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RESEARCH ARTICLE

AN ANALYSIS OF PAP AND PAP - HPV TESTING FOR CERVICAL CANCER SCREENING IN TERTIARY CARE CENTER A RETROSPECTIVE STUDY IN A TEACHING INSTITUTION OF GOVT. MADURAI MEDICAL COLLEGE HOSPITAL, MADURAI, TAMIL NADU

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Key words:-

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Abstract

Background: To prevent cancer cervix, cervical cancer screening is one of the emerging health programme in all primary as well as tertiary care institution. In 2012, updated cervical cancer screening recommendation was released with consensus on Pappnicolaou (PAP) testing every 3 years for women aged 21 – 65 years (or) PAP – Humen Pailloma Virus (HPV) co testing at 5 – year intervals for women aged 30 – 65 years.

Materials and Methods: This prospective study was done at the tertiary care hospital from January 2017 to December 2017. 51 women were selected for screening HPV. The laboratory results were reported according to the new Bethesda system for reporting cervical cytology 2014.

Results: Out of 51 cases, 17 HPV positive cases showed high risk genotype. Commonest high risk genotype detected was HPV 16 followed by HPV 35. And also 11 cases showed HPV positivity even with normal Pap smear study.

Conclusion: HPV Testing along with pap smear are mandatory since there is high detection rate of HPV even in those with normal Pap smear.

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Introduction:-

According to GLOBOCON 2018, cervical cancer ranks fourth among women in both newly detected cases and cancer deaths worldwide. In developing countries, Cancer cervix is a major cause for cancer mortality in women [1].The incidence of cervical cancer cases differs in developing and developed countries. The burden of cervical cancer is still high in developing countries like India. Cervical cancer can be prevented through simple cost effective measures, such as creating awareness, and regular screening with the Pap smear. [3] Early detection and appropriate treatment are possible with simple and robust screening.[2] Early cervical epithelial changes can be identified by a Pap smear test, which is the primary screening test for detection of precancerous cervical intraepithelial neoplasia and the early stage of invasive cervical cancer.[4] There is a need to spread cervical cancer screening awareness programs, educate women regarding the symptoms of cancer, and motivate them to visit the hospital for a cancer screening. Women and all family members should be counseled about the need for cancer screening. Pap smear positive women need adequate treatment and regular follow up. Thus, we have to strengthen our health services and health care system to include screening at primary health centers. A Pap screening done in association with an HPV

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DNA test increases the sensitivity for early detection of precancerous lesions.[5] The aim of the present study was to evaluate women for precancerous lesions using the Pap smear test and HPV DNA study.

Materials and Methods:-

The prospective study was done at the tertiary care hospital from January 2017 to December 2017. 51 women were selected to offer screening for HPV positivity. A detailed history, per speculum and vaginal examinations were done by the department of Obstetrics and Gynecology. Women with different complaints, including vaginal discharge, blood mixed discharge, foul-smelling discharge, postcoital bleeding, intermenstrual bleeding, postmenopausal bleeding, abdominal pain, infertility, and secondary amenorrhea, were included in this study. Those not willing to participate in the study, had a frank growth or were pregnant were excluded from the study. A sample was taken from the ectocervix by rotating a wooden Ayre spatula 360°. The sample was quickly smeared onto a labeled glass slide and fixed with 95% ethyl alcohol in a jar and was sent to our Department for cytopathological examination. Laboratory results were reported according to the new Bethesda System for Reporting Cervical Cytology 2014. The system broadly divides the cervical lesions into those negative for intraepithelial neoplasia and epithelial cell abnormalities (ECA) that include squamous and glandular cells. HPV testing was done in parallel with Pap smear. HPV testing was done using a low cost FDA approved real time PCR strategy.

