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Research Article

Study of Clinicopathological Features in Perimenopausal Women with Abnormal Uterine Bleeding (M).

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Background: Abnormal uterine bleeding (AUB) is the most common health issue in women, defined as any bleeding pattern that differs in frequency, duration, and amount. AUB(M) is when the cause is due to malignancy or hyperplasia. Endometrial sampling and its histopathological examination is the first-line test in patients presenting with AUB(M). The aim of this study was to analyse the histopathological patterns of endometrium in women with AUB(M) and to find the predominant histopathologic pattern in perimenopausal women with AUB.
Methods: The cross-sectional study was conducted at the JSS Medical College , mysore, from November 2019 to June 2021. Endometrial biopsies of patients with AUB(M), in whom other causes were ruled out, were included in this study.
Results: Our analysis showed that maximum women were in the age group of 41 to 45 years (38.6%) with Heavy menstrual bleeding, being the most common clinical presentation (72.9%). 75.7% of the women on whom the Ultrasound scan was done, showed Endometrial thickness >12mm. Non-atypical Endometrial hyperplasia (50%) was the most common type of endometrial hyperplasia diagnosed on histopathology, followed by proliferative change(30%). Histopathological findings also included 1 case of endometrial adenocarcinoma.
Conclusion: Although a regular cyclical pattern is observed commonly, endometrial sampling should be considered in the peri menopausal age groups wherein the incidence of endometrial hyperplasia and endometrial carcinoma is more common.

Keywords: Abnormal uterine bleeding, Endometrium, Endometrial biopsy, Endometrial carcinoma, Hyperplasia.

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INTRODUCTION

Abnormal uterine bleeding (AUB) is defined as any bleeding pattern that differs in frequency, duration, and amount from a pattern observed during normal menstrual cycles or menopause. In addition; it is also the commonest cause of iron deficiency anaemia and chronic malaise around the world. It is a disorder which is both medically and socially debilitating.[1] AUB is due to several factors deranging homeostasis like hormonal imbalances, infections, structural lesions, and malignancy. Based on these possible underlying etiologies, the International Federation of Gynaecology and Obstetrics (FIGO) in 2011 devised a classification named PALM-COEIN for the etiology of AUB. PALM accounts for structural features like polyps, adenomyosis, leiomyoma, and malignancy. COEIN addresses non-structural causes like coagulation defects, ovulatory dysfunction, endometrial causes, iatrogenic causes, and non-classified ones.[2] Endometrial biopsy is used as a diagnostic aid in AUB. It is done as a first-line test in women >45 years of age presenting with AUB.[3] The present study was done to determine the histopathological spectrum of endometrium in women presenting with abnormal uterine bleeding.

Primary Objective:
To evaluate the clinic-pathological features of abnormal uterine bleeding in perimenopausal women.

Materials And Methods

Study Design: This is a cross sectional study conducted in the department of OBG in a tertiary care hospital over a period of 1.5 years from November 2019 to June 2021 with the approval from Ethical Committee.

The clinical data were obtained from history taking which included the history of presenting complaints, duration of cycles, flow, passage of clots, intermenstrual bleeding, unscheduled bleeding, age at menarche, any important obstetric history, physical examination, after which ultrasound pelvis with endometrial thickness is assessed whenever she presents with the complaints of AUB.

Those with structural causes such as fibroids, polyps, adenomyosis and non-structural causes (such as Coagulopathy, Ovulatory and Iatrogenic) were excluded. A total of 70 patients were included in this study.

Then, endometrial specimens obtained from endometrial biopsy and curettage from those satisfying the inclusion criteria were put in 10% formalin and sent to histopathology lab, for formalin fixation and staining with Haematoxylin and Eosin stains (H and E). These slides were examined by pathologist and reported according to the WHO 2014 classification.
The data was analysed and percentage for each category calculated. Summary statistics done by measuring the mean and standard deviations and inferential statistics done using Chi square test. All analysis was done by SPSS software 21.0 with P value <0.05 considered as significant.

