International Journal of
Recent Innovations in Medicine and Clinical Research
Open Access, Peer Reviewed, Abstracted and Indexed Journal

ISSN: 2582-1075
https://ijrimcr.com/
Volume-5, Issue-1, 2023: 17-26

Research Article

Histomorphological Profile of Endometrium with Abnormal Uterine Bleeding in Perimenopausal and Postmenopausal Women

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Received: January 02, 2023 **Accepted:** February 02, 2023 **Published:** February 16, 2023

Abstract: Background: Abnormal Uterine Bleeding (AUB) is any uterine bleeding that is more than the normal volume (50-80 ml) or duration. It includes both organic and nonorganic causes. The PALM COEIN classification system helps us in understanding various etiological causes of AUB and can be used by clinicians and researchers for international comparisons. Increased risk of endometrial hyperplasia and endometrial carcinoma is more evident in perimenopausal and post-menopausal women with AUB. Histomorphological examination of endometrial biopsies and curetting is considered to be the gold standard in the diagnosis of its etiology. Many women with AUB undergo unwanted hysterectomy without a definitive diagnosis, so early diagnosis for cause of AUB is crucial as various uterine pathologies can be picked up and timely treatment can improve patient quality of life. **Methods:** A prospective study was conducted in department of Pathology, BPS GMC for Women, Khanpur Kalan over a period of 1 year. A total of 205 cases of AUB with a probable endometrial cause in women in perimenopausal and postmenopausal age group were included in the study. **Results:** Out of all cases of AUB non organic contributes maximum 52% followed by organic cause (48%) in patients presenting with AUB. Dysfunctional uterine bleeding were most common (103 cases) as per clinical diagnosis followed by bleeding with pain in 34. Perimenopausal age group (80.9%) contributes maximum towards both nonorganic and organic cause (AUB) in 56.7% and 43.3% cases respectively followed by postmenopausal age group in 19.1% cases. Maximum incidence of AUB in multiparous (70.2%) followed by 28.3% cases of grand multiparous and least in nulliparous women (1.5%). Endometrial carcinoma is most commonly seen in grand multiparous in 72.7% cases where as endometrial hyperplasia and leiomyoma were

commonly seen in multiparous women in 40.7% and 31.2% cases respectively. The most common presenting complaint was HMB; Heavy Menstrual Bleed (menorrhagia) (57.56%). **Conclusions:** Endometrial sampling is now considered as first line diagnostic tool because of its diagnostic accuracy, safety, quickness and convenience. Histomorphological study of endometrium plays an important role in assisting in right treatment. The histopathological examination revealed significantly more cases of COEIN component of AUB.

Keywords: Abnormal Uterine Bleeding (AUB), Heavy Menstrual Bleed (HMB), Menorrhagia, Perimenopausal, Postmenopausal.

Introduction

Abnormal Uterine Bleeding (AUB) is any uterine bleeding that is more than the normal volume (50-80 ml) or duration. It includes both organic and nonorganic causes. Dysfunctional uterine bleeding (DUB) is sub group of AUB that includes abnormal bleeding due to nonorganic or functional causes, which is present in 50% cases with AUB.[1] Multiparity is an important risk factors for development of abnormal uterine bleeding.[2] FIGO in 2011 formulated and classified AUB as "PALM-COEIN'' which is Polyp; adenomyosis; leiomyomas; Malignancy and hyperplasia; coagulopathy; Ovulatory disorders; Endometrial factors; Iatrogenic causes; and Not classified. This system describes PALM as the structural causes and COIEN as the non-structural causes of AUB[1]. In the 2018 FIGO system, AUB secondary to anticoagulants was moved from the coagulopathy category to the iatrogenic category, also the committee added intermenstrual bleeding and defined irregular bleeding as outside the 75th percentile[3].

The prevalence of AUB among reproductive aged women internationally is estimated to be between 3% to 30%, with a higher incidence occurring around menarche and perimenopause[3]. In the order of 30% of all gynaecological consultations are of abnormal uterine bleeding.[4] Abnormal perimenopausal or postmenopausal bleeding is associated with endometrial carcinoma in approximately 10% of cases.[5] In India, the reported prevalence of AUB is around 17.9% according to National Health Policy (NHP), 2017 data.