Result:-

In this study, 29% of women are in the 31-40 years age group followed by 21% between 41-50 years age group and 75% of them are premenopausal age group. [Table 1]. Abnormal vaginal discharge was the most common symptom found in 45%, lower abdominal pain in 23%, back ache in 17% and postcoital bleeding in 3% of the women. On per speculum vaginal examination, 47% had normal looking cervix whereas abnormal cervix was seen in 53% [Table 2]. In Pap smear examination out of 51 cases, 42 cases were normal (82.3%) (fig 1), while two cases (3.9%) showed features of ASCUS (Atypical Squamous Cells of Undetermined Significance) (fig 2), three cases (5.8%) showed features of LSIL (Low grade Squamous Intraepithelial Lesion) (fig 3) and four cases (7.8%) showed features of HSIL (High grade Squamous Intraepithelial Lesion) (fig 4). VIA/VILI positivity was seen in three cases of HSIL, three cases of LSIL and two cases of ASCUS [Table 3]. Out of 17 cases, HPV positivity was seen in three cases of HSIL (17.6%), two cases of LSIL (11.7%), one case of ASCUS (5.8%), and 11 cases (64.7%) with inflammatory smear. (fig 5). All the 17 HPV positive cases showed a high risk genotype. Commonest high risk HPV detected was HPV 16 followed by HPV 35 [Table 4].

Discussion:-

The incidence of cervical cancer is high because of nonexistent or poorly implemented prevention programs. The Pap smear test, a screening method used to detect cervical cancer, is an effective way to prevent the development of cervical cancer. The awareness about the Pap smear test within the community is very low [4]. According to the American Cancer Society (2012), the Pap smear test is a routine cancer screening method that should be done every 3 years, and a Pap smear with HPV DNA test is recommended every 5 years. [6]

HR-HPV (High risk – Human Papilloma Virus) types are associated with dysplastic and neoplastic lesions in the uterine cervix. [7] Low risk HPV types are usually found in benign epithelial lesions like genital warts (condylomata acuminata), but not in malignant lesions. [8]

Out of more than 100 types of HPV identified till date, mainly types 16 and 18, along with types 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, and 82 are considered as potentially carcinogenic and are thus referred to as HR-HPV types. [9,10]. Clearly HPV 16 and 18 account for the most of the cases. In our study it is in well correlation with the literatures.

Viral gene expression, and particularly that of the viral oncogenes E6 and E7, is in most instances restricted to the intermediate or superficial cell layers. Apparently, control mechanisms suppress their expression in the basal or parabasal cell layers, i.e. in those epithelial cells that retain the capacity to replicate. This mechanism prevents a concomitant expression of viral and cellular genes in genome replication and proliferation. [11] If these negative regulating mechanisms lose their function, concomitant expression of viral oncogenes and cellular replication may occur. [8]

Cytologically, in LSIL /Mild dysplasia/CIN I exfoliate superficial and intermediate squamous epithelial cells show enlarged , hyperchromatic and irregularly contoured nuclei. Nucleoli are absent and koilocytic changes are common. In HSIL/Modrate to severe dysplasia/CIN II lesion exfoliate parabasal –type cells are arranged singly or in sheets with thick, well-defined cytoplasm and enlarged hyperchromatic nuclei showing smooth or irregular nuclear contours. The chromatin is evenly distributed and may be finely or coarsely granular. Nucleoli are absent and koilocytic changes may be present.[12]

In severe CIN III lesions, the epithelial fragment show abundant, well or ill defined cytoplasm and enlarged , hyperchromatic and irregular nuclear contour cells arranged in syncytial clusters.[12]

ASC-US cells show cellular features that are more severe than the squamous cells with reactive changes but less than those of a SIL. The cells show enlarged uni or binuclei that are 2-5 to 3 times larger than the nucleus of normal intermediate squamous cells. Mild increase in nuclear cytoplasmic ratio, slightly hyperchromatic nuclei with irregular chromatin distribution, focal irregular nuclear contour, dense and eosinophilic (keratinized)cytoplasm, and nucleoli may be seen in ASC-US repair cells.[13] Though Pap smear remains the typical example of an important preventive intervention, the reduction in cervical cancer relies on regular serial screening test. Generally, HPV DNA testing has a higher sensitivity but a lower positive predictive value (PPV) than cervical cytology.[14] Since human papillomavirus (HPV) has been established as a well-recognized etiologic agent of cervical neoplasia, HPV DNA testing is a promising alternative or complementary test to improve the efficacy of cervical screening and probably cost-effective, as it reduces the screening interval.[15]

