

**CYTO-HISTO CORRELATION OF ATYPICAL GLANDULAR CELLS OF ENDOMETRIAL ORIGIN ON CERVICAL CYTOLOGY IN ABNORMAL UTERINE BLEEDING CASES**Lopa Mudra Kakoti<sup>1</sup>, Nandini N. Manoli<sup>2</sup>, Nandish S. Manoli<sup>3</sup>**HOW TO CITE THIS ARTICLE:**

Lopa Mudra Kakoti, Nandini N. Manoli, Nandish S. Manoli. "Cyto-Histo Correlation of Atypical Glandular Cells of Endometrial Origin on Cervical Cytology in Abnormal Uterine Bleeding Cases". Journal of Evolution of Medical and Dental Sciences 2015; Vol. 4, Issue 13, February 12; Page: 2153-2157, DOI: 10.14260/jemds/2015/309

**ABSTRACT: BACKGROUND:** An association has been reported with presence of endometrial cells on cervical smears and clinically significant uterine lesions. Hence for early detection of endometrial pathology, the 2001 Bethesda system has suggested the mandatory reporting of presence of any atypical endometrial cells regardless of age and menstrual status and out of phase normal looking endometrial cells in women aged 40 years or more. **OBJECTIVES:** To assess the association between atypical glandular cells of endometrial origin in cervical cytology and histopathological findings in abnormal uterine bleeding cases. **SETTINGS AND DESIGN:** The study was conducted at JSS hospital, Mysore in the department of pathology. This was a descriptive type of study. The sample was collected from patients attending the gynecology OPD with the complaints of abnormal uterine bleeding in JSS hospital. **MATERIALS AND METHODS:** Smears for cervical cytology are collected using either pap smear or manual liquid based smear from 82 patients in the age group of 20-75 years with complaints of abnormal bleeding history. The results of cervical cytology were compared and confirmed with the endometrial pathology. **RESULTS:** Out of 82 abnormal uterine bleeding cases 14 showed atypical endometrial cells. On follow up of these cases, the results indicated an association between atypical endometrial cells in cervical cytology with endometrial carcinoma in 8 cases (60%), 1 case with complex hyperplasia with atypia (10%). **CONCLUSION:** Presence of atypical endometrial cells in all women with abnormal uterine bleeding has considerable clinical implications & further diagnostic evaluation by endometrial sampling is of utmost importance.

**KEYWORDS:** Atypical glandular cells, endometrial cells, abnormal uterine bleeding, the Bethesda system, pap smear.

**INTRODUCTION: BACKGROUND:** About 10% cases of Abnormal Uterine Bleeding is associated with endometrial cancer, but it can be caused by many other conditions such as polyps, myomas, hormonal dysfunction and most commonly in post-menopausal women atrophy.<sup>1,2,3</sup>

Endometrial cells are present incidentally on many pap tests, providing cytopathologists an opportunity to examine these cells in specimen that may have been obtained for other reasons.<sup>4</sup>

Spontaneously exfoliated, benign endometrial glandular cells are a normal component of the Papanicolaou (Pap) tests obtained in premenopausal women during the first half of the menstrual cycle (Days 1-14). The presence of exfoliated benign endometrial cells in any other clinical scenario is considered an abnormal finding.<sup>5</sup>

An association has been reported with presence of endometrial cells on cervical smears and clinically significant uterine lesions. Hence The Bethesda system 2001 has mandated multiple reporting categories meant to apply to endometrial cells.<sup>6</sup>

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There are 3 types of endometrial cells usually reported on Pap cytology: normal endometrial cells (nEMCs), atypical endometrial cells (aEMCs), and endometrial carcinoma cells (EMCCs).<sup>7</sup>

Guidelines from the 2001 Bethesda system suggested, in addition to reporting of atypical glandular cells (AGC) and adenocarcinoma, the reporting of benign appearing endometrial cells in women aged above 40 years is mandatory and a review of literature supports this recommendation.<sup>8</sup>

Literature reviewed a number of studies that have examined the findings on surgical pathology follow-up of benign, atypical, and malignant endometrial cells in Pap tests. But very few studies showed analysis of pap tests preceding the histopathological diagnosis.