RESULTS

Table1: Distribution of Age group among the study subjects

		N	%
Age group	Lessthan40years	20	28.6%
	Between41to45Years	27	**38.6%**
	Between46to50Years	20	28.6%
	Morethan50years	3	4.3%

Patients with AUB ranged from 38 to 52 years. Based on their age, the patients were categorized into 4 categories. In this study, maximum number of study subjects were in the age group of 41 to 45 years (38.6%).

Table2: Distribution of Mean age of menarche among study subjects

	Mean(years)	Standard Deviation
MENARCHE	12.16	1.10

mean age of menarche at 12.16 $\pm$ 1.10 years of age.

Table3: Distribution of study subjects based on the complaints at the time of presentation

		N	%
COMPLAINTS	Heavy menstrual bleeding	51	72.9%
	Heavy menstrual bleeding + dysmenorrhea	12	17.1%
	Inter menstrual bleeding	7	10.0%

In the present study nearly 72.9% of them presented with Heavy menstrual bleeding symptoms at the time of presentation.

Table 4: Distribution of study subjects based on the parity

		N	%
Parity	Multiparous	55	78.6%
	Nulliparous	15	21.4%

In the present study, nearly 78.6% of the study subjects were multiparous and 21.4% were nulliparous.

Table 5: Distribution of Mean height, Weight and BMI among study subjects

	Mean	**Standard Deviation**
HEIGHT(m)	156	4
WEIGHT(kg)	67	7
BMI (kg/m^2)	27.8195	3.2947

The mean BMI in the study was **27.8kg/m^2**, with more than **80%** belonging to the category of BMI >25kg/m^2.

Table 6: Distribution of study subjects based on the Endometrial Thickness

		N	**%**
ET	Less than equal to12mm	17	24.3%
	More than12mm	53	75.7%
		Mean	**Standard Deviation**
	ET Thickness (in mm)	15.74	4.19

On Ultrasound evaluation the mean endometrial thickness obtained was 15.74 mm with maximum women (75.7%) having an endometrial thickness Of > 12mm.

Table 7: Distribution of study subjects based on the Histopathology Report

REPORT OF HISTOPATHOLOGY	**N**	**%**
Proliferative Endometrium	21	30.0%
Early Proliferative Phase	2	2.9%
Secretory	3	4.3%
Late Secretory	3	4.3%
Pill Endometrium	1	1.4%
Hyperplasia Without Atypia	35	50.0%
Atypical Hyperplasia	4	5.7%
Endometrial AdenoCarcinoma	1	1.4%

On Histopathological evaluation, of the Endometrial samples 42.9% of the samples were reported as variants of Normal endometrium while **50%** of the samples were reported as **endometrial hyperplasia without atypia**. Only 5.7% of the samples were reported as atypical hyperplasia and 1.4% reported as Endometrial Adenocarcinoma.

Table 8: Association between age group and Histopathology report among the study subjects

HISTOPATHOLOGY REPORT	**Age group**							
	Less than 40 years		**Between 41 To 45 Years**		**Between 46 To 50 Years**		**More than 50 years**	
	N	%	N	%	N	%	N	%
Proliferative Endometrium	7	35.0%	8	29.6%	6	30.0%	0	0.0%
Early Proliferative Phase	0	0.0%	1	3.7%	1	5.0%	0	0.0%
Secretory	1	5.0%	1	3.7%	1	5.0%	0	0.0%
Late Secretory	2	10.0%	1	3.7%	0	0.0%	0	0.0%
Pill Endometrium	0	0.0%	1	3.7%	0	0.0%	0	0.0%
Hyperplasia Without Atypia	9	45.0%	15	55.6%	10	50.0%	1	33.3%
Atypical Hyperplasia	1	5.0%	0	0.0%	2	10.0%	1	33.3%
Endometrial Adeno Carcinoma	0	0.0%	0	0.0%	0	0.0%	1	33.3%

ChiSquare=35.410p=0.025

In the present study, maximum number of study subjects belonged to the age group of 41 to 45 years and among these maximum (55.6%) had a histopathology report of Non atypical Endometrial hyperplasia (Hyperplasia without atypia) which was found to be statistically significant with p value of 0.025.

