and had Colposcopy . Of them 101 had adequate Colposcopy and significant acetowhite lesions with a score of ≥5. A total of 101 women had LLETZ under SEE AND TREAT approach. The mean age(years) of these women was 38.12 (SD 6.51) with median(IQR) of 37 (32-42). The mean age at marriage was 19.08 (SD 1.99) with median(IQR) of 18(18-19). All of them were non-smokers. The mean parity observed was 2.58 (SD 1.03). There were 2 out of 101 women who were nulliparous (1.98%) and 7.92% had a single child; however accepted the treatment after counselling.

The most common presenting complaint was pain in lower abdomen observed by 43.56% of women. Other complaints included persistent discharge per vaginum (30.69%), heavy menstrual bleeding (6.93%), postcoital bleeding (3.96%) and intermenstrual bleeding (3.96%). Even in women with CIN 2/3, the most common symptom was pain in lower abdomen(27.72%) followed by persistent discharge per vaginum(22.77%).

Colposcopy and Swede Score: The mean score in this group was 6.07 (SD 1.09) and the median was 6(5-7).Transformation Zone(TZ) type 1 was seen in 34.44% of women with CIN 1, 54.44% of women with CIN2 and 11.11% of women with CIN 3 while TZ type 2 was seen in 36.36% of women with CIN 1, 54.55% of women with CIN2 and 9.09% of women with CIN 3. During LLETZ, a single pass was taken in 80.20% (81 out of 101) of the women;11.88% (12 out of 101) of the women had two passes taken and 7.92% (8 out of 101) women required three passes due to a large lesion size. Blood loss observed ranged from minimum 10 ml to a maximum of 80 ml. The mean blood loss was 36.58 (SD 12.82). After excising the LLETZ specimen, monsel's paste was applied and ball cautery was used which was sufficient for haemostasis in all but one case where sutures were taken. No vaginal packing or additional anaesthesia or analgesia was required in any case. Also none of them had secondary hemorrhage or required admission post procedure. Post LLETZ 3.96% of the women had discharge per vaginum. There were no major complications observed during the procedure or within 2 weeks of follow up.

The LLETZ specimen was sent for HPE; histopathology showed CIN 1 in 35 of 101 women (34.6%), 55 (54.5%) had CIN 2 and 11 (10.9%) has CIN 3 (Figure No. 1).The resection margin status was positive in 3.96%(4 out of 101 women). Thus, complete excision was achieved in 96.04% of these women.

Discussion:-

Owing to the vast population and limited resources in low and middle-income countries, modalities like "Screen and Treat" following a VIA positive test and "See and Treat" following colposcopy have been devised. See and Treat approach after colposcopy in VIA positive womenreduces the overtreatment of Screen & Treat as benign lesions like ectropion and squamous metaplasia can be detected.

The commonest presenting complaint noted in our women was pain in lower abdomen. The low rate of post-LLETZ complications may be due to prophylactic prescription of oral antibiotics to all women in the present study(as per IARC guidelines) and adherence of the treated women to the advice given post LLETZ.No obvious lesions on Colposcopy were present post LLETZ but on microscopic (histopathological) examination, resection margin was positive in 4 of these women.

Overtreatment was defined if there was no CIN or low grade CIN (CIN 1) found during histopathology analysis in the LLETZ specimen.[10,11] An acceptable treatment was defined as the HPE report of CIN2+ in the excisedspecimen.As per the guideline of the European Federation for Colposcopy and Pathology of the Lower

Genital Tract (EFC), the standard for women who underwent treatment under SEE and TREAT approach was taken as proven Cervical Intraepithelial Neoplasia (CIN) on histology for ≥90% of them.[12] The PPV of Colposcopy as defined by NHS Cervical Screening Programme is 65% for high grade leisons with an adequate colposcopic examination and complete visualization of the upper extent of the lesion and squamocolumnar junction.[13]Although for quality control, See-and-Treat management should be used for CIN2/3 or high-grade cervical glandular intraepithelial neoplasia present in ≥90% of the excised specimens as specified by the NHSCSP.[14]

As per NHSCSP guidelines, overtreatment was found to be 34.65%. However, none of the women had normal histology, indicating that treatment was needed albeit later. Also as per EFC there was no overtreatment and a 100% acceptable treatment rate. In a low resource setting and in the absence of a follow up system, this could be considered as acceptable treatment.The overtreatment rate in our study was found to be higher compared to other studies.[10,11,12]Singla et al conducted one study where they screened with VIA/VILI and Pap smear followed by Reid Colposcopic index evaluation on Colposcopy and SVA(Single Visit Approach). 16 women underwent SVA in their study and they observed an overtreatment rate of 12.5%. Remko et al conducted a similar study with cytology as screening modality and observed an overtreatment rate of 18.1%. Nessa et al in their study observed an overtreatment rate of 51.1%. This could be due to the differences in the study population and screening methods.

In a limited resource setting, See and Treat approach is very useful. The entire process of screening, colposcopy and treatment can be completed in one or two visits to minimize loss to follow up and delayed treatment. It also decreases the anxiety of a screen positive women and provides psychological benefits and is thus acceptable by the patient. As centers for Colposcopy and treatment are limited in lower income countries, this approach helps reduce the costs on an already overburdened healthcare system.

