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Study of Significance of Endometrial Cells in Routine Cervicovaginal Smears in Women Aged 40 Years and Older

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Abstract: *The role of cervical cytology in cancer & pre cancer is well known . Due to early detection by Papanicolaou Screening, the incidence of cervical cancer has declined. However benign endometrial cells when seen in cervical cytology outside the proliferative phase & in post menopausal women must be specially noted in women above 40 yrs as it may indicate endometrial pathology. Purpose of study is to determine the significance of benign endometrial cell in pap smear test in women aged 40 years & above in patients attending Gynaecology Department of N.R.S.M,C.&H as a screening test for detection of endometrial pathology .So the present study will help in early detection of endometrial pathology by screening benign endometrial cells in women aged 40 years & above.*

Keywords: *cervicovaginal smears, Endometrial cell , exfoliated, Post menopausal.*

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I. Introduction

The role of cervical cytology in cancer & pre cancer is well known . Due to early detection by Papanicolaou Screening, the incidence of cervical cancer has declined. However benign endometrial cells when seen in cervical cytology outside the proliferative phase & in post menopausal women must be specially noted in women above 40 yrs as it may indicate endometrial pathology.

Every year, thousands of new cases of endometrial malignancies are diagnosed making endometrial carcinomas the most common malignancy of gynaecological tract in the Western countries (Jemal A,Tiwary R.C , Murray T et al)30.Due to change in lifestyle & hormone replacement therapy, Endometrial carcinoma is on the rise in Indian population also.

In 2001 , the reporting of benign endometrial cells was further modified (The Bethesda System 2001) to include all women 40 years & above (Solomon D, Devey D, Kurman R et al & Forum Group Members)17 as these women are considered to be at risk for endometrial pathology specially endometrial carcinoma.

In spite of increased prevalence of exfoliated benign endometrial cells in cervicovaginal smear, lower incidence of endometrial pathology was noted in patients on hormone replacement therapy in comparison to patients who did not take hormone replacement therapy. But the presence of benign endometrial cells in cervico vaginal smear in patients on Tamoxifen therapy was associated with increased risk of endometrial carcinoma(Abadi M.A , Barakat R.R et al)31

So the present study will help in early detection of endometrial pathology by screening benign endometrial cells in women aged 40 years & above.

II. Aims And Objectives

Purpose of study is to determine the significance of benign endometrial cell in pap smear test in women aged 40 years & above in patients attending Gynaecology Department of N.R.S.M,C.&H as a screening test for detection of endometrial pathology

1) To determine the significance of presence benign endometrial cells in routine cervico vaginal smears with conventional pap staining above 40 years..
2) To find out the significance of presence of benign endometrial cells in cervico vaginal smears of post menopausal women aged above 50 years

III. Materials And Methods

This study was performed in the Department of Pathology of N.R.S.M.C &H. Study population includes patients attending Outpatient Department of NRSMC &H Gynaecology & Obstetrics Department.Study period was between February 2016 to July 2017with a sample size of 100 patients.

Sample design: Inclusion Criteria patients who give consent,patients 40 years and above outside the proliferative phase .Exclusion Criteria includes patients who do not give consent,patients below 40 years of age and patients with bleeding disorders.Study design was a Prospective observational study.Parameters to be studied were Clinical History, cervico vaginal examination **,** Laboratory investigations **,** Treatment records , Electronic Database, Statistical analysis with patient consent forms.

A detail history in terms of Last Menstrual Period ,Menopause, associated symptoms & any treatment including hormone replacement therapy. History of Diabetes ,Hypertension & any malignancies were also noted.

Cervico vaginal smears were taken from the women (> 40 years of age)who came to attend Gynaecology Outpatient Department, using vaginal speculum Ayer's spatula & endocervical brush. The smears were fixed in 90% Alcohol for 15 minutes. Method of staining used is Papanicolaou Stain(regressive)and mounted in DPX & cover slipped . The smears were studied under light microscope. Thorough searchwas made for benign endometrial cells.

Patients showing benign endometrial cells in cervico vaginal smears were subjected to dilation & curettage for endometrial tissue & histopathological examination of the tissue after processing was performed with Haematoxylin & Eosin stain .