Abnormal Uterine Bleeding (AUB) is an important symptom of both benign and serious gynaecological disease. AUB is the single most common reason for gynaecological referral.[4] The most common presentation of AUB is menorrhagia followed by polymenorrhea, metrorrhagia.[6] Menorrhagia refers to excessive or prolonged bleeding occurring at regular interval of time objectively defined as blood loss greater than 80 ml[7] and menstrual period lasting longer than seven days. Polymenorrhea refers to shortened cycles that is <24 days. Metrorrhagia also known as intermenstrual bleeding is used to define any acyclic bleeding from the genital tract (uterus only). These older terms (menorrhagia, polymenorrhoea, metrorrhagia) including DUB should be discarded in favour of using simple terms to describe the nature of AUB.[8]

AUB is a very common gynaecological condition that affects all age groups, most common in reproductive age group. The increased risk of endometrial hyperplasia and endometrial carcinoma is more evident in perimenopausal and postmenopausal women with AUB. In women more than 45 years of age[9] and postmenopausal age group adenocarcinoma of endometrium is most common genital cancer often preceded by proliferative precursor lesion like endometrial hyperplasia[10].

Endometrial sampling is now considered as first line diagnostic tool because of its diagnostic accuracy, safety, quickness and convenience[11]. Currently the most commonly used technologies for outpatient evaluation of the endometrium are biopsy, hysteroscopy, and Trans Vaginal Ultrasound (TVS). Endometrial biopsy by Dilatation and Curettage or office endometrial biopsy is considered the gold standard in AUB.

Histomorphological examination of endometrial biopsies and curetting is considered to be the gold standard in the diagnosis of its etiology. It is also equally important in evaluating patients for

infertility in terms of the dating of the endometrium. Its histological appearance used to document the ovulation and to assess the hormonal status[8]. Histomorphological study of endometrium plays an important role in its treatment[12]. Various endometrial patterns on histopathology were classified as nonorganic and organic cause. Nonorganic cause includes proliferative pattern, secretory pattern, disordered proliferative endometrium, menstrual phase, atrophic endometrium, hormonal changes, irregular shedding. Organic cause includes hyperplasia, chronic endometrities, polyp, carcinoma, endometrial metaplasia, secretory hyperplasia and granulomatous tuberculosis.

Perimenopause is a period three to four years before menopause followed by one year of amenorrhea. However a better practical definition is the phase preceding the menopause generally occurring around 40-50 years (average 45.52- 47.5 years). Normally a one year period of amenorrhea after age of 40 is considered as menopause. Postmenopause is any time after six months amenorrhea in a menopausal women[1].

PALM-COEIN classification has an advantage of the entire range of possible etiologies but should be followed by further investigation to arrive at a more accurate and consistent diagnosis in perimenopausal group of women so as to rule out organic cause particularly precancerous lesions and cancers[13]. This system aids in classification of women with AUB in a systemic manner which in turn useful for both the clinicians and researchers in providing reliable information for research like epidemiological and prevalence studies along with accurate diagnosis and treatment. This system also helps in selecting appropriate treatment for the women with different pattern of menstrual bleeding as well[14].

Aim of the study to evaluate histomorphological profile of endometrium with abnormal uterine bleeding in perimenopausal and postmenopausal women.

Methods

Place of Study-Department of pathology, BPS GMC, Khanpur Kalan
Duration-August 2020 to August 2021 (1 year)
Type of study-Prospective study
Methodology-Endometrial curettage, endometrial biopsies and hysterectomy specimens of the females of age group of perimenopausal (41-50 years) and postmenopausal (>50 years) presenting with AUB were sampled in the study. Written Informed consent was obtained from all participants. A structured proforma was used to collect the medical history and examination findings of the patients.

The samples along with relevant clinical details were received in 10% formalin, gross findings were noted and multiple representative sections were taken. The specimens were processed by standard technique. Four to six micron thick paraffin embedded sections were taken and stained by haematoxylin and eosin using standard protocols. Stained slides were examined under microscope for various histopathological patterns.

Results

A total of 205 numbers of endometrial samples were received during the study period. Maximum numbers of patients were in the age group of 40-49 years (72.2%). Among causes of AUB; non organic cause contributes maximum 106 cases followed by organic cause in 99 cases. The bleeding pattern and clinical characteristics of the study population were shown in Table 1 and Figure 1 respectively.

The commonest symptoms presented were menorrhagia (HMB) 118(57.56%) followed by postmenopausal bleeding 39(19%) and most common clinical diagnosis was fibroid in 103(50.2%) cases. The maximum incidence of AUB was in multiparous patients (parity 1-3) of 70.2%, followed by grand multiparous (parity>3) patients (28.3%) and least in nulliparous patients 1.5% (Table 1).