Table 9: Distribution of Mean Endometrial thickness among the study subjects based on Histopathology Report

		ET Thickness (mm)	
		Mean	**Standard Deviation**
	Proliferative Endometrium	15.81	4.02
	Early Proliferative Phase	13.00	4.24
HISTO REPORT	Secretory	10.67	2.31
	Late Secretory	10.00	.00
	Pill Endometrium	10.00	.00
	Hyperplasia Without Atypia	15.86	2.93
	Atypical Hyperplasia	22.25	2.87
	Endometrial Adeno Carcinoma	28.00	.00

This study shows that the mean endometrial thickness in case of Non atypical endometrial hyperplasia was **15.86+/-2.93mm** while that of Atypical hyperplasia which was 22.25+/-2.87mm and Endometrial Adenocarcinoma was 28mm.

As compared to the normal Histopathological findings where in the maximum mean ET was 15.81+/-4.02mm.In the present study, none of the Histopathology reports that reported as Secretory endometrium (including the Late Secretory changes or pill endometrium) had and endometrial thickness of >12mm.

However, an almost comparable number of Histopathology reports of Proliferative endometrium and early proliferative endometrium had an ET below and above 12mm (29.4% and 30.2% respectively).

Table 10: Association between Endometrial Thickness with Histopathology Report among the study subjects

		Endometrial Thickness			
		Less than equal to 12 mm		More than 12 mm	
		N	**%**	**N**	**%**
	Proliferative Endometrium	5	29.4%	16	30.2%
	Early Proliferative Phase	1	5.9%	1	1.9%
	Secretory	3	17.6%	0	0.0%
	Late Secretory	3	17.6%	0	0.0%
	Pill Endometrium	1	5.9%	0	0.0%
	Hyperplasia Without Atypia	4	23.5%	31	58.5%
	Atypical Hyperplasia	0	0.0%	4	7.5%
	Endometrial Adeno Carcinoma	0	0.0%	1	1.9%

ChiSquare=27.29p=0.0001

Majority of the cases of Non atypical endometrial hyperplasia (58.5%) and all the cases of atypical hyperplasia and Endometrial Adenocarcinoma had an ET>12mm. Hence, there was an association between the Endometrial Thickness and Histopathology report which was statistically significant. (p value of 0.0001).

DISCUSSION

Endometrial hyperplasia, being the precursor of Endometrial carcinoma, is necessary that clinicians keep a high lookout for its signs and symptoms and treat this precursor accordingly.

The present study shows that among clinical features, maximum women in perimenopausal age group belonged to age group of 41 to 45 years. This is in line with the previous data reported in literature. (**JohnsyMerla J, Srijanaki M et al., 2015; Thapa S, Acharya I et al., 2021; Raychaudhuri G, Bandyopadhyay A et al., 2013)[4,5,6].** Contrary to this a meta-analysis by **EsmerAC, AkbayirO et al., 2014**[7] has shown that there is no cutoff age group for women with AUB in whom Endometrial biopsy is a must.

In this study, the mean age of women at the time of menarche was 12 years, with majority of women included in study (80%) who were Obese (with Mean BMI - 27.8kg/m^2). This is in agreement with another study by **Lee et al., 2020** [8] where in the mean BMI was 26.9kg/m2 in those with Atypical endometrial hyperplasia. This analysis supports the fact that majority of women who have factors that lead to hyperestrogenism, can lead to precursors of endometrial cancer that is Endometrial Hyperplasia. In this study, we see that majority of women had two positive factors and thereby they were at increased risk of developing Endometrial Carcinoma. A study by **Wise et al, 2016**[9]. showed as the number of risk factors increase the risk of Endometrial hyperplasia and thereby Endometrial carcinoma increases.

In contrast to few studies including the one by **Bhattacharya AB, Jha Met al,. 2019**[10]**,** which enumerated nulliparity and presence of Past history of Diabetes mellitus and Hypertension as a risk factor for Endometrial hyperplasia, this study showed majority of the women were multiparous (78.6%) and 65.7% women had no significant medical history.

