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CLINICOPATHOLOGICAL EVALUATION OF ENDOMETRIAL CURETTAGE SPECIMENS FROM A TERTIARY CARE CENTRE

Dr Sandhya Baliram Narwade[1], Dr. Sanjivani Sahebrao More[2], Dr Supriya Rahul Muneshwar[3*]

[1]Assistant professor, Dept. Of Pathology, Dr. Shankarrao Chavan Government Medical College & Hospital - Vishnupuri, Nanded, MS.
[2]Assistant professor, Dept. Of Pathology, Dr. Shankarrao Chavan Government Medical College & Hospital - Vishnupuri, Nanded, MS.
[3*]Assistant professor, Dept. Of Pathology, Dr. Shankarrao Chavan Government Medical College & Hospital - Vishnupuri, Nanded, MS.

[*]**Corresponding Author:** Dr Supriya Rahul Muneshwar,
[*]Assistant professor, Dept. Of Pathology, Dr. Shankarrao Chavan Government Medical College & Hospital - Vishnupuri, Nanded, MS.

Abstract:
Introduction: Endometrial sampling stands as the benchmark for diagnosing abnormal uterine bleeding (AUB), chiefly aimed at uncovering its origins, particularly to ascertain the presence of cancerous or precancerous conditions. AUB ranks as the most frequent complaint encountered in gynecological clinics. This paper delves into an analysis of endometrial curettage specimens, focusing on their clinicopathological characteristics, based on a study encompassing numerous cases.
Objectives: The primary goal of this investigation was to conduct a clinicopathological assessment of a substantial collection of endometrial curettage specimens within a tertiary healthcare setting.
Methods: The study meticulously examined 400 endometrial curettage specimens, applying Hematoxylin and Eosin (H&E) staining as the fundamental technique. Additional special stains and immunohistochemistry (IHC) were utilized as necessary. A thorough clinicopathological comparison was performed for each case, with findings benchmarked against previous research.
Results: The age range of subjects in this study spanned from 18 to 70 years, with a predominant age bracket of 31-40 years. The most frequent observations included cyclical endometrial changes, followed by various endometrial pathologies and trophoblastic diseases.
Conclusion: The endometrial biopsy emerges as a crucial diagnostic instrument for gynecological disorders. Recognizing the histopathological patterns of the endometrium associated with AUB across different age groups is vital for patient management. Bleeding post-menopause should be treated with suspicion for malignancy until proven otherwise.

Keywords: Endometrial curettage, Clinicopathological analysis, Abnormal uterine bleeding.

Introduction

The lining of the uterine cavity, known as the endometrial mucosa, is subject to the influence of hormones throughout a person's life. These hormones may originate from the ovaries or the pituitary gland[1]. The assessment of endometrial conditions is optimally performed through the examination of endometrial biopsies, scrapings, or curettage samples.

There are numerous indications for obtaining endometrial biopsies, including but not limited to abnormal uterine bleeding in specific age demographics, instances of incomplete abortions, or the suspicion of neoplastic growth. Additionally, endometrial sampling may be conducted before certain infertility treatments to ascertain the menstrual cycle phase, which can inform subsequent diagnostic or therapeutic measures. Within the context of a hysterectomy, the endometrium is also evaluated, potentially revealing primary or secondary neoplastic changes[2].
Regarded as a minimally invasive and highly sensitive method, endometrial sampling stands as a pivotal initial step in the investigation of abnormal uterine bleeding (AUB). AUB is characterized by any deviation in the amount or pattern of menstrual flow. Specifically, bleeding that occurs more than one year after menopause is classified as postmenopausal bleeding (PMB)[1].