Table 1. Distribution of total number of 205 cases according to pattern of bleeding

Pattern of Bleeding	No. of Cases	Percentage (%)
HMB	118	57.56%
Postmenopausal Bleeding	39	19.00%
Irregular menstrual bleeding/Intermenstrual bleeding	32	15.5%
Prolonged and HMB	08	4.0%
Frequent menstrual bleeding	04	2.00%
Infrequent menstrual bleeding	03	1.50%
Postcoital bleed	01	0.50%
Total	205	100 %

Both the organic and non-organic causes are more common in perimenopausal age group patients in 94 and 72 cases of perimenopausal age group (166) respectively. Overall the predominant histopathological finding was secretory endometrium in 53(25.8%) followed by leiomyoma in 32(15.5%) among total 205 cases. Hyperplastic endometrium with or without atypia was in 29(14%). In nonorganic causes, among perimenopausal age group most common pattern was secretory endometrium in 51 cases followed by DPE (21cases) and among postmenopausal age group maximum cases were of proliferative pattern (four cases) followed by three cases of atrophic endometrium (Table 2).

Table 2. Distribution of 106 cases according to nonorganic causes (DUB)

Histopathology	Perimenopausal (% in group)	Postmenopausal (% in group)	Total (Percentage %)
Secretory	51 (96.3%)	02 (3.7%)	53(50%)
Disordered Proliferative Endometrium (DPE)	21 (95.4%)	01 (4.6%)	22 (20.8%)
Proliferative	14 (77.7%)	04 (22.3%)	18 (16.9%)
Fragmented	06 (75%)	02 (25%)	08 (7.5%)
Atrophic	00	03 (100%)	03 (2.9%)
Irregular shedding	02 (100%)	00	02 (1.9%)
Total	**94 (88.6%)**	**12 (11.4%)**	**106 (100%)**

In organic cause most of the cases were in perimenopausal age group (72.7% cases) and 27.3% in postmenopausal age group. In perimenopausal age group leiomyoma and endometrial hyperplasia was commonly seen in 81.3% cases each and all cases of endometrial carcinoma and granulomatous inflammation was seen in in postmenopausal age group (100% cases (Table 3).

Table 3. Distribution of cases according to organic causes (99 cases)

Histopathology	Perimenopausal (% in group)	Postmenopausal (% in group)	Total (Percentage %)
Leiomyoma	26 (81.3%)	06 (18.7%)	32 (32%)
Endometrial Hyperplasia	26 (81.3%)	06 (18.7%)	32 (32%)
Adenomyosis	10 (90.9%)	01 (9.1%)	11 (11%)
Polyp	10 (90.9%)	01 (9.1%)	11 (11%)
Endometrial Carcinoma (Ca)	00	11 (100%)	11 (11%)
Granulomatous Inflammation (Inf)	00	02 (100%)	02 (03%)
Total	72 (72.7%)	27 (27.3%)	99 (100%)

Endometrial hyperplasia were more common in perimenopausal age group 81.3% cases followed by 18.7% in postmenopausal age group. Simple hyperplasia without atypia was most common finding

(88.5%) in perimenopausal age group while simple hyperplasia with atypia were most common in postmenopausal age group (50%) (Figure 1).