IV. Figures And Tables

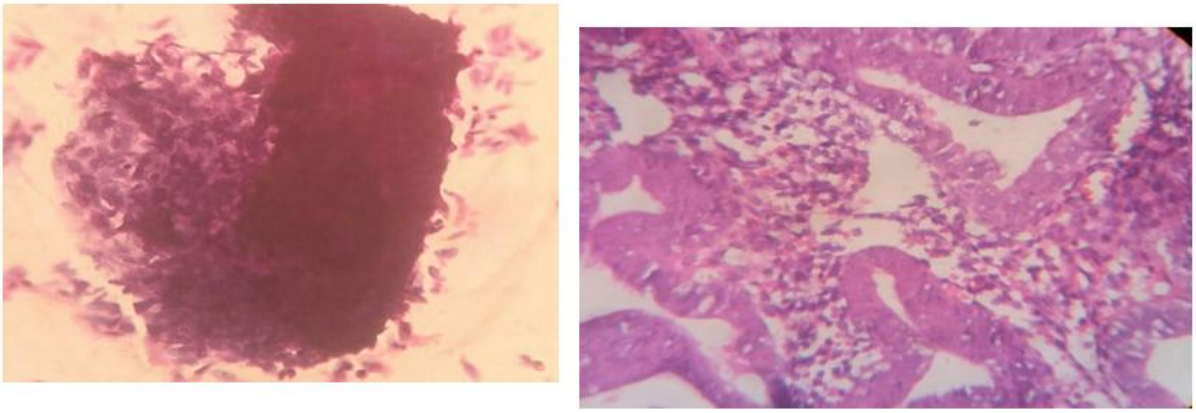


Fig 1: Exfoliative cytology of normal endometrium(Pap x 100)
FIG-2 HPE OF ENDOometrial Hyperplasia with Atypia (H & E X 400)

TABLE-1. Distribution of study subjects according to age

Age In Years	No. of cases	Percentage
40-50	52	52%
51-60	38	38%
>60	10	10%
Total	100	100%

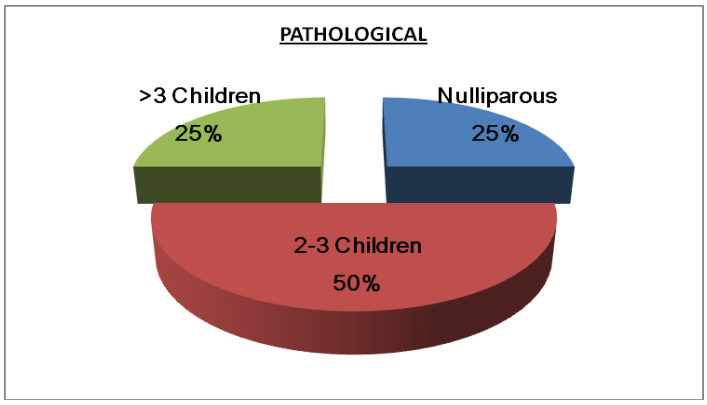
Among the study subject out of 100 patients maximum (52%) are in the age group 40-50 years.

TABLE-2 Pap Smear showing EMCs in Pre-menopausal & Post – menopausal women

Pap Smear showing EMCs	Pre-menopausal (28.57%)	Post-menopausal (71.42%)
14	4	10

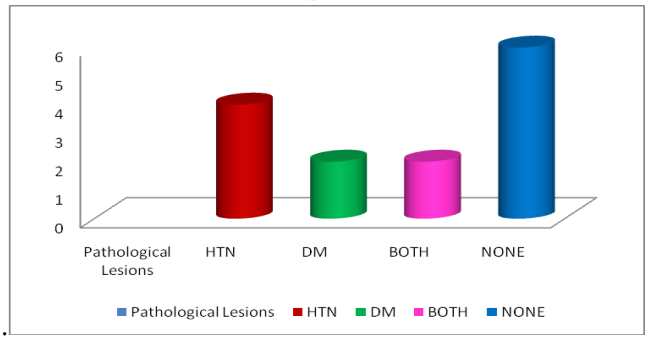
Out of 14 cases with EMCs 28.57% were pre-menopausal and 71.42% were post-menopausal women. Maximum women showing EMCs were in the post-menopausal group.

TABLE 3



Pie Chart Showing maximum no. of endometrial pathology was among women with 2-3 children

TABLE 4



Bar chart showing presence of pathological lesions according to Co-morbidity

Inference : shows out of 14 women of which 28.57%were Hypertensive, 14.28% were Diabetic & 14.28% were Both and 42.28% were not hypertensive or diabetic.

TABLE 5 **Distribution of endometrial lesions in study subjects according to presence of Endometrial Cells in Pap smear**

Endometrial Lesions	Hyperplasia Without Atypia (14.28%)	Hyperplasia With Atypia (28.57%)	Endometrial Carcinoma (14.28%)
	2	4	2

V. Discussions

Benign appearing endometrial cells are normal components in exfoliative gyaneocological preparation obtained from women of reproductive age in the proliferative phase (1-14days) of the menstrual cycle ; the presence of benign endometrial cells in cervical smears is considered abnormal under any other circumstance (Demay RM).In particular the presence of benign endometrial cells in exfoliative specimens from post-menopausal women may disclose serious uterine pathology and warrants further evaluation.