Methods
This cross-sectional prospective study was conducted within the Pathology Department of a tertiary care facility. The duration of the study extended from January 2022 to June 2023, centering on the analysis of 400 endometrial curettage samples received by the histopathology laboratory. The selection of cases was guided by defined inclusion and exclusion criteria, with a clear stipulation that only endometrial curettage or biopsy specimens were to be considered, thereby excluding any samples derived from hysterectomies. A thorough collection of patient data, including age, parity, menstrual history, and any relevant drug history, was undertaken to support the study's objectives. Following collection, the curettage specimens were preserved in 10% formal saline for optimal tissue preservation and then processed using an automatic tissue processor to prepare paraffin-embedded blocks. Tissue sections, cut to a thickness of 4 to 6 micrometers, were stained with Hematoxylin and Eosin (H&E) for initial histopathological examination under a light microscope. In instances where further diagnostic clarification was required, additional methodologies, such as special stains and Immunohistochemistry (IHC), were employed to substantiate the diagnoses, thereby ensuring the study's diagnostic rigor and precision.

Observations and Results:
The present study includes a total of 400 endometrial curettage samples received from January 2022 to June 2023. In specimens where no endometrial tissue was seen or no conclusion could be arrived at, despite the presence of some tissue, a diagnosis of inadequate evaluation was given. Normal cyclical changes in endometrium and abnormal histopathological findings such as hyperplasia, polyps, features suggestive of AUB/ DUB, pregnancy complications (molar or retained products of conception), malignancy, etc. were noted.

Table 1: Distribution of patients in various age groups:

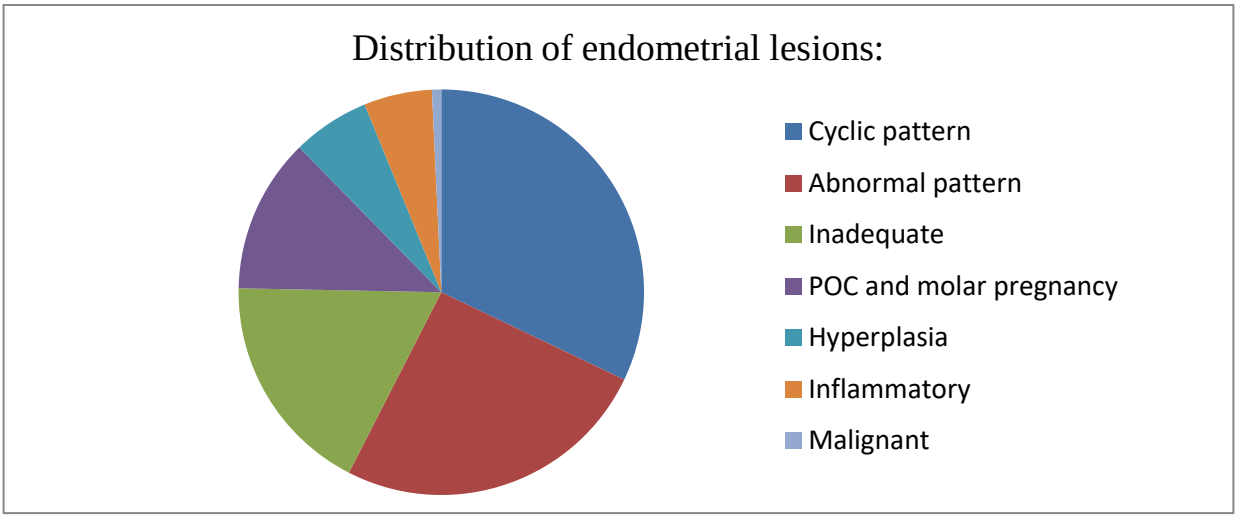
Age [years]	No. of patients	Percentage [%]
< 20	01	0.25
20- 30	86	21.5
31- 40	135	33.75
41- 50	117	29.25
51- 60	54	13.50
61- 70	04	1.00
> 70	03	0.75

Most of the biopsy specimens were received in the age group of 30- 50 years followed by 20- 30 years and 51- 60 years of age.

