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Histopathological Spectrum Of Endomyometrium And Correlation With Mast Cells In Abnormal Uterine Bleeding

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Abstract:
Background*: Abnormal uterine bleeding (AUB) is defined as any uterine bleeding that is more than the normal volume, longer duration and varying in regularity or frequency. Human uterus is considered to be relatively rich in mast cells than other tissues of the body. Myometrium is richer in mast cells compared to endometrium. Mast cells are present in endometrial stroma in fairly constant number throughout the menstrual cycle. Mast cells undergo activation prior to menstruation having a role in regulation of menstruation*.
Materials and Methods*: Uterine hysterectomy specimens sent to histopathology lab of our institution were evaluated, following gross examination, both the endometrium and myometrium in each hysterectomy specimen were histopathologically examined. All specimens were stained with Harris Hematoxylin and Eosin (H&E) stain for routine histological examination and Toluidine Blue for examining the mast cells. Number of mast cells in 10 consecutive high power fields (HPF) were counted in all sections of endometrium and myometrium and tabulated*.
Results*: A total of 110 hysterectomy specimens were examined. The majority of the patients attributing to abnormal uterine bleeding were from perimenopausal age group with menstrual disturbances corresponding mainly to menorrhagia. Mean mast cell count in myometrium were fairly higher in myometrium compared to endometrium.*
Conclusion: *Mean mast cell count varies in different lesions of endometrium and myometrium with significantly higher number in myometrial lesions.*
Key Word: *Endometrium, Myometrium, Mast cells, Abnormal Uterine Bleeding, Hematoxylin and Eosin, Toluidine Blue.*

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I. Introduction

Abnormal uterine bleeding is a deviation from the normal menstrual cycle in terms of duration, volume, frequency, or regularity is a leading cause of gynaecological consultation. It affects up to one-third of women at some point in their lives and spans a wide spectrum of etiology ranging from benign functional disturbances to overt structural pathologies[1]. The International Federation of Gynecology and Obstetrics (FIGO) systems (e.g., PALM-COEIN) have standardized the classification of AUB; however, detailed histopathological characterization is essential for both treatment and prognosis[2].

Mast cells, primarily known for their role in allergy, inflammation, and tissue remodelling, have recently been implicated in the pathophysiology of AUB. These cells release biologically active mediators—such as histamine, cytokines, and proteases—that can influence vascular permeability and uterine contractility, both of which are critical in menstruation and tissue repair[3]. While several studies have reported variable mast cell densities in normal versus pathological uterine tissues, controversy remains regarding their precise distribution in the endometrium versus the myometrium, especially in the context of AUB.

This study aimed to investigate the histopathological spectrum of the endometrium and myometrium in AUB cases and to correlate these findings with the density of mast cells. By elucidating these histological patterns and cellular profiles, we hope to provide insights into the potential mechanistic role of mast cells in abnormal uterine bleeding and pave the way for future targeted therapeutic approaches.

II. Material And Methods

Study design: Hospital-based observational study.

Study place: Department of Pathology, Muzaffarnagar Medical College, Muzaffarnagar (U.P.).

Study population: The cases of Abnormal Uterine Bleeding coming to OPD of Obstetrics and Gynecology undergoing hysterectomy and their hysterectomy specimens sent to Department of Pathology, Muzaffarnagar Medical College for histopathological examination.

Duration of Study: 18 months (12 months for data collection and 6 months for data analysis.)

Sample size: 110 cases were studied

Sampling technique: Purposive.

Study Methods: All AUB cases recommended for hysterectomy and histopathological examination within specific duration of time were evaluated. Histopathological studies of all hysterectomy specimens from 1st january 2023 to 30th june 2024, were taken. Patient's clinical data comprising of clinical features and laboratory investigation reports were collected from year 2023-2024.

Inclusion criteria: All hysterectomy specimens

Exclusion Criteria:
1. Specimens with retained products of conception.
2. Biopsy specimens consisting mainly of autolyzed or necrosed tissue.

