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Spectrum of histomorphological pattern of endometrium in different age groups in abnormal uterine bleeding in a tertiary care centre of western Uttar Pradesh

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***Abstract*---**Objectives: The aim of the study was to find out the histomorphological pattern of endometrium in different age groups presenting with abnormal uterine bleeding. Methods: This is a hospital based cross - sectional study which was performed on 569 cases (120 endometrial curettings and 449 hysterectomy specimens) received in department of pathology NCR Institute of Medical Sciences, Meerut during a period of two years (1st august 2020 to 31st july 2022). Specimens were fixed in 10% formol saline, routine processing was done and sections were stained with haematoxylin and eosin stain (H&E stain). Results were expressed as percentages and p value was calculated. Results: The age range of these patients was from 25-75 years with mean age of 43 years. Majority of patients were in the perimenopausal age group.The most common pattern in reproductive age group was secretory phase (51.28%) whereas in

perimenopausal females it was proliferative phase (68.04%) and in post menopausal females it was atrophic phase (84.85%). Precancerous lesions such as endometrial polyp and endometrial hyperplasia was dominant in perimenopausal age group. Conclusions:- Abnormal Uterine Bleeding is a common cause of morbidity amongst woman of all age groups. Spectrum of endometrium varies in different age groups from cyclical endometrium to carcinoma. Therefore, histopathological examination of endometrium remains gold standard for early diagnosis and treatment of these cases.

***Keywords*---**abnormal uterine bleeding, spectrum histomorphological pattern, endometrium.

Introduction

The endometrium is a dynamic, hormonally sensitive and responsive tissue that is uniquely endowed throughout the female reproductive lifespan with complex of periodic proliferation, differentiation, breakdown and regeneration. Menstruation is the physiologic shedding of the endometrium, associated with uterine bleeding that occurs at monthly intervals from menarche to menopause.[1] Abnormal uterine bleeding (AUB) is defined as changes in frequency of menstruation, duration of flow or amount of blood loss.[2] Normal menstruation is defined as bleeding from secretory endometrium associated from an ovulatory cycle not exceeding a length of 8 days. According to Munro MG[3] AUB is defined as prolonged bleeding for more than 8 days and bleeding volume sufficient to interfere with the womens quality of life. AUB occurs in 9 to 14% of women of all age groups between menarche and menopause, significantly impacting quality of life.[4] The causes of abnormal uterine bleeding (AUB) include a wide spectrum of diseases of the reproductive system and non-gynaecologic causes as well. It might be part of normal physiological state such as adolescence, perimenopausal, lactation and pregnancy or it may be caused by a pathological process that is not directly related to the uterus such as hyper andreogenic and ovulation in patients with polycystic ovaries, hypothalamic dysfunction, hyperprolactinemia, hypothyroidism, pituitary disease, premature ovarian failure and iatrogenic causes such as irradiation or tumour.[5] AUB after the age of 40 years requires further evaluation to exclude endometrial polyp, hyperplasia, fibroid or carcinoma.[1,2,6] In about 25% of the patients, the abnormal uterine bleeding is the result of a well defined organic abnormality.[7] It can be associated with endometrial carcinoma in approximately 10% of the cases and its precursor lesions. The aim of the study was to find out the histomorphological pattern of endometrium in different age groups presenting with abnormal uterine bleeding.

Material and Methods

This is a hospital based cross - sectional study which was performed on 569 cases (120 endometrial currettings and 449 hysterectomy specimens) received in department of pathology NCR Institute of Medical Sciences, Meerut during a period of two years (1st august 2020 to 31st july 2022).

Inclusion criteria- All endometrial currettings and hysterectomy specimens were included in the study.
Exclusion criteria- Specimens received as products of conception, inadequate samples consisting of blood clots and mucous were excluded from the study.
Demographic data like age of the patient, menstrual history was recorded. Specimens were fixed in 10% formol saline, routine processing was done and sections were stained with haematoxylin and eosin stain (H&E stain).

Statistical analysis

Descriptive statistics was applied for demographic data and represented as percentage. Chi square test was applied to calculate the p value. p value of <0.05 was accepted as statistically significant.