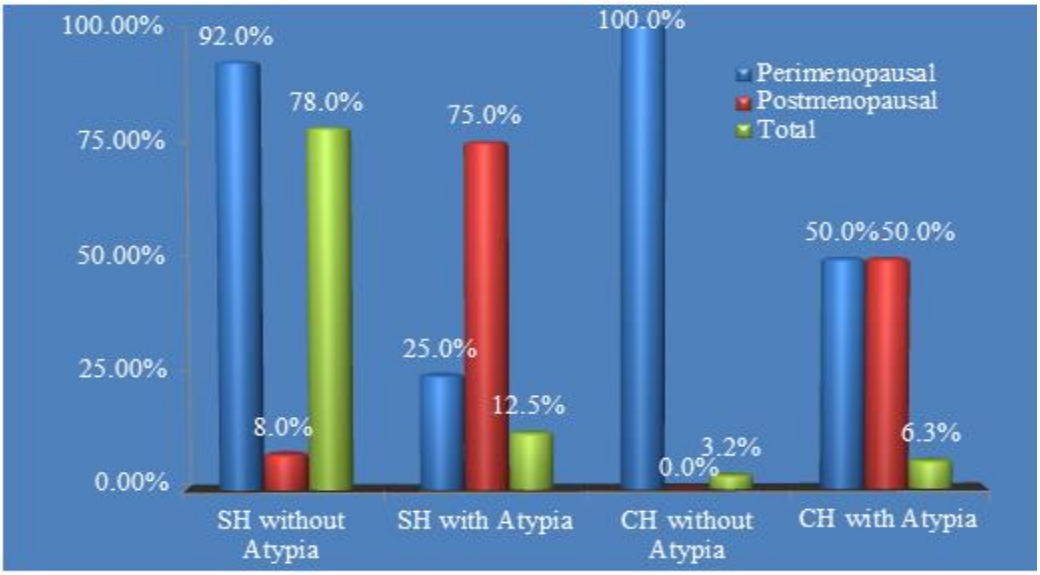

Figure 1. Distribution of cases of endometrial hyperplasia (SH-Simple Hyperplasia; CH-Complex Hyperplasia)

Discussion

Abnormal uterine bleeding at any stage in a woman's life is disruptive and worrisome. Postmenopausal bleeding is of special concern because it is the only common clinical indication for the presence of endometrial carcinoma. Several different approaches have been clinically useful screening methods for early detection of endometrial abnormality in women with irregular uterine bleeding. These include dilatation and curettage (D&C), hysteroscopy, and micro-hysteroscopy. In our study majority of patients were between 40-49 years (72.2%) age group which compared with other studies[15,16] were much higher. The menstrual disorders increase with advancing age. The most common symptoms were menorrhagia (Heavy menstrual bleed) [57.5%] followed by postmenopausal bleeding.[19] Similar findings were also noted by Singh et al[15] and Desai et al[17]. In the present study among causes of AUB; non organic causes contribute maximum (52%) cases followed by organic cause (48%). In concordance to our study, Devi et al[2] found maximum cases 70.4% were of nonorganic origin followed by 22.8% of organic origin.

In the present study, among nonorganic causes, secretory (including shedding change) was the most common in 50% cases followed by 20.8% of DPE and proliferative in 17%. All these pattern was more common in the perimenopausal age group and atrophic endometrium was in postmenopausal age group. Secretory endometrium was present in 96.3% cases of the perimenopausal age group. In concordance to our study Desai et al[17] found that this pattern was more common in perimenopausal age group (95%). In contrast to this study Vaidya et al[18] showed maximum incidence of this pattern in reproductive age group (18-40 years) followed by peri and postmenopausal age groups. Bleeding in the secretory phase is due to ovulatory dysfunction uterine bleeding. This ovulatory bleeding is explained by the inability of the corpus luteum to synthesize adequate amount of progesterone, although it remains active throughout the entire period of 12-14 days. The exact aetiology of ovulatory bleeding can be further clarified by daily serum progesterone assay. Among organic causes, both leiomyoma and endometrial hyperplasia (32% each) were the most common followed by 11% cases each of endometrial carcinoma, adenomyosis and polyp. Only 3% cases of granulomatous inflammation. No case of chronic non-specific endometritis was seen in the present study. All these pattern were common in the perimenopausal age group (88.6%) than postmenopausal (11.4%) except all cases of endometrial carcinoma and granulomatous inflammation (100%) were in postmenopausal age group.

Endometrial hyperplasia is common in perimenopausal women (26 cases out of 32 cases; 81.3%) causing symptom of irregular and prolonged bleeding due to anovulatory cycles in majority of cases. This was consistent with the study by Desai et al[10]. Simple hyperplasia without atypia was the most common finding (92%) in perimenopausal age group while simple hyperplasia with atypia (75%) was the most common in postmenopausal age group whereas complex hyperplasia with or without atypia were common in perimenopausal age group. In concordance to our study Shukla et al and Desai et al (31 out of total 39 cases) found that hyperplasia was common in perimenopausal age group. Shukla et al[19] also showed endometrial hyperplasia was the most predominant pattern in contrast to our study which showed hyperplasia was second predominant pattern, first was secretory (25.8%). Similar observations (16% cases of hyperplasia) were made by Suneet.[20]

In the present study endometrial carcinoma contributes 5.5% of all the cases of AUB. Present study showed that all the cases of endometrial carcinoma were in postmenopausal age group; 11(100%) out of total 205 cases. In contrast to our study lower incidence (2%) of carcinomas were reported by Desai et al[17] and study also showed that all were in postmenopausal age group similar to our study. Shukla et al[19] and Singh et al[15] also reported lower incidence of hyperplasia in 2.38% and 0.94% cases respectively. Out of total 11 cases, 4 cases were of adenocarcinoma including 1 was of serous morphology followed by 3 cases of squamous cell carcinoma, 2 suspicious for adenocarcinoma. 1 each of poorly differentiated and adenosquamous carcinoma.