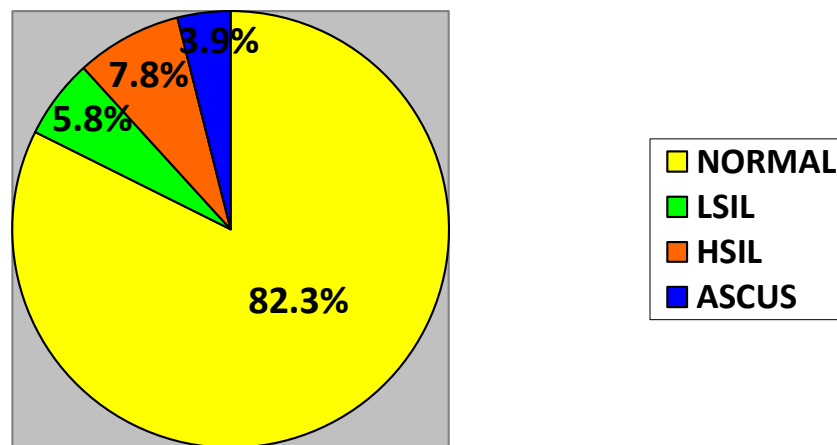


Figure 1:- Distribution of pap test results,

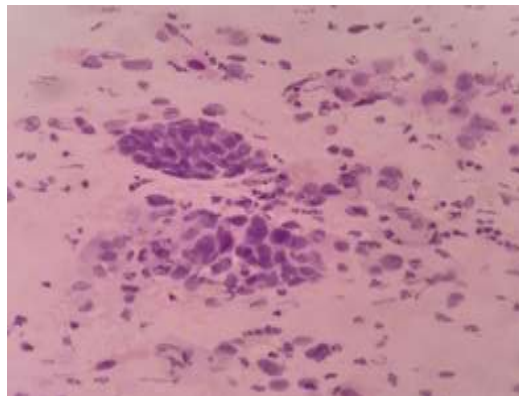


Figure 2:- ASC- US . LBP ,Thin prep , (H&E Stain) A group of cells with nuclear enlargement showing nuclear membrane irregularity and hyperchromatia ,X 40.

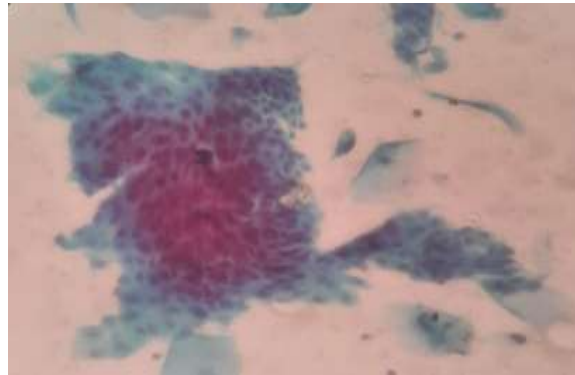


Figure 3:- LBP, Thin prep,(pap stain) . LSIL on cytology shows mature squamous epithelial cells with enlarged nuclei with variable chromatin and nuclear membrane. X 40

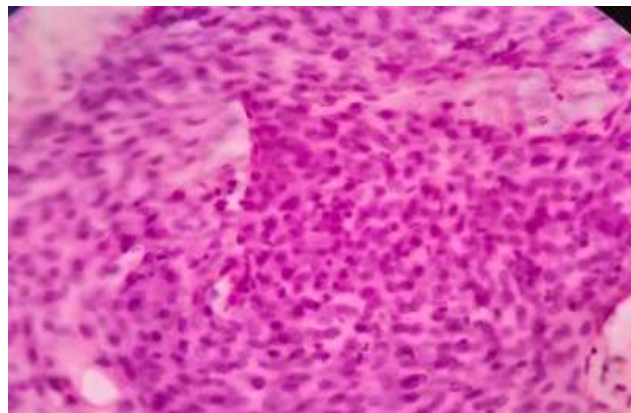


Figure 4:- HSIL. LBP, Thin prep, (H&E Stain) A syncytial clusters of dysplastic cells showing hyperchromatic overlapping nuclei. X 40.