Table 2: Distribution of number of patients based on histopathological diagnosis:

Histopathological Diagnosis	**Number of patients**	**Percentage [%]**
Inadequate Samples/ Biopsies	72	*18.0*
Proliferative Phase	78	*19.5*
Secretory Phase	52	*13.0*
Menstrual endometrium	01	*0.25*
Atrophic endometrium	02	*0.5*
Senile cystic glandular hyperplasia	10	*2.5*
Hyperestrogenic state	01	*0.25*
Disordered proliferative phase	14	*3.5*
Abnormal secretory phase	18	*4.5*
Luteal phase defect (Hormonal imbalance)	16	*4.0*
Pill endometrium/Progestin effect	22	*5.5*
Endometrial polyp	19	*4.75*
Simple endometrial hyperplasia without atypia	24	*6.0*
Complex hyperplasia without atypia	02	*0.5*
Glandular and stromal breakdown	13	*3.25*
Products of conception and molar pregnancy	50	*12.5*
Acute endometritis	02	*0.5*
Chronic endometritis	01	*0.25*
Endometrioid adenocarcinoma	01	*0.25*
Mucinous carcinoma	01	*0.25*
Papillary serous carcinoma	01	*0.25*
Total	**400**	**100%**

Out of 400 specimens, 72 samples received were inadequate followed by normal cycling endometrium, which was the commonest pattern observed. Among these 131 cases of cyclic endometrium [Fig 1],78 was proliferative 52 were secretory, and 1 was in the menstrual phase. Senile cystic glandular hyperplasia was seen in 10 cases while a hyperestrogenic state was observed in a single case. Atrophic endometrium was seen in 2 cases.



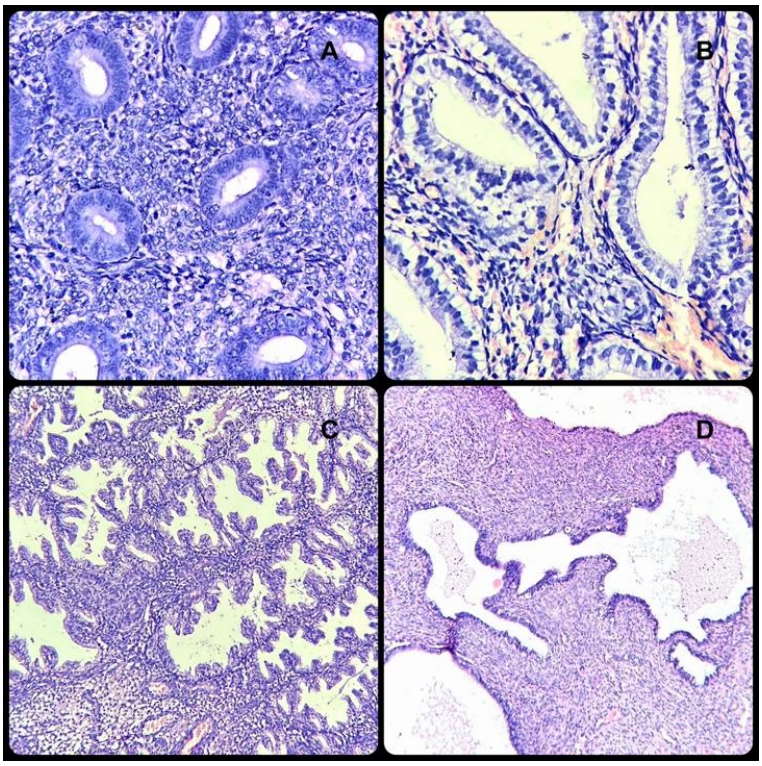


Fig 1: Shows [A] proliferative phase, [B] early secretory phase, [C] secretory phase and [D] senile cystic atrophy of endometrium. [H&E: 40X]