Endometrial carcinoma most often occurs in women in the sixth and seventh decades of life at an average age of 60 years. Seventy five percent cases occur in women older than 50 years of age and 90% of women with endometrial carcinoma have vaginal bleeding or discharge as their only presenting complaint. Less than 5% of women diagnosed with endometrial cancer are asymptomatic. The incidence of adenocarcinoma is 0.1% per year in postmenopausal women but rises to 10% in presence of abnormal uterine bleeding. In our study there were 2 cases of adenocarcinoma amongst 17 patients with postmenopausal bleeding and none in perimenopausal group.

In our study the histopathological examination revealed significantly more cases of COEIN compartment (51.7%) of AUB while PALM contributes 48.3% cases of AUB. In contrast to our study other studies by Mishra et al[13], Singh et al[21] and Singh et al [22] found maximum cases of AUB belonged to PALM group in 63.98%, 58.3% and 69.4% cases respectively while COEIN contributes 36.01%, 41.7% and 30.6% respectively.

Conclusion

The histopathological evaluation of endometrial curettings and hysterectomy specimens yielded various patterns ranging from physiological to pathological lesions. Endometrial evaluation in different age groups helps in the management, especially in perimenopausal and postmenopausal age groups. As endometrial hyperplasia is a precursor of endometrial cancer, overall risk of progression to cancer being 5-10%. Its identification is important in perimenopausal patients. Occurrence of malignancy increased with increasing age of patients. The PALM COEIN classification system helps us in understanding various etiological causes of AUB and can be used by clinicians and researchers for international comparisons.

Declarations

Acknowledgements: Not applicable
Funding: None
Conflict of interest: None Declared
Ethical approval: Taken

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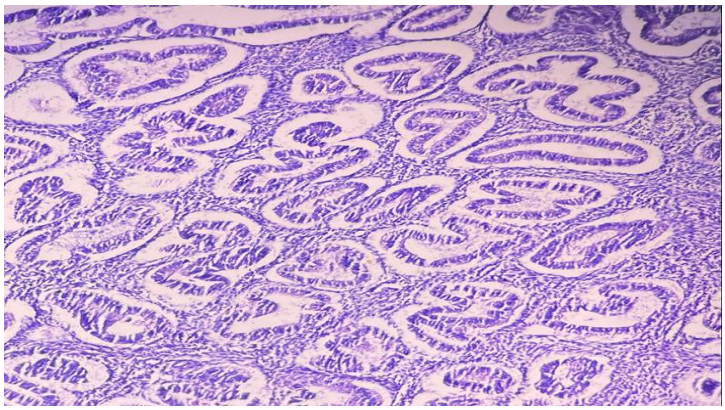

Figure 2. Simple hyperplasia endometrium-(H&E 100X magnification): H&E stained slide (100X magnification) shows tissue section with increased gland to stroma ratio with back to back arrangement of glands.

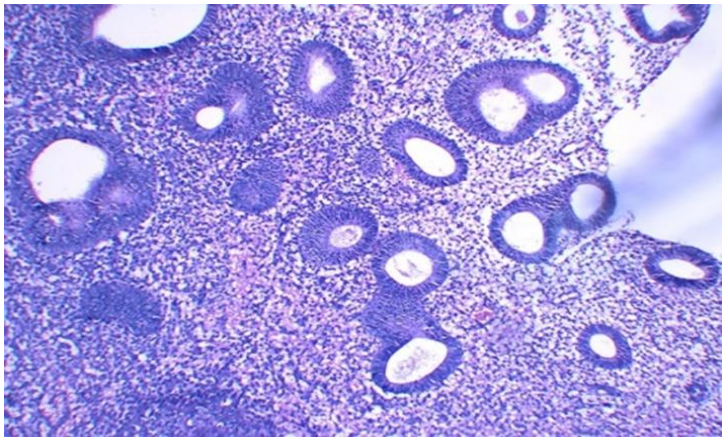

Figure 3. Complex hyperplasia endometrium without atypia-(H&E 100X magnification): H&E stained slide (100X magnification) shows tissue section showing increased gland to stroma ratio.