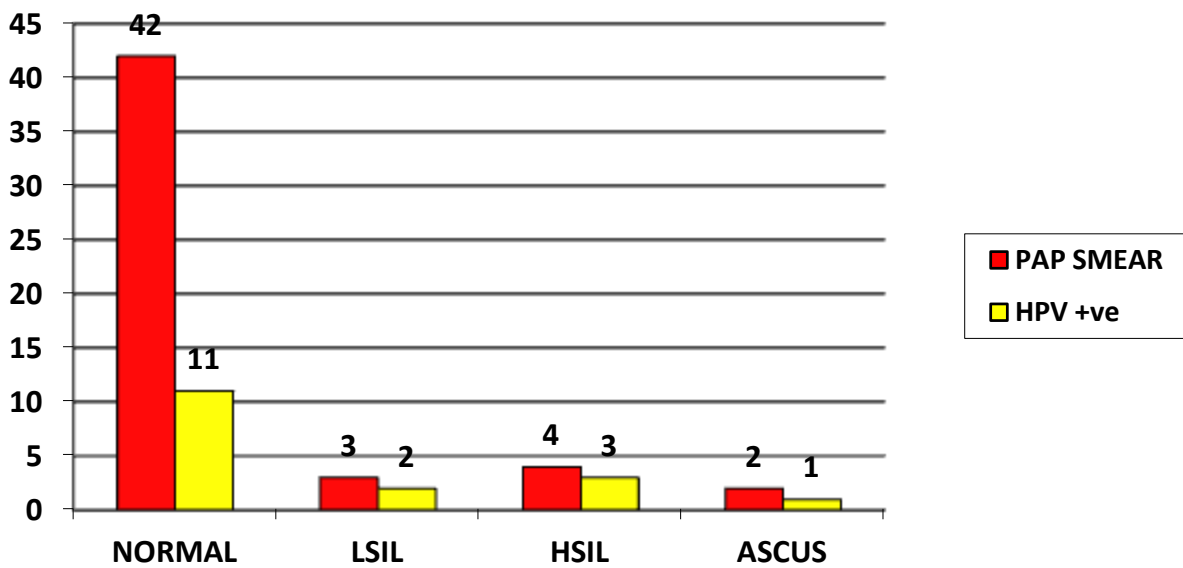


Figure 5:- Distribution of HPV Test results.

Table 1:- Distribution Of Clinical Symptoms.

| Clinical symptoms | Number of cases | Percentage |
|----------------------------|-----------------|------------|
| Lower abdominal pain | 12 | 23% |
| Abnormal vaginal bleeding | 5 | 9% |
| Abnormal vaginal discharge | 23 | 45% |
| Post coital bleeding | 2 | 3% |
| Backache | 9 | 17% |
| Others | 5 | 9% |

Table 2:- Per -Speculum Examinatio.

| Clinical sign | Number of cases | Percentage |
|-----------------|-----------------|------------|
| Normal cervix | 24 | 47% |
| Abnormal cervix | 27 | 53% |

Table 3:- Distribution of Test Positivity.

| Test result | Normal | ASCUS | LSIL | HSIL | INVASIVE |
|-------------------|--------|-------|------|------|----------|
| PAP TEST | 42 | 2 | 3 | 4 | - |
| VIA/VILI POSITIVE | 4 | 2 | 3 | 3 | - |
| HPV POSITIVE | 11 | 1 | 2 | 3 | - |

Table 4:- Results of Hpv Testing.

| HPV Types | Number of Positive cases |
|-----------|--------------------------|
| 16 | 12 |
| 31 | 5 |
| 35 | 9 |
| 39 | 2 |
| 51 | 1 |
| 56 | 1 |
| 58 | 2 |
| 59 | 1 |

Conclusion:-

To prevention of cervical cancer, HPV Testing along with PAP smear are mandatory and gold standard procedure since there is high rate of detection of HPV even in normal and inflammatory smear.

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Competing interests:

None declared

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