The present study being a single-center, prospective interventional study has its limitaions. Though the study population was similar to the local population but the findings cannot be extrapolated for the generalized population. Only patients coming to the OPD were included in the study instead of general population. A larger multicentric study would help in setting the cut-off. Also the sample size was small and not a true representative of our country's total population. The period of follow up was only 2 weeks due to limited tenure, so any information regarding late complications like cervical stenosis, preterm labor or recurrence is not available.

In see and treat approach, treatment in dependent on colposcopy examination which may have variation of interpersonal skills. Extensive training in colposcopy can help decrease this limitation. In future, artificial intelligence (AI) could help in making a decision. The main disadvantage of this approach is the risk of overtreatment, however this could be reduced with greater experience in colposcopy and incorporation of AI.

See and Treat approach includes both ablation and excision based on the Colposcopic score. Ablative method like cryotherapy is simple, safe and easy to perform procedure but there are obstacles like gas unavailability and leakage. Also thermocoagulation is not widely available. While the electrosurgical equipment are widely available and LLETZ is an easy to learn and safe to perform procedure. It can be done as a day-care procedure under local anesthesia thus excision procedures can be performed with wider application. However the drawback remains of overtreatment. Studies pertaining to colposcopy directed LLETZ and long term sequalae can help us derive further conclusions.

In the present study, the advantages outweigh the disadvantages as the approach was efficacious with 96.04% women having complete excision and minimal short term complications. We find it acceptable pertaining to the advantages provided by the see and treat approach and the acceptability by these women to the provided treatment.

To conclude, SEE AND TREAT approach when based on an appropriate criteria proves to be of great value in the management of preinvasive lesions of cervical cancer and has an acceptable efficacy. It saves time and financial resources of both health care providers and of the women who undergo treatment as per this approach.

Thus we recommend a SEE AND TREAT approach based on Colposcopic Swede score with a cut-off of 5 for excisional treatment. The use Colposcopic Swede score and both LLETZ and Cryotherapy as treatment modalities can work hand in hand and help us achieve our goal to reduce the burden of cervical cancer in our country.

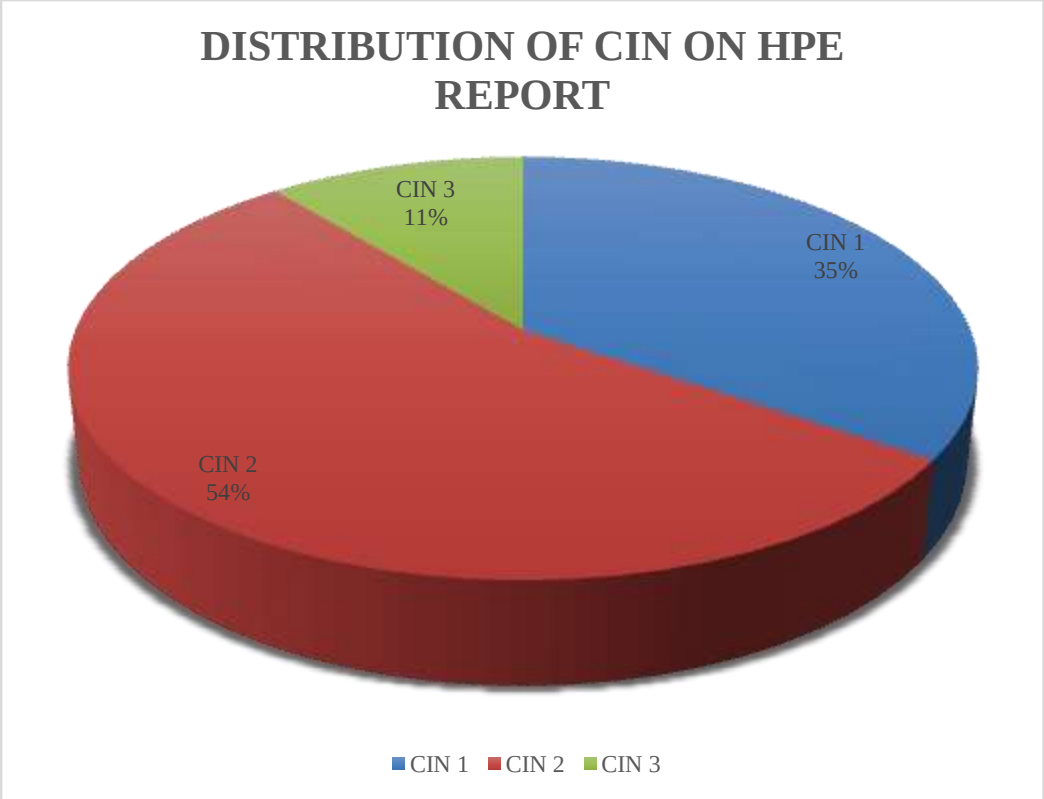

Figure No. 1:- Distribution of CIN on HPE report.

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