Results

Table (1)- age wise distribution of the cases

Age Groups	No. of cases	Percentage %
<40 Years	151	26.54
40–50 Years	334	58.70
>50 Years	84	14.76
Total	569	100.00

The age range of these patients was from 25-75 years with mean age of 43 years. Majority of patients were in the perimenopausal age group.

Table (2)- Distribution of cases according to age and type of menstrual disturbance

Menstrual disturbances	Age Groups						P Value *
	<40 years		40–50 years		>50 years		
	No of cases	Percentage (%)	No. of cases	Percentage (%)	No of cases	Percentage (%)	
Menorrhagia	58	38.41	130	38.92	0	0.00	<0.001
Metrorrhagia	29	19.20	52	15.57	0	0.00	
Menometrorrhagia	13	8.61	34	10.18	0	0.00	
Polymenorrhagia	15	9.93	27	8.08	0	0.00	
Polymenorrhoea	4	2.65	12	3.59	0	0.00	
Postmenopausal bleeding	0	0.00	23	6.89	84	100.00	
Dysmenorrhoea	26	17.22	47	14.00	0	0.00	
Amenorrhoea	3	1.99	5	1.50	0	0.00	
Absent	3	1.99	4	1.20	0	0.00	
Total	151	100.00	334	100.00	84	100.00	

X^2 Chi-square test applied. **Statistically significant difference between menstrual disturbances and age groups <0.001

Table (3)- Histopathological status of the endometrium

S.No	Histopathological status of endometrium	No of cases	Percentage (%)
1.	Proliferative	291	51.14
2.	Secretory	78	13.71
3.	Atrophic endometrium		
	Atrophic inactive	66	11.60
	Atrophic/Non inactive	40	7.03
		131	23.02
	Mixed atrophic	13	2.28
	Cystic atrophic	12	2.11
4.	Chronic endometritis	09	1.58
5.	Endometrial polyp	18	3.16
6.	Endometrial hyperplasia		
	Simple hyperplasia with atypia	00	0.00
	Simple hperplasia without atypia	28	4.92
		40	7.03
	Complex hyperplasia with atypia	05	0.88
	Complex hyperplasia	07	1.23
7.	Endometrial carcinoma	02	0.36
	Total	569	100.00

The most common histopathological pattern was proliferative phase of endometrium followed by atrophic endometrium.

Table (4): Comparison of endometrial histopathology in Reproductive, Perimenopausal and postmenopausal age groups

S. No	Histopathology of Endometrium	No of cases	Reproductive age group (<40 years)	Peri-menopausal (40-50 years)	Post-menopausal (>50 years)	P-Value*
1	Proliferative	291	90 (31.62%)	198 (68.04%)	1(0.34%)	<0.001
2	Secretory	78	40(51.28%)	3848.72%)	–	<0.001
3	Atrophic endometrium					
	Atrophic	66	–	10 (15.15%)	56(84.85%)	<0.001
	Atrophic/Non inactive	40	5(12.5%)	32(80.0%)	3(7.50%)	<0.001
	Mixed atrophic	13	–	6(46.15%)	7(53.85%)	<0.001
	Cystic atrophic	12	–	7(58.33%)	5(41.67%)	<0.001
4	Chronic endometritis	9	3(33.33%)	3(33.33%)	3(33.33%)	1.00
5	Endometrial polyp	18	2(11.11%)	14(77.78%)	2(11.11%)	<0.001
6	Endometrial hyperplasia					
	Simple hyperplasia with atypia	0	–	–	–	–

	Simple hyperplasia	28	6(21.43%)	17(60.71%)	5(17.86%)	<0.001
	Complex hyperplasia with atypia	5	2(40.0%)	3(60.0%)	–	<0.001
	Complex hyperplasia	7	1(14.29%)	6(85.71%)	–	<0.001
7	Endometrial carcinoma	2	00	00	2(100%)	<0.001
	Total	569	151	334	84	

X^2 Chi-square test applied. Statistically significant difference for uterine lesions in different age groups $p<0.001$. A statistically significant difference was observed for the prevalence of endometrial lesions among the different age groups (Table 4).