Methodology: Following gross examination, both the endometrium and myometrium of hysterectomy specimen were histopathologically examined for uterine lesions. All the cases received were stained with Harris Hematoxylin and Eosin (H&E) stain for routine histological examination and Toluidine Blue stain for examining the mast cells. They were stained with Toluidine blue and analyzed for the mast cells prior to analysis of the uterine tissue for the same. Categorization of the lesions was done on histological grounds. Number of mast cells in 10 consecutive high power fields (HPF) were counted in all sections of endometrium and myometrium and tabulated. Paraffin blocks were made using Leukhart's L moulds and multiple sections were cut by Spencer's rotary microtome. 5-micron thick sections were mounted on the slides for H&E stain.

Statistical analysis and software: Suitable statistical significance tests were used for statistical analysis along with SPSS17/20 statcal2 software. The statistical methods were applied for percentage and mean values which were calculated and compared using Pearson's Chi-square tests, ANOVA one way T-test and calculating the value of significance (*p* value). *p*-value of ≤ 0.05 was considered as statistically significant

III. Result

Patient Demographics and Clinical Presentation: Among the 110 cases, the age distribution is summarized in **Table 1**. The majority of patients (62.7%) were in the 40–49 years age group, with the remainder spanning reproductive (<40 years) and postmenopausal (>50 years) stages. All patients presented with abnormal uterine bleeding; additional symptoms included abdominal pain (8.2%), abdominal lump (9.1%), and other complaints (2.7%).

Table 1. Age Incidence of AUB Cases

Age Group (years)	Number of Cases	Percentage (%)
20–29	4	3.6
30–39	14	12.7
40–49	69	62.7
50–59	17	15.5
60–69	5	4.5
70–79	1	0.9
Total	**110**	**100**

Table 2 indicates that menorrhagia was the most common presentation. Histologically, the endometrium predominantly showed a proliferative phase pattern (45.4%), followed by mid-secretory phase changes (15.5%) and hyperplasia (9.1%). In the myometrium, structural lesions were common: leiomyoma (31.8%), adenomyosis (28.2%), and non-specific pathology (36.4%) were noted.

Table 2 Types of menstrual disturbances encountered:

Menstrual Disturbance	Number of Cases	Percentage (%)
Menorrhagia	44	40.0
Dysmenorrhea	25	22.7
Polymenorrhea	12	10.9
Metrorrhagia	3	2.7
Postmenopausal Bleeding	26	23.6
Total	**110**	**100**

Table 03 shows mast cell distribution across different endometrial changes. The highest mean mast cell count was in the late secretory phase (8.33), followed by mid secretory phase (7.88), and hyperplasia (7.8). Biphasic endometrium (7.17) and proliferative phase (7.7) also showed significant mast cell infiltration. Lower counts were seen in cystic atrophy (5.67), and endometrial polyp (4.86, total 34), with endometritis (5.0, total 25) having the least mast cell presence. The proliferative phase recorded the highest total mast cell count (311 cases), reinforcing the role of mast cells in endometrial remodeling and inflammation in AUB pathogenesis.

Mast cell counts varied with the histological phase and lesion type. In the endometrium, the distribution is summarized in **Table 3**.

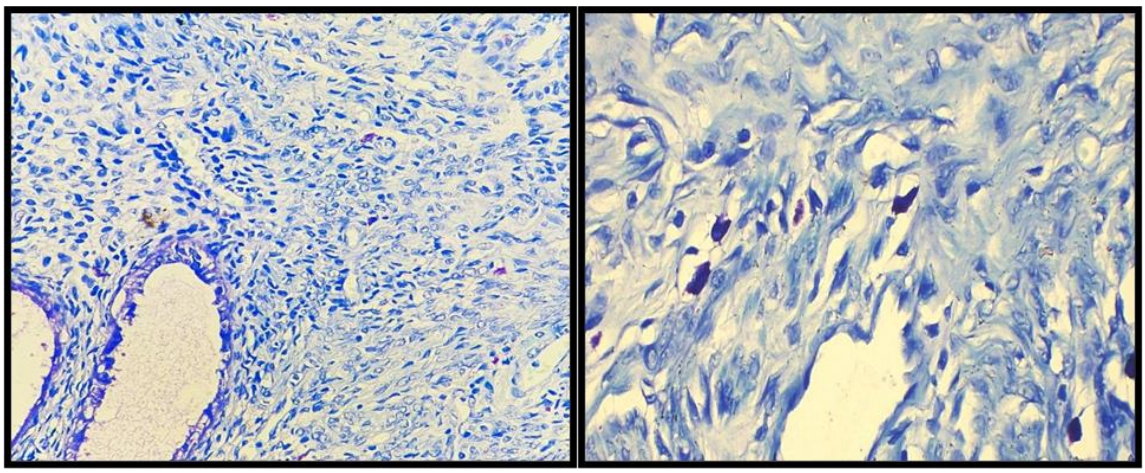
Table 3. Mean Mast Cell Count in Endometrial Changes (per 10 HPF)