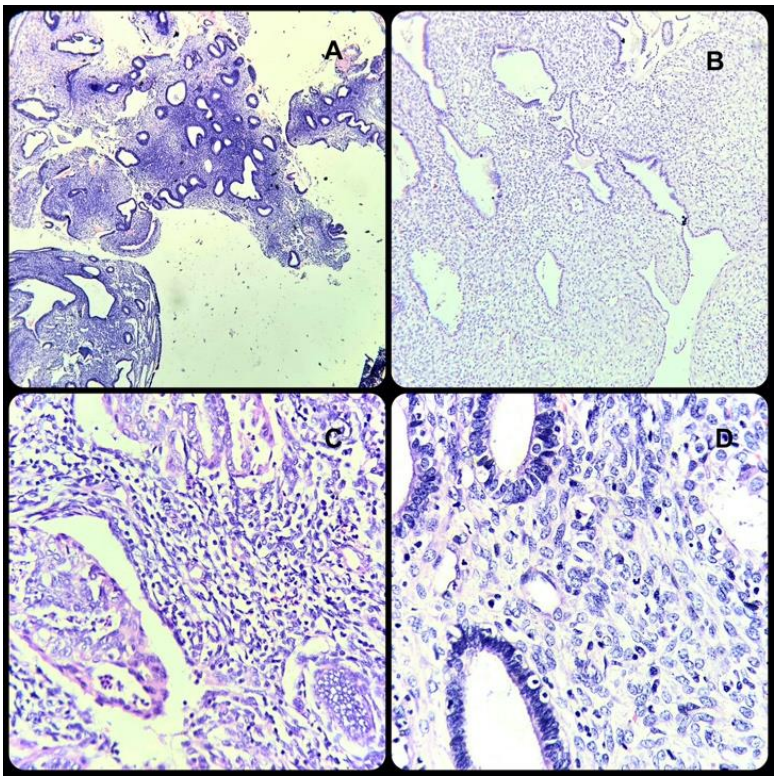


Fig 2: Shows [A] disordered proliferative phase, [B] abnormal secretory phase, [H&E: 10X] [C] acute endometritis and [D] chronic endometritis. [H&E: 40X]

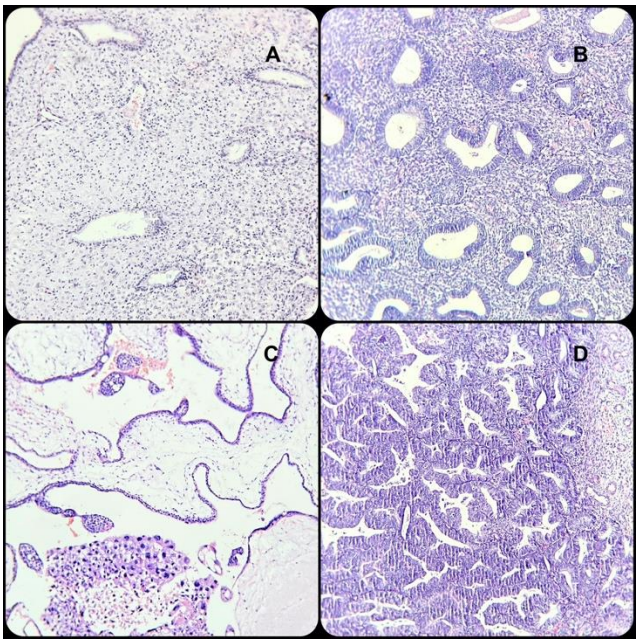


Fig 3: Shows [A] pill endometrium, [B] endometrial hyperplasia, [C] vesicular mole and [D] endometrial carcinoma. [H&E: 40X]

Disordered proliferative phases and abnormal secretory phases [Fig. 2 A,B] in the endometrium were observed in 14 and 18 cases respectively. Luteal phase defect was seen in 16 cases. Pill endometrium [Fig.3A] was observed in 22 cases while endometrial polyps were seen in 19 cases. Simple endometrial hyperplasia without atypia [Fig.3B] was observed in 24 patients while complex endometrial hyperplasia without atypia was seen in 2 cases. Glandular and stromal breakdown suggestive of AUB was seen in 13 cases. Trophoblastic lesions were seen in 50 cases with molar pregnancy [Fig.3C] being the predominant cause. Endometritis [Fig.2C,D] was seen in 3 cases. Three cases of malignancy [Fig.3D] were seen during study period.