On analysing the menstrual symptoms and cycle duration, majority(72.9%) had complained of Heavy menstrual bleeding

which were painless with 60% of women had Irregular cycle duration of >30 days, implying these women had anovulatory cycles, which is seen more in perimenopausal women.

Studies on Endometrial Ultrasound showing thickened endometrium showed that there was 25% increased Endometrial hyperplasia/ carcinoma (EH/EC) **Lacey Jr JVet al., 2009[11].**

Interestingly, presence of diabetes, obesity with increased Endometrial thickness (>11mm) increases the risk of premalignant or malignant endometrial pathology by 25%.

The mean ET for the present study was 15.7mm. Some studies show some minor variation in the mean value, with median ET of 10.5mm (Getpooket al), 9.4mm (Minagawa et al)[12] in asymptomatic women.

Another study by **Giri SK et al 2020[13] and Özdemir S et al., 2010[14]** showed similar findings wherein the median ET was 9.4mm and 8mm respectively. A study done by **Minagawa Y et al.,[12]** analyzed 367 premenopausal women where in median ET for symptomatic women (with AUB) was 12.2 mm while in asymptomatic women it was 9.4mm. Endometrial carcinoma was detected in all cases with ET > 20mm and in one case where in ET was 17.3mm in**.**

In another study, by **Patel K et al, 2020[15],** 120 women of perimenopausal age group (40 to 45 years), Endometrial hyperplasia was detected when ET of > 11mm and simple hyperplasia with atypia was detected when ET was of >/= 11 to 16mm. There was no Endometrial pathology in cases <11mm.

In agreement with the hypothesis on sonographic evaluation, wherein ET> 12mm is a risk factor for Endometrial hyperplasia, and other studies including one by **Patel K et al., 2020[15]**, our study showed an association between Histopathology report of Endometrial biopsy and Endometrial hyperplasia (p value - 0.001).

Also, in the study, 50% of the Histopathology reports were reported as Endometrial Hyperplasia without atypia /Non-atypical hyperplasia. Similar to these results, a retrospective Histopathological study in the endometrial samples of women with Abnormal uterine bleeding, where the majority (29.88%) among 87 samples obtained reported as Non atypical Hyperplasia in **Pramana C et al,. 2020[16]** study.

The results from this study indicate that there is no association between parity and Endometrial biopsy report. This study, goes hand in hand with the meta- analysis done where in no association was found between parity and endometrial cancer risk.**(WuQJ,LiYY et al, 2015[17]).** Also, there was an association between Endometrial thickness and Histopathology reports. It was noted that all the cases of Endometrial hyperplasia with atypia (4) and Endometrial carcinoma (1) had an ET >12mm. Additionally, all cases of Secretory endometrium (including early, late and pill endometrium) had and ET <12mm.

CONCLUSION

AUB is the most common complaint found among the patients in the gynecology outpatient department. The increased awareness and better accessibility to healthcare facilities also contribute to the increase in cases presenting with AUB. AUB requires thorough and prompt evaluation as it can be a clinical manifestation of underlying fatal diseases like endometrial carcinoma. A prompt diagnosis made by correlating the clinical history and radiological findings can help in providing the right treatment to the patient.

. In the present study, we found that women in the perimenopausal age with AUB presented mainly with heavy menstrual bleeding. The most common histopathological feature was hyperplasia without atypia followed by proliferative endometrium. Endometrial carcinomas was seen in one case. Endometrial sampling is an effective diagnostic tool and it needs to be considered in all patients in perimenopausal age groups with AUB.