Discussion

The human reproductive system has remained a subject of fascination for centuries owing to its uniqueness as well as vulnerability towards a wide spectrum of benign and malignant diseases. In the present study 569 cases presenting with abnormal uterine bleeding were analysed. Age range of 25-75 years with mean age of 43 years which was comparable to the mean age of 41 years reported by Agarwal et al.[6] These patients were categorised into 3 categories reproductive (<40 years), perimenopausal (40-50 years) and post menopausal (>50 years). A majority of females belong to the perimenopausal age group (58.70 %) followed by reproductive age group (26.54 %) and the post menopausal bleeding age group (14.76 %). A large number of workers in the past[1,6-14] also reported maximum number of cases in perimenopausal age groups (41-50 years).

The reason for increased incidence of abnormal uterine bleeding in premenopausal age group (41–50 years) may be attributed to the fact that these patients are in their climacteric period. As women approach menopause, cycles shorten and often become intermittently anovulatory due to a decline in the number of ovarian follicles and the estradiol level.[7] Another reason maybe that AUB without structural pathology is more common in reproductive age group while the causes of bleeding in the perimenopausal and postmenopausal women are hormonal or associated with local pathology including malignancy, benign tumours and infections.

Among the different types of menstrual disturbances, menorrhagia was the most prominent (33.045) followed by postmenopausal bleeding (18.81%), metrorrhagia, (14.24%), menometrorrhagia (8.26%), polymenorrhagia (7.38%), polymenorrhoea (2.81%) and amenorrhoea (1.41%). While in other studies menorrhagia was predominantly confined to perimenopausal age,[6,11,15-19] in the present study no marked difference was observed in the reproductive and premenopausal age groups. Jairajpuri et al[15] also reported menorrhagia as the most common presenting complaint accounting for 41% patients with most of them in the 41-50 year age group gradually increasing from the 21-30 year age group. Moghal[8] also reported an incidence of 41%. Other studies have also found menorrhagia as the most common complaint with varying prevalence between 25.9% and 50.25%.[6,16-20]

The most predominant histopathological finding in this study showed normal physiological phases. Proliferative phase was present in 51.14% cases followed by atrophic endometrium in 23.02% and secretory phase in 13.71% cases. Our findings were consistent with a large number of workers who reported that the proliferative phase was the most prevalent finding in patients with AUB[1,2,7,20,22,49] while others observed secretory phase to be most common histological finding.[5,15,19,20] The proliferative and secretory phases were more prominent in the reproductive and perimenopausal age groups while atrophic endometrium was the most common finding in the postmenopausal age group.

This study also significantly revealed that the occurrence of endometrial pathology increases with increasing age with maximum number of cases of endometrial polyp and endometrial hyperplasia were in the perimenopausal age group (40-50 years) while 2 cases of endometrial carcinoma observed in this study were in postmenopausal age group (>50 years). Similar trends were also reported in other studies with the highest prevalence of uterine lesions in the perimenopausal age group.[1,2,5-7,15,19] The lower incidence in the postmenopausal age group may be attributed to the fact that usually by this age the uterine lesions are diagnosed and adequately treated. Non specific endometritis is a histopathologic lesion that may be the consequence of a variety of bacterial and nonbacterial insults to the endometrium.[23]

In the present study, chronic endometritis was found in 9 cases with equal distribution of cases in all the three age groups. Eight out of nine cases were associated with menstrual irregularities like menorrhagia, metrorrhagia, polymenorrhagia, postmenopausal bleeding, dysmenorrhoea and uterine tenderness. These findings were consistent with those of Greenwood and Moran[23] who reported some sort of vaginal bleeding in 94% of endometritis. The detection rate of chronic endometritis in this study was lower compared to other reports. In the study by Sarfaraz and Tariq[24] on patients presenting with menorrhagia, chronic endometritis was seen in 3% cases. Jairajpuri et al.[15] diagnosed endometritis in 39 cases (6.1%) with a higher detection rate in the 41-50 year age group (51.2%). Doraiswami et al,[7] Damle et al,[16] Solapurkar,[19] Mirza et al[25] found chronic endometritis in 4.2%, 5.68%, 2.68% and 13.0% cases respectively. On the other hand Sajitha et al[26] reported an incidence of only 0.64%. No specific infection like tuberculosis was noted in any case in the present study which was similar to the findings of Sharma et al.[27]