Table 3: Age wise histopathological diagnosis:

Histopathological diagnosis	**< 20 Years**	**20-30 Years**	**31-40 Years**	**41-50 Years**	**51-60 Years**	**>61 Years**
Proliferative Phase Endometrium	0	11	26	34	7	0
Inadequate	0	5	25	21	20	1
Secretory Phase Endometrium	1	8	22	15	5	1
Products of conception and molar pregnancy	0	48	2	0	0	0
Simple endometrial hyperplasia without atypia	0	3	13	3	4	1
Pill endometrium/ Progestin effect	0	4	9	8	1	0
Endometrial polyp	0	0	10	5	4	0
Abnormal secretory phase	0	0	10	6	1	1
Luteal phase defect (Hormonal imbalance)	0	4	5	6	1	0
Disordered proliferative phase	0	2	4	5	3	0
Glandular and stromal breakdown	0	0	3	8	2	0
Simple cystic glandular hyperplasia	0	0	2	3	4	1
Complex hyperplasia without atypia	0	0	2	0	0	0
Atrophic endometrium	0	0	0	0	2	0
Acute endometritis	0	0	0	2	0	0
Chronic endometritis	0	0	1	0	0	0

Menstrual endometrium	0	0	1	0	0	0
Hyperestrogenic state	0	1	0	0	0	0
Endometrioid adenocarcinoma	0	0	0	1	0	0
Mucinous carcinoma	0	0	0	0	0	1
Papillary serous carcinoma	0	0	0	0	0	1
Total [400]	1	86	135	117	54	7

Table 4: Distribution of cases according to clinical presentation

Chief complaints	**Number**	**Percentage**
Menorrhagia	128	32
Metromenorrhagia	91	23
Polymenorrhea	80	20
Inability to conceive	55	14
Discharge and bleeding per vaginum	41	10
Post menopausal bleeding	5	1
Total	400	100

Discussion:

The endometrial lining is divided into a deeper basal layer and a superficial functional layer. The superficial functional layer is under the influence of pituitary and ovarian hormones. Any deviation from the normal menstrual cycle can be attributed to: Disorders of endometrial origin, disorders of hypothalamic-pituitary-ovarian axis.[4]

A normal menstrual cycle has a frequency of 24-38 days, last 7-9 days with 5-80 ml of blood loss. Variations in any of these parameters constitute abnormal uterine bleeding (AUB)[5]. The FIGO Working Group on Menstrual Disorders has classified the various causes for AUB into structural/organic lesions and non-structural entities. Endometrial sampling and subsequent histopathological study remain the gold standard for diagnosis of causes of AUB.[6]

Histopathological examination of endometrial biopsies is gold standard diagnostic tool in evaluation of AUB and a specific diagnosis helps to plan the therapy for successful, resourceful management of AUB.[7]

The age distribution of AUB in our study revealed that 33.75% of cases belonged to 4th decade (31-40 years) as mentioned in Table 1. Puneet Kaur et al. in 2016 reported that 27% of cases belonged to 31-40 years which was similar to our study. Similarly the study conducted by Baral R et al., 2011 showed higher incidence in 4th decade which coincides with the present study. In this study, our patients presented with different types of AUB; the commonest presenting feature was menorrhagia (47.6%). Nayak et al., 1996 found menorrhagia in 49.1% of cases similar to our study. Similarly Bagle et al., 2013 reported in their study that 48.8% of cases had menorrhagia. The study conducted by Aseel Ghazi Rifat et al., 2014 reported 47.2% of cases with menorrhagia, which is similar to our study.