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REFERENCES

1. Howitt BE, Nucci MR. Mesonephric proliferations of the female genital tract. Pathology. 2018 Feb 1;50(2):141-50.
2. Fraser IS, Critchley HO, Broder M, Munro MG. The FIGO recommendations on terminologies and definitions for normal and abnormal uterine bleeding. Seminars in reproductive medicine 2011 Sep (Vol. 29, No. 05, pp. 383-390)
3. Munro MG, Critchley HO, Broder MS, Fraser IS, FIGO Working Group on Menstrual Disorders. FIGO classification system (PALM-COEIN) for causes of abnormal uterine bleeding in nongravid women of reproductive age. In- ternational Journal of Gynecology & Obstetrics. 2011 Apr 1;113(1):3-13.
4. Johnsy Merla J, Srijanaki M, Suresh Durai J, Shantaraman K, Swaminathan K. Histomorphological Profile and Immunohistochemical Analysis of Endo- metrium in Perimenopausal Bleeding: A 2 Year Study in a Tertiary Care Center: IOSR(JDMS). 2015 Dec; 14(12): 38-44
5. Thapa S, Acharya I. Endometrial Histopathology in Abnormal Uterine Bleed- ing: A Retrospective Analysis. Medical Journal of Shree Birendra Hospital. 2021 Feb 2;20(1):1-5
6. Raychaudhuri G, Bandyopadhyay A, Sarkar D, Mandal S, Mondal S, Mitra PK. Endometrial hyperplasia: a clinicopathological study in a tertiary care hospital. The Journal of Obstetrics and Gynecology of India. 2013 Dec 1;63(6):394-8.
7. Smer AC, Akbayir O, Goksedef BP, Gunduz N, Kisacık S, Dagdeviren H, Guraslan B, Ark C. Is there an appropriate cutoff age for sampling the en- dometrium in premenopausal bleeding?. Gynecologic and obstetric investi- gation. 2014;77(1):40-4.
8. Hui LS, Chin SH, Goh C, Hui LX, Mathur M, Kuei TL, Xian FC. Non- atypical endometrial hyperplasia: risk factors for occult endometrial atypia and ma- lignancy in patients managed with hysterectomy. Obstetrics & Gynecology
9. Gong TT, Wang YL, Ma XX. Age at menarche and endometrial cancer risk: a dose-response meta-analysis of prospective studies. Scientific reports. 2015 Sep 11;5(1):1-

0.
10. Bhattacharya AB, Jha M, Agarwal A, Gupta V, Shukla M, Kumar R. Histo- pathological and Immunohistochemical Study of Endometrial Lesions Ob- tained from D&C and Hysterectomy Specimens at a Tertiary Care Hospital.
11. Lacey Jr JV, Chia VM. Endometrial hyperplasia and the risk of progression to carcinoma. Maturitas. 2009 May 20;63(1):39-44
12. Minagawa Y, Sato S, Ito M, Onohara Y, Nakamoto S, Kigawa J. Transvagi- nal ultrasonography and endometrial cytology as a diagnostic schema for endometrial cancer. Gynecologic and obstetric investigation. 2005;59(3):149-54
13. Giri SK, Nayak BL, Mohapatra J. Thickened Endometrium: When to Inter- vene? A Clinical Conundrum. The Journal of Obstetrics and Gynecology of India. 2021 Feb 2:1-0.
14. Özdemir S, Çelik Ç, Gezginç K, Kıreşi D, Esen H. Evaluation of endometrial thickness with transvaginal ultrasonography and histopathology in premen- opausal women with abnormal vaginal bleeding. Archives of gynecology and obstetrics. 2010 Oct;282(4):395- 9
15. Patel K, Srivastava M. The Comparative Study of Transvaginal Sonography and Endometrial Biopsy. International Journal Of Scientific Study. 2020;8(6):82-5.
16. Pramana C, Damayanti L, Latuheru EP, Ningtyas DR, Michell C, Angelina J. A Histopathological Study of Endometrium in Abnormal Uterine Bleeding: A Retrospective Study. International Journal of Psychosocial Rehabilitation. 2020;24(05).
17. Wu QJ, Li YY, Tu C, Zhu J, Qian KQ, Feng TB, Li C, Wu L, Ma XX. Parity and endometrial cancer risk: a meta-analysis of epidemiological studies. Scientific reports. 2015 Sep 16;5(1):1-7