To our knowledge studies from India has hardly been reported in this issue.

**OBJECTIVE:** The present study aimed to assess the association between atypical glandular cells of endometrial origin in cervical cytology and histopathological findings in abnormal uterine bleeding cases.

**MATERIALS AND METHODS:** Samples were collected using split- smear technique from 82 patients with bleeding history in the age group of 20 to 70 years attending the gynaecology out-patient clinic at JSS Hospital, Mysore, prospectively from July 2012 to July 2014 for a period of two years. Manual Liquid Based Cytology is strongly advocated as it improves sample quality and reduces the likelihood of false negative results by removing obscuring factors.

Scrape smears were collected using plastic Ayre's spatula. The scrapings were first put into MLBC vial containing liquid fixative and later evenly spread onto a glass slide, and immediately fixed in ethyl-alcohol fixative (95% ethyl alcohol). After fixation, smears were stained using conventional Pap stain.

**RESULTS:** Among the 82 bleeding history cases, 14 cases showed presence of atypical endometrial cells. The mean age of the patient was 45.4 years. On follow up with histopathology 8 cases were diagnosed to have endometrial malignancy (4 cases as type 1 endometrial carcinoma followed by 3 cases of squamous cell carcinoma and 1 case of type 2 endometrial carcinoma) 1 case of precancerous lesions of complex hyperplasia with atypia and rest were benign lesions like 2 adenomyomatous polyp, 1 atrophic endometrium and 1 endometritis. The youngest patient with diagnosis of endometrial carcinoma was 36 year. All other patients were postmenopausal women.

**DISCUSSION:** It has been generally accepted that the cervical cyto-histological correlation can be considered as one method to access the quality assurance for cytology laboratories.

Many studies have associated the presence of atypical endometrial cells on Pap cytology (conventional and liquid-based Pap cytology) with increased rates of underlying endometrial malignancy: 9% to 52%.<sup>7</sup>

Chhieng DC et al. found approximately one-third of women with a diagnosis of atypical glandular cells of endometrial origin had a significant uterine lesion on subsequent biopsy and suggested that Patients with a diagnosis of atypical endometrial cells on cervicovaginal smears should be followed closely, and endometrial curettage or biopsy should be included in their initial work-up.<sup>9</sup>

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René Scheiden et al had 56% of the patients with significant cancerous and precancerous conditions emphasising the requirement of complete and careful evaluation.<sup>10</sup>

Our study revealed 9cases (64.3%) with significant precancerous (1case) and cancerous lesions (8 cases) on histopathology follow up, out of 14 atypical endometrial cells in cytology. Increased rate of detection of precancerous and cancerous lesion was because we included only symptomatic patients as study group.

We had 3 cases of squamous cell carcinoma of endometrium. Some studies have also documented high-grade squamous cervical lesions or squamous carcinomas in women with reports of atypical endometrial cells.<sup>7,11</sup>

Though the sensitivity and specificity of pap smear in detection of glandular lesions is not as high as squamous lesions, there is importance of further diagnostic evaluation for endometrial status when these atypical glandular cells shows their presence.<sup>12,13</sup>

Our data also indicates the similar findings.

**CONCLUSION:** With changing life style, increasing women life span and drastic reduction of historically commoner cervical cancer by the successful implementation of pap smear screening programs, the increased incidence of endometrial carcinoma is becoming an important challenge. Presence of atypical endometrial cells in cervical smears in all aged women indicates an underlying endometrial pathology which warrants further diagnostic evaluation. Hence, The Bethesda system of reporting endometrial cells in cervical cytology can also be a help in detecting early endometrial pathology in abnormal bleeding or postmenopausal bleeding cases.