Endometrial polyps were seen in 18 cases (3.16%) in the present study which was comparable to Dhamle et al.[16] Lower incidence of the endometrial polyps in the younger age group may be attributed to a possible spontaneous regression mechanism, which is characteristic of the cycling endometrium in reproductive age group.[7] Although the etiology and pathogenesis of the endometrial polyps are not understood, it is believed that they are generally estrogen-dependent lesions with higher concentrations of estrogen and progesterone receptors observed in the glandular epithelium in endometrium of women with endometrial polyps.[28] A polyp should always be considered if abnormal bleeding persists after curettage, because a polyp on delicate pliable stalk maybe easily missed by the curette.[29]

Atrophic endometrium (84.85%) was seen predominately in the >50 years age group and was the most common cause of bleeding in postmenopausal age. Choo et al[30] also observed that atrophic endometrium was a predominant cause of postmenopausal bleeding with an incidence of 82%. However, a variation in the incidence of atrophic endometria in postmenopausal bleeding patients from 5.12% to 82% has been reported in the literature.[31,32]

Atrophy of endometrium occurs as a consequence of the prolonged absence of any endogenous or exogenous estrogenic stimulation. The thin atrophic endometrium is susceptible to minor injury and thus may be responsible for postmenopausal bleeding even in the absence of an identifiable lesion. Superficial large, dilated venules are situated under a thin endometrium which may rupture to cause excessive uterine bleeding.[1,7,33,34] Other etiological factors of postmenopausal bleeding from the atrophic endometrium postulated may be atrophic endometritis, vitamin deficiency, chronic passive congestion of the uterus, blood dyscrasias and anticoagulation, endometrial capillary or venous modifications or systemic diseases like atheroscelerosis, hypertension and diabetes.[35]

Overall incidence of hyperplastic endometrium observed in this study was 7.03% out of which 28 (4.92%) cases were of simple hyperplasia, 7 cases (1.23%) of complex hyperplasia and 5 (0.88%) cases of complex hyperplasia with atypia. The frequency was higher than reported by Agrawal et al[6] and Jairajpuri et al[15] who reported a low incidence and concluded that 4.75% and 5.79% of abnormal uterine bleeding was diagnosed as precursor lesions. Other workers have found an incidence of 7.7% to 26.18% of hyperplastic endometrium in post menopausal patients with or without bleeding problems.[5,19]

Identification of endometrial hyperplasia is important because they are precursor of endometrial cancer.[4] The risk is especially seen with atypical endometrial hyperplasia which carries the risk of associated endometrial carcinoma more than hyperplasia without atypia.[4] Kurman et al[36] observed that the progression to carcinoma occurred in 1% of patients with Simple Hyperplasia, 3% of patients with Complex Hyperplasia, 8% of the patients with Simple Hyperplasia with Atypia, and in 29% of the patients with Complex Hyperplasia with Atypia. The risk of coexistent cancer may be as high as 20-50%, leading some authors to recommend that all women with atypical hyperplasia should receive definitive surgical management. In this study only 02 cases (0.36%) of endometrial carcinoma were observed. Incidence of endometrial carcinoma ranged from as low as 0.47%[15] to as high as 17.6%.[37] The most common clinical presentation in these patients was postmenopausal bleeding which was similar to the findings of other authors.[8,18,30,37]

Conclusion

AUB is a common cause of morbidity amongst woman of all age groups. Histopathological examination of endometrium remains gold standard in diagnosing these cases and excluding the possibility of precancerous lesions in advancing age groups. Early diagnosis and treatment in these cases prevents progression to cancer.

Ethics approval and consent to participate

Institutional ethics clearance was taken before starting the study and written and informed consent was taken from the patients participating in the study.

Competing interest
There is no competing interest.

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NIL

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