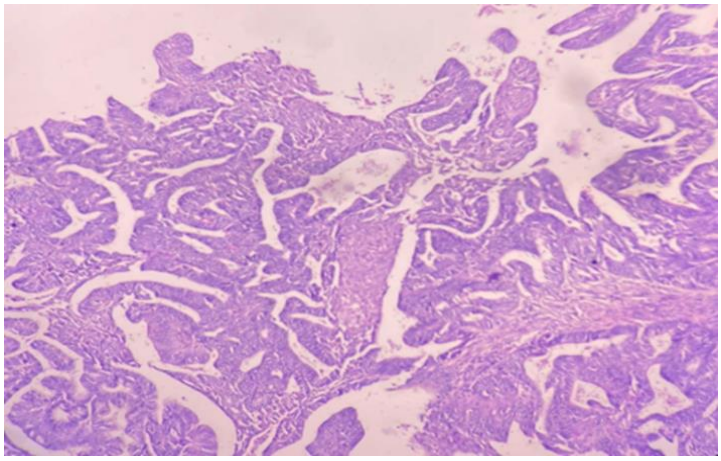

Figure 4. Adenosquamous carcinoma endometrium-(H&E 100X magnification): H&E stained slide (100X magnification) shows tissue section shows adenomatous as well as squamous component.

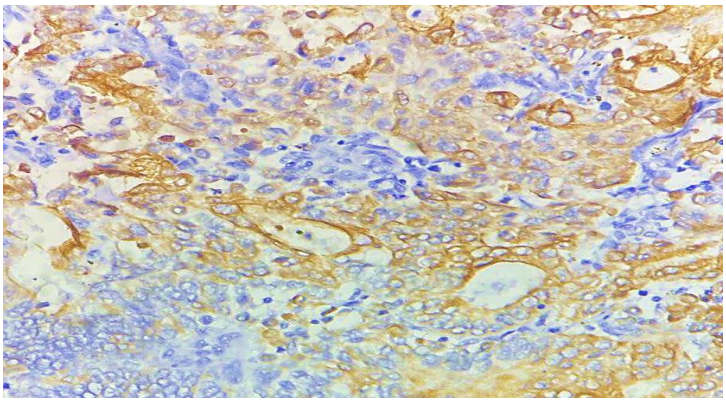

Figure 5. Adenosquamous carcinoma endometrium (100X magnification): Tissue section glands showing cytokeratin cytoplasmic positivity (Cytokeratin IHC 100X)

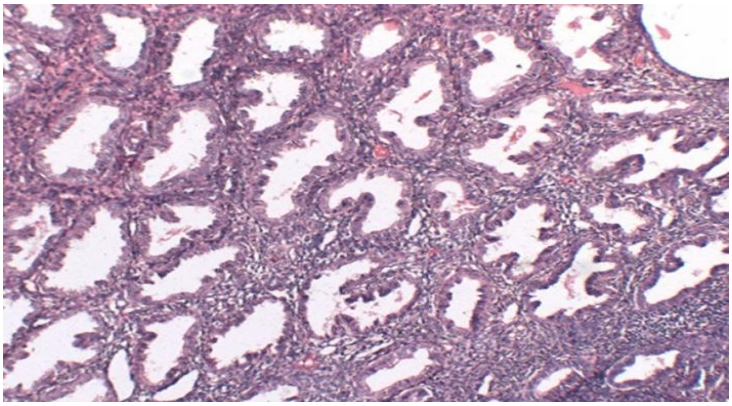

Figure 6. Late secretory phase endometrium-(H&E 200X magnification): H&E stained slide (200X magnification) shows tissue section with sawtooth appearance of glands.