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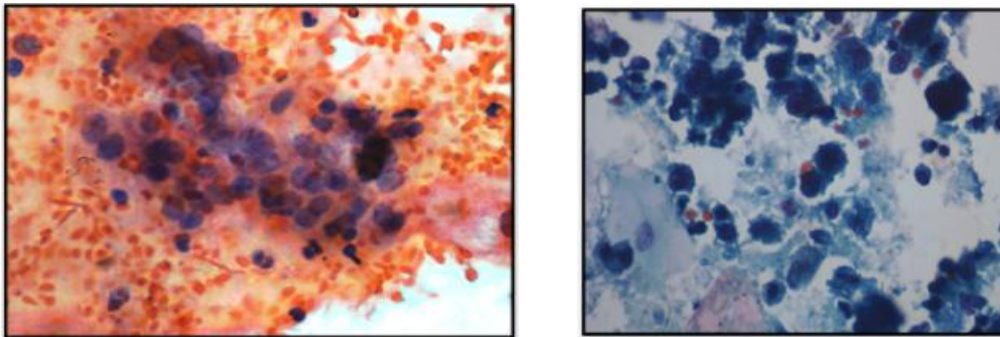
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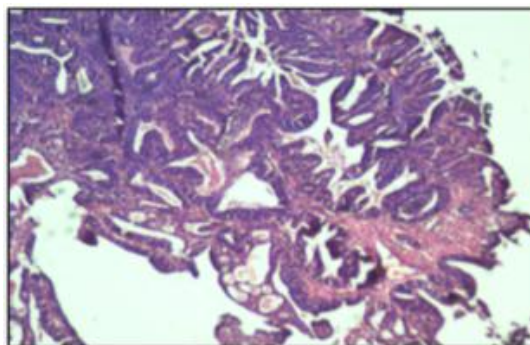
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**Fig. 1 & 2:** CPS and MLBC (Pap, X400)-Atypical Endometrial Cells - Smear shows cells with high N/C ratio arranged in clusters with enlarged hyperchromatic nuclei and fairly abundant cytoplasm.



**Fig. 1 & 2**

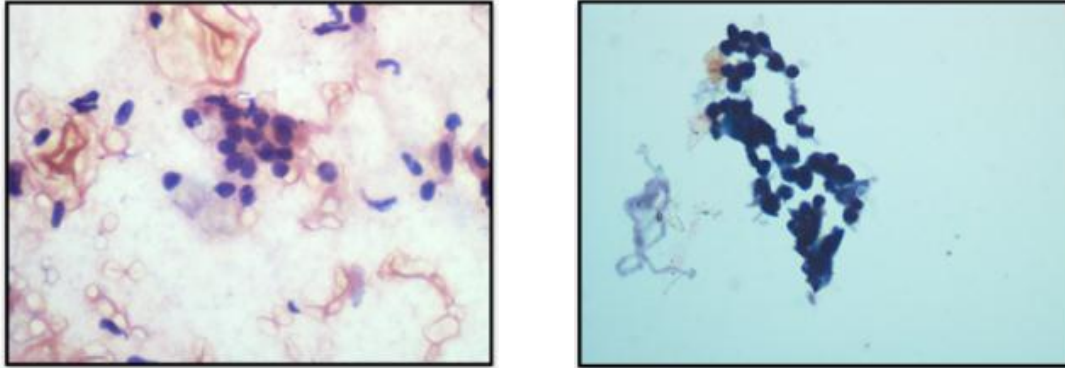
**Fig.3:** HPE (H & E, X100) - Endometrial Adenocarcinoma type 1 -Section shows a tumor displaying features of endometrial adenocarcinoma.



**Fig. 3**

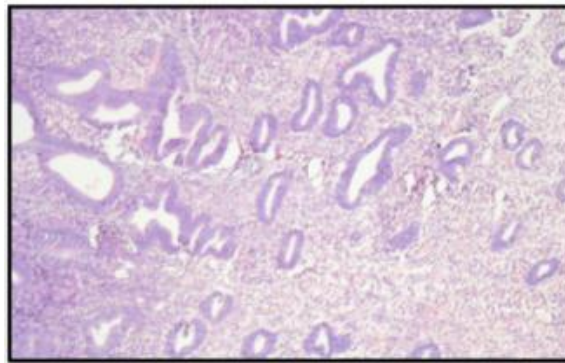
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**Fig. 4 & 5:** CPS & MLBC (Pap, X400) benign endometrial Cells - Smear shows endometrial cells in acinar pattern. Cells are small with round nuclei and scant cytoplasm.



**Fig. 4 & 5**

**Fig. 6:** HPE (H & E, X100) - Proliferative Endometrium -Section shows round tubular endometrial gland and compact stroma.



**Fig. 6**

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