Three types of endometrial cells are usually reported on Pap cytology: normal endometrial cells (NEMCs), atypical endometrial cells (AEMCs), and endometrial carcinoma cells (EMCCs). Unlike AEMCs and EMCCs, NEMCs are reported only in women 40 years and older based on the Bethesda system 2001, because age is more consistently available than menopausal status or clinical symptoms and the incidence of significant endometrial pathology in women under 40 years is extremely low.[17]

Edi Brogi et all found that benign endometrial glandular cells in cervical smears from PMP women may indicate endometrial pathology, especially if vaginal bleeding is present. Although atypical endometrial hyperplasia or carcinoma was not identified in the group of PMP women on HRT, endometrial abnormalities of a lesser degree were present in 8.5%of patients. Thus, the authors favour continued classification of benign endometrial glandular cells in cervical smears of PMP women, whether or not they are on HRT, as a glandular cell abnormality.[8]. Aylin Simsir et all ,found that the reporting of benign endometrial cells in CV cytology specimens of premenopausal women 40 years and older has no clinical significance. This is in contrast with findings for postmenopausal women. who shed cytologically normal-appearing endometrial cells have a significant risk of preneoplastic and neoplastic endometrial disease regardless of their hormonal intake status

and lack of symptoms. Therefore, although premenopausal women can be safely followed up conservatively in the absence of symptoms, all postmenopausal women with spontaneously exfoliated endometrial cells in their CV specimens should undergo endometrial sampling regardless of HRT status and symptoms.[9]

In the studies on the significance of benign endometrial cells encountered in Pap smears, Ng [10,11] and Gondos and King[3] used a retrospective single-arm design to examine the prevalence of endometrial pathology among women with benign endometrial cells seen on Pap smears. Among women _ 40 years of age with endometrial histology follow-up, Gondos and King found that 17% had either endometrial hyperplasia or adenocarcinoma. Cherkis and coworkers[4,12]conducted studies of the same type among postmenopausal women and women in the second half of their cycle who had benign endometrial cells on their Pap smears. They found that this was associated with endometrial hyperplasia or adenocarcinoma in 24.1% of cases that had endometrial follow-up. Yancey and coworkers[13]found an endometrial hyperplasia or adenocarcinoma rate of 13.5% in a similar study of postmenopausal women with surgical pathology correlation.

Changed reporting guidelines brought about by Bethesda 2001 has also increased the attention given by cytotechnologists and pathologists to identification and classification of endometrial cells on Pap tests.Bean and coworkers32 have shown that, in fact, the percentage of Pap tests for which benign endometrial cells were reported increased from 0.4% to 0.7% following initiation of the Bethesda 2001 System. Even higher prevalence figures of 1.1% and 1.3% endometrial cells in postmenopausal women were recently reported.[14,15.] These figures are in striking contrast to those of older and some newer studies, in which only 0.01%,21 0.03%,14 0.06%,10 and 0.11%11 of Pap smears showed benign endometrial cells that were either out of- phase or occurred in postmenopausal women. A study contemporary with the last two studies [12,13]specifically examining the frequency of finding endometrial cells in Pap smears[16] found endometrial cells in 0.6% of postmenopausal women.

Large reviews demonstrate seven to 16 percent of Pap tests with normal endometrial cells in women age 40 and older were associated with endometrial hyperplasia or carcinoma.[18,19.]

Normal endometrial cells on Pap tests are rarely associated with significant pathology in premenopausal women without abnormal bleeding.[14,20,21,22-24]

VI. Conclusion

This study is a consecutive observational study to find out the risk of precancerous and cancerous endometrial lesions in women aged 40 years and older, with presence of EMCs in this Cervicovaginal Papaniculaou smears.The important observations that was obtained are -most common age group presented with endometrial pathology was 51-60 years, endometrial hyperplasia with atypia (28.57%), endometrial hyperplasia without atypia (14.28%) and endometrial carcinoma (14.28%)., post-menopausal women were at higher risk (71.42%).Hypertension and diabetes are risk factors for endometrial carcinoma, Nulliparous women are more susceptible for endometrial carcinoma,significant risk of underlying endometrial abnormality regardless of lack of symptoms.According to Bethesda 2001, the cut-off age of 40 years has reduced the burden of Cervicovaginal Papaniculaou test studies and reduced the screening load. Out of the 1100 cases routine cervicovaginal smears in one and half year period considering the exclusion and inclusion criteria the study could be done on 100 women only which is a low sample volume.

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