The most common endometrial histopathologic pattern observed was normal cyclic endometrium. Normal cyclical endometrium including proliferative phase (19.5%) and secretory phase (13%) was seen in 32.5% of total cases and comparable to studies conducted by Vaidya et al (40.94%) & Sajitha et al (38.99%). Doraiswamy et al and Sushila Devi et al have also documented normal cyclical endometrium as the commonest observation in their studies. This pattern was high between 30 and 49 years of age.[6] Muzzafar et al. and Fakhar S et al. also reported proliferative phase in 46.6% and 54% cases respectively.[8]

Disordered proliferative endometrium accounted for 3.5% of our cases with the highest incidence in 40-49 years age group. It is common in the perimenopausal years because of anovulatory cycles. Morphologically disordered proliferative endometrium resembles normal proliferative tissue consisting of glands lined by cytologically bland, pseudostratified, proliferative, mitotically active epithelium and having a normal ratio of glands to stroma, but the glands may be cystically dilated or show shallow budding or tubular within abundant stroma. Metaplastic ciliated epithelium and

evidence of endometrial breakdown may be seen. It differs from hyperplasia without cytologic atypia by virtue of its relatively normal gland: stroma ratio of 1:1.[6]

Pregnancy related complications accounted for 12.5% of our cases and the majority of them were in 20 to 30 years age group. It is imperative that they occur in the reproductive period of life. The incidence correlates with other studies.

In our study, endometrial hyperplasia amounts to 6% of the total cases and most commonly seen in 30-49 years of age. Vani BS et al. in 2019 reported that 19.47% of cases belonged to 30-49 years which was similar to our study.

Endometrial hyperplasia which is an intraepithelial nonneoplastic proliferative lesion was said to peak around the perimenopausal and menopausal period with variable incidence in other studies.[2]There are many benign entities that simulate endometrial hyperplasia and need to be excluded before giving the diagnosis. Some such benign entities include cystic atrophy, disordered proliferative endometrium, secretory endometrium or Arias-Stella reaction, endometritis, endometrial polyps and benign papillary proliferations.[6]

To differentiate between benign uterine lesions and atypical hyperplasia or EIN morphological criteria is taken which may be further supported by additional immunohistochemical (IHC) markers.[1]

Acute endometritis was seen in 0.5% of cases and chronic endometritis was seen in 0.25% cases. The histologic criteria for chronic endometritis in the literature has been somewhat variable with respect to the number of plasma cells present in the endometrial stroma as well as to secondary characteristics including neutrophils in the surface endometrium and gland lumina, increased lymphocytes, or lymphoid aggregates.[9]

Chronic endometritis is usually encountered in the context of pelvic inflammatory disease, in association with the use of intra uterine device or in connection with retained products of conception.[6]

Atrophic endometrial pattern was seen in 3% cases with more than half of them occurring after 50 years of age. Various studies like Sajitha K et al., Vaidya S et al., Shah RJ et al., on women of all age groups have shown an incidence of atrophic endometrium ranging from 1.1, 4.1 to 5.13% respectively. In atrophic endometrium the epithelium lining the glands are mitotically inactive and bland in terms of cytological appearance. The glandular architecture may be cystic or budded. These glands are embedded in a inactive spindled stroma. Cystic atrophy is the term applied to endometria composed of cystically dilated glands lined by cuboidal to flattened epithelial cells.[6]

Atrophic endometrium was seen predominantly in the 51–60 years age group. The exact cause of bleeding from the atrophic endometrium is not known.[10]

Endometrial polyps are polypoid structures with a fibrous stroma containing large, thick-walled, coiled vessels showing cystically dilated and occasionally crowded glands lined by inactive, atrophic to weakly proliferative endometrium. Many undergo spontaneous regression. Endometrial tissue from lower uterine segment may be confused with endometrial polyp as the stroma has a fibrous appearance and glands are few in number. The absence of thick-walled stromal blood vessels and the characteristic admixture of mucinous endocervical epithelium suggests an origin from the lower uterine segment.[11] Endometrial polyps were seen in 4.75% of our patients. In similar studies by Mahapatra et al, Sajitha et al, and Khan et al endometrial polyps were seen in 3.6%, 5.12%, and 3.9% patients respectively, which is comparable to the findings in present study.

Out of 400 cases, malignancies were found in three cases which accounts for 0.75% of total cases. Endometrioid adenocarcinoma is the most common type of endometrial carcinomas encountered.

Conclusion:

Endometrial biopsy is an important tool to diagnose gynaecological conditions in patients. Postmenopausal bleeding should be considered as an indication of malignancy until proved otherwise.

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