Endometrium changes	Number of cases	Total Mast cell count	Mast cells range	Mean Mast cell count
Early secretory phase	1	1	0-1	1
Mid Secretory Phase	17	134	1-15	7.88
Late secretory phase	3	25	5-14	8.33
Proliferative phase	50	385	1-14	7.7
Biphasic	6	43	4-9	7.17
Endometritis	5	25	1-11	5
Atrophic endometrium	8	51	1-11	6.38
Endometrial Polyp	7	34	2-8	4.86
Hyperplasia without atypia	05	78	2-8	7.8
Hyperplasia with atypia	05	78	2-8	7.8
Cyst Atrophy	3	17	1-3	5.67

Table 04 presents mast cell distribution in myometrial changes. Leiomyoma had the highest mean mast cell count (78), followed by necrosed blood vessels (76.3) and no specific pathology (67.5). Adenomyosis showed the lowest mean count (65.2). These quantitative findings reveal a statistically significant variation between different lesions ($p < 0.05$) [4].

Table 4. Mean Mast Cell Count in Myometrial Lesions (per 10 HPF)

Myometrium changes	Number of cases	Total Mast cell count	Mast cell range	Mean Mast cell count
Adenomyosis	31	2022	01-14	65.2
Leiomyoma	35	2729	01-30	78
Necrosed blood vessels	4	305	01-11	76.3
No specific pathology	40	2700	01-19	67.5