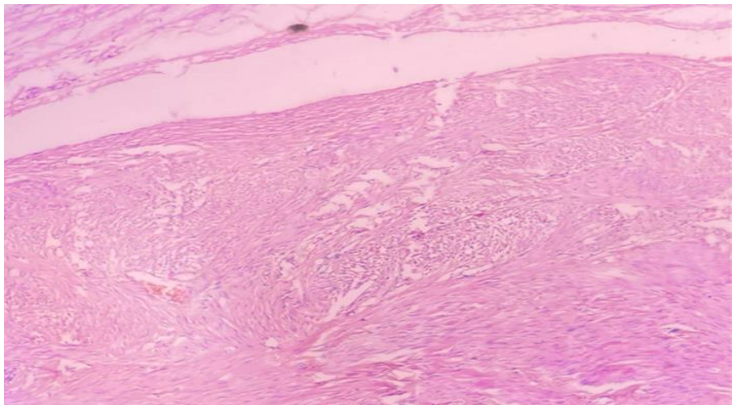

Figure 7. Leiomyoma-(H&E 100X magnification): H&E stained slide (100X magnification) shows Tissue section with well capsulated leiomyoma.

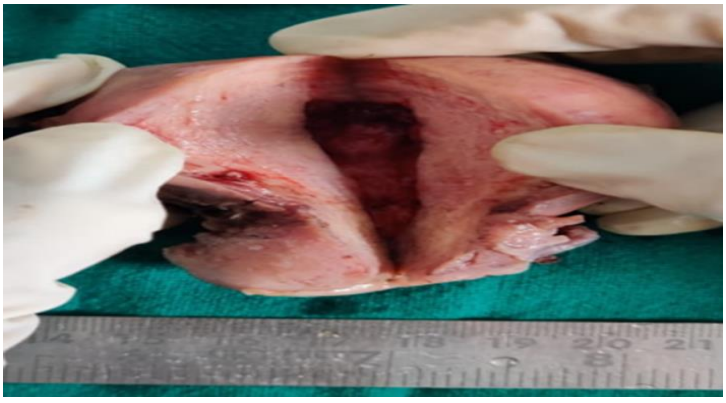

Figure 8. Gross: Simple hyperplasia: Cut section shows thickened endometrium

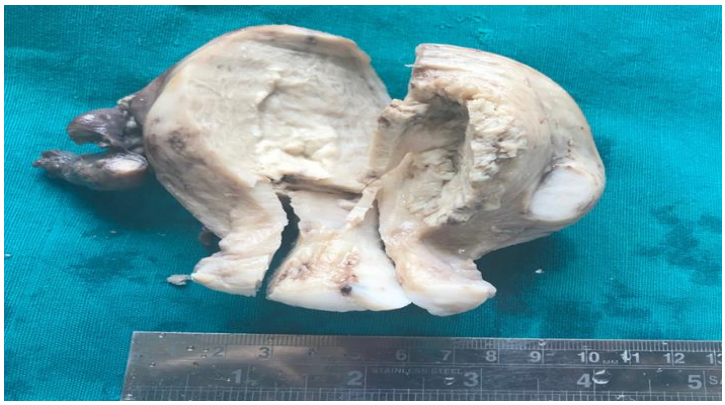

Figure 9. Gross: Endometrial adenocarcinoma: Cut section of uterus showing papillary excrescences arising from uterine cavity.

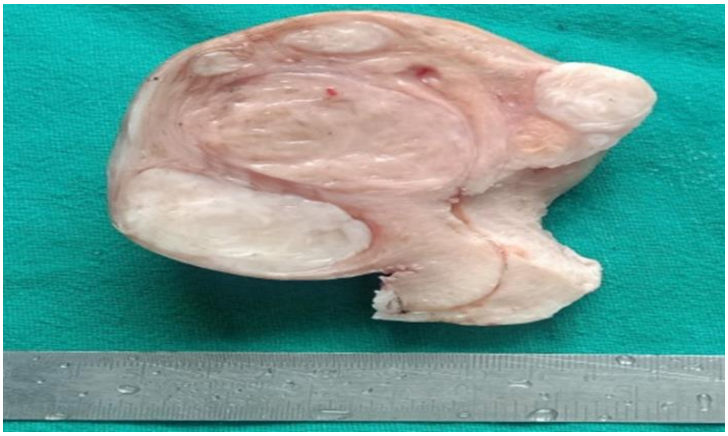

Figure 10. Gross: Uterine leiomyoma: Cut section of uterus shows multiple intramural fibroid arising from myometrium.

Citation: Rathore R, Kundu PR, Siwach S, Agarwal D, Kulhariya A, Singh H, Parul. Histomorphological Profile of Endometrium with Abnormal Uterine Bleeding in Perimenopausal and Postmenopausal Women. Int J Rec Innov Med Clin Res. 2023;5(1):17-26.