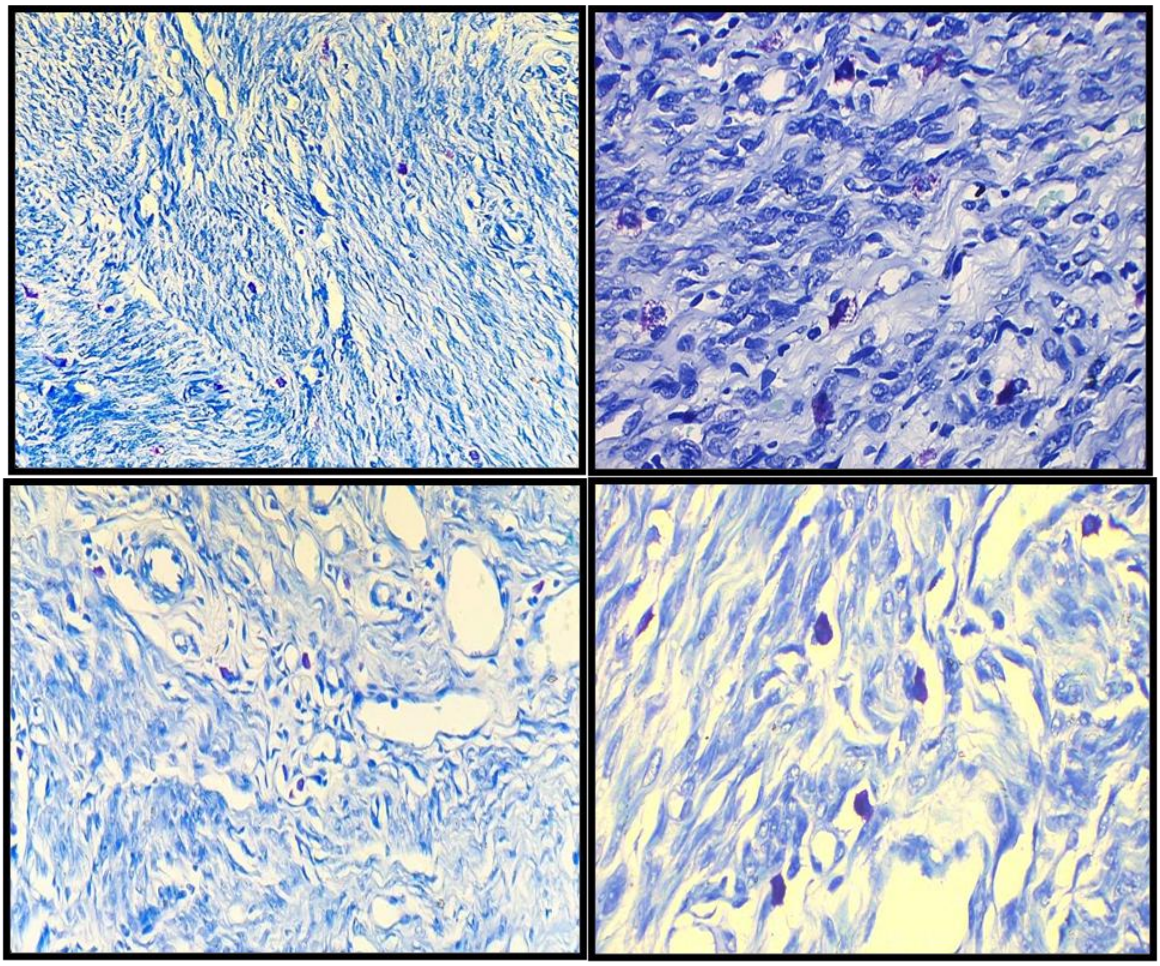


FIGURE 1.

1. Mast cells in endometrium, (Toluidine blue stain, 40X)
2. Mast cells In Endometrium, Toluidine Blue Stain 100X
3. Mast cells In Myometrium, Toluidine Blue Stain 40X
4. Mast cells In Myometrium, Toluidine Blue Stain 100X
5. Mast cells In endomyometrial junction, (Toluidine blue stain, 40x)
6. Mast cells In endomyometrial junction, (Toluidine blue stain, 100x)

IV. Discussion

Our study, **"Study of Histopathological Spectrum of Endomyometrium and Its Correlation with Mast Cells in Abnormal Uterine Bleeding,"** focused on understanding the histopathological changes in the endometrium and myometrium in cases of abnormal uterine bleeding (AUB).

Since AUB is one of the most common gynecological complaints, investigating its underlying causes is crucial[4].

Mast cells, known for their role in inflammatory and vascular processes, were analyzed to assess their potential contribution to the pathogenesis of AUB. Studying their distribution in different endometrial and myometrial lesions helps in understanding their role in menstrual regulation and abnormal bleeding patterns.[5]

This study confirms that AUB is most prevalent in perimenopausal women in our research study conducted that demonstrates increasing incidence with age. The predominance of menorrhagia—with 40% of cases—and the corresponding proliferation phase in the endometrium underscores the complex interplay between hormonal regulation and tissue response[6]. Importantly, the histopathological examination revealed that nearly half of the cases (45.4%) maintained a normal proliferative pattern, while other cases showed secretory phase alterations, hyperplasia, or atrophic changes. These findings are in agreement with prior studies where proliferative endometrium was frequently observed in AUB.

Mast cells, known for their role in inflammation, were found to vary across different histological phases and lesions. In the endometrium, higher counts in the late secretory phase may be linked to increased local degranulation and mediator release prior to menstruation. In contrast, lower mast cell counts in conditions such as endometrial polyps and endometritis suggest a differential inflammatory milieu[5]. Among myometrial lesions, leiomyomas exhibited the highest mast cell count. Previous studies have similarly demonstrated increased mast

cell densities in leiomyomatous tissues, which may contribute to enhanced angiogenesis and fibrosis through the release of tryptase and other mediators[5].

In our study, we found that the majority of patients with abnormal uterine bleeding (AUB) belonged to the perimenopausal age group (40-49 years), accounting for 69 cases (62.72%), followed by the postmenopausal group (>50 years) with 23 cases (20.90%) and the reproductive age group (<40 years) with 18 cases (15.38%). Chi square test was applied and a statistically significant association ($p < 0.001$) was observed, indicating a strong correlation between increasing age and AUB occurrence.

In our study, menorrhagia was the most common menstrual disturbance, affecting 44 cases (40%), followed by postmenopausal bleeding (26 cases, 23.63%), dysmenorrhea (25 cases, 22.75%), polymenorrhea (12 cases, 10.90%), and metrorrhagia (3 cases, 2.72%). A statistically significant correlation ($p < 0.001$) was found, confirming that menorrhagia is the predominant clinical presentation in AUB cases.

Our study also closely matches Sharma et al[8]. where menorrhagia was found in 38.92% of cases, dysmenorrhea was reported in 14.00% of cases, polymenorrhea accounted for 3.59% of cases, postmenopausal bleeding was observed in 6.89% cases.

Our findings are strongly aligned with Suneja P, Saldanha P[8], where menorrhagia was also the most frequent symptom, found in 35 cases (55.56%) while dysmenorrhea (4.76%) and menorrhagia prevalence was (55.56%). A statistically significant association ($p < 0.001$) highlights that heavy menstrual bleeding / menorrhagia is the predominant clinical presentation in AUB.

In our study, we evaluated mast cell density in different endometrial patterns and found that the highest mean mast cell count was seen in the late secretory phase (8.33), followed by mid secretory phase (7.88), and hyperplasia (7.80) and proliferative phase (7.7). The lowest mast cell counts were observed in endometrial polyp (4.86) and cyst atrophy (5.67). However, the ANOVA test ($p = 0.807$) indicated no statistically significant correlation between mast cell counts and endometrial changes.

Our findings correlate well with Renuka M.Patil[9], who found that mast cell counts in the endometrium varied across menstrual phases, with maximum mean mast cell count 19.43 /10hpf in secretory phase followed by proliferative phase with mean mast cell count of 12.43/ 10hpf.

In our study, we found that leiomyoma (35 cases, 31.8%) was the most frequent histopathological finding in the myometrium, followed by adenomyosis (31 cases, 28.2%), no specific pathology (40 cases, 36.4%), and necrosed blood vessels (4 cases, 3.6%). A statistically significant correlation ($p < 0.001$) was observed between myometrial pathology and AUB, indicating that structural abnormalities like leiomyoma and adenomyosis play a major role in the etiology of AUB.

Our findings reported that leiomyoma and adenomyosis were the most common myometrial abnormalities in AUB patients. Similarly, Sharma et al[7]. emphasized that leiomyomas and adenomyosis were among the most frequent causes of AUB, reinforcing our findings.

Thus, our study strongly aligns with Sharma et al[7].confirming that leiomyoma and adenomyosis are the most common histopathological findings in AUB patients. The discrepancies in no-specific pathology prevalence between our study and MN Singh et al[10.] may be attributed to variations in study populations, diagnostic criteria, and histopathological evaluation methods.

The correlation between mast cell density and specific histopathological patterns in both the endometrium and myometrium suggests that these immune cells could be integral in the pathogenesis of AUB. Their secretory products may alter vascular tone and promote extracellular matrix remodelling, thereby contributing to abnormal bleeding. Although the study is limited by its observational design and the inherent biases of case selection, the results support the notion that mast cells are not merely bystanders but active participants in the uterine microenvironment of AUB patients.

Future investigations could focus on the molecular pathways that regulate mast cell activation in uterine tissues. Moreover, therapeutic strategies—such as mast cell stabilizers—may be explored as adjuncts in managing AUB cases that show high mast cell infiltration.

V. Conclusion

This study demonstrates that in AUB patients, the most common histopathological finding in the endometrium is a proliferative pattern, primarily in perimenopausal women. Mast cell counts vary significantly among different lesions; notably, leiomyomas in the myometrium exhibit the highest mast cell density, suggesting a role in the pathogenesis of AUB. Targeted histopathological evaluation inclusive of mast cell profiling may enhance diagnostic accuracy and could hint at potential therapeutic interventions aimed at modulating inflammatory mediators. Overall, these findings stress the multifactorial nature of AUB and underline the need for further research into mast cell–mediated pathways in uterine pathology.

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