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To study the clinico-pathological correlation in abnormal uterine bleeding

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Abstract
Introduction: Abnormal Uterine Bleeding may occur in women of all age groups, responsible majorly (69%) in peri or postmenopausal age group. These complaints may significantly affect the quality of life, result in surgical intervention intending hysterectomy and ultimately have a significant impact on the health care system. Thus, there is a need for noninvasive or minimally invasive technique to study the endometrial pathology. The present study was designed to study the clinico-pathological correlation in abnormal uterine bleeding.
Material and Methods: This study was a hospital based study, conducted in the Department of Obstetrics and Gynecology, SRMS IMS Bareilly. Around 150 patients with a clinical diagnosis of AUB were enrolled & were subjected for transvaginal ultrasound followed by endometrial sampling.
Results: Majority of the patients were multiparous and in peri-menopausal age, presented menorrhagia being the most common pattern. More than half of the patients were obese. Simple hyperplasia and malignancy of endometrium was majorly seen among patients with endometrial thickness of >9mm.
Conclusion: A visual assessment by the transvaginal sonography and histopathological assessment of the endometrium, remains the cornerstone in the current practice. Women with endometrial thickness of ≥ 8mm on TVS, can be further subjected for endometrial sampling and remaining women can be individualized for biopsy.

Keywords: Abnormal uterine bleeding, transvaginal sonography, endometrial sampling, perimenopausal women

Introduction
Endometrium is a hormonally sensitive, functional and responsive tissue which constantly undergoes changes mainly during the reproductive period. Menstrual disorders are common gynecological problem accounting about one-third of all outpatient visits.
Abnormal Uterine Bleeding is any variation in the normal menstrual cycle such as changes in regularity and frequency, duration of flow or amount of blood loss. It is one of the most frequently encountered and perplexing condition in adult women. It may occur in women of all age groups, responsible for around 20-30% in reproductive age group and 69% in peri or postmenopausal age group [1]. These complaints may significantly affect the quality of life, result in time off work, lead to surgical intervention intending hysterectomy and ultimately have a significant impact on the health care system.
The first imaging modality for AUB indicated should be transvaginal ultrasound [2]. TVS is non invasive, cost effective easily accepted by the women without any complications and further we can see the myometrium, endomyometrial junction, adnexae and ovaries. It is useful for the measurement of endometrial thickness and pattern, hyperplasia, organic causes like leiomyomas and endometrial malignancies [3]. In perimenopausal women and postmenopausal women, endometrial biopsy is to be considered in order to detect endometrial hyperplasia or carcinoma in early stage. Though newer surgical diagnostic and therapeutic techniques are available to aid in the management of patients with abnormal uterine bleeding, endometrial curettage was found to be the best investigation for endometrial pathology. But it was found to be less effective in diagnosing focal lesions like polyps, atypical hyperplasia and malignant lesions. Thus, the diagnosis should be made with judicious use of ultrasound examination, magnetic resonance imaging and other imaging modalities.
There is a need for noninvasive or minimally invasive technique to study the endometrial pathology.

Therefore, the present study was designed to study the clinico-pathological correlation in abnormal uterine bleeding.

Material and methods

It was a hospital based study. All patients presented to the Department of Obstetrics and Gynecology, SRMS Bareilly, from November 2018 to May 2020 with a clinical diagnosis of AUB were enrolled in this study. Women of age more than or equal to 35years, with clinical diagnosis of abnormal uterine bleeding and no palpable pelvic pathology. Patients having acute pelvic infection, abnormal pap smear, palpable pelvic pathology, known case of thyroid dysfunction, hyperprolactinemia, blood dyscrasias, known or suspected case of genital malignancy and those who refuse to participate where excluded from the study. A detailed clinical assessment of patient was performed. All patients were subjected for transvaginal sonography with empty bladder, which was done using 7.5 MHZ intravaginal transducer. Two layer thickness of endometrium in A-P dimension at maximum thickness area was taken. The caliper of the ultrasound machine was placed on the outer border of highly echogenic endometrium; from the basalis anterior to the contralateral basalis posterior.

After this initial workup, informed consent for procedure was obtained, pre-procedure medication was done and they were subjected for emdometrial sampling. The tissue obtained was sent for histopathological examination in 10% formalin, to the Department of Pathology, for further evaluation. All the clinical details and investigation reports were endorsed on the predesigned proforma.

Results and observations

The present study was conducted in the Department of Obstetrics and Gynecology, SRMS Bareilly with the objective to study the clinico-pathological correlation in abnormal uterine bleeding. A total of 150 patients were included in the study.

Table 1: The baseline characteristics of the study participants

Parameters	No. (n=150)	Percentage (%)
Age (35-40years)	85	56.7
Socio-Economic Status(UL)	60	40.0
Parity (Multi)	132	88.0
BMI (>29.9Kg/m2)	61	40.7

Table 2: Distribution of patients according to type of menstrual disorder

Type of menstrual disorder	No. (n=150)	Percentage (%)
Menorrhagia	93	62.0
Metropathia haemorrhagica	20	13.3
Oligomenorrhea	17	11.4
Polymenorrhea	20	13.3

Table-2 shows the distribution of patients according to type of menstrual disorder. Menorrhagia was the most common type of menstrual disorder (62%) followed by Metropathia haemorrhagica & Polymenorrhea (13.3%) and Oligomenorrhea (11.4%).

Table 3: Distribution of patients according to endometrial thickness on TVS

Endometrial thickness (mm)	No. (n=150)	Percentage (%)
<4 mm	13	8.7
4-8 mm	85	56.7
9-15 mm	43	28.7
>15 mm	9	6.0

Table-3 shows the distribution of patients according to endometrial thickness. Endometrial thickness 4-8 mm was among more than half of patients (56.7%) followed by 9-15 mm (28.7%), <4 mm (8.7%) and >15 mm (6%).

Table 4: Distribution of patients according to HPE findings

HPE findings	No. (n=150)	Percentage (%)
Menstrual phase	49	32.7
Disordered proliferative endometrium	34	22.6
Secretory phase	23	15.3
Chronic endometritis	16	10.7
Proliferative phase	14	9.3
Simple hyperplasia without atypia	10	6.7
Malignancy	4	2.7

Table-4 shows the distribution of patients according to HPE findings. Menstural phase was the most common HPE finding (32.7%). Disordered proliferative endometrium was the second most common HPE finding (22.6%). Secretory phase was the third most common HPE finding (15.3%).

Table 5: Association of HPE with age

HPE findings	No. of patients	Age in years								p-value
		35-40		41-45		46-50		51-55		
		No.	%	No.	%	No.	%	No.	%	
Chronic endometritis	16	9	56.2	4	25.0	2	12.5	1	6.2	0.971
Disordered proliferative endometrium	34	19	55.9	9	26.5	3	8.8	3	8.8	0.620
Malignancy	4	1	25.0	0	0.0	0	0.0	3	75.0	0.059*
Menstrual phase	49	25	51.0	15	30.6	7	14.3	2	4.1	0.341
Proliferative phase	14	8	57.1	1	7.1	4	28.6	1	7.1	0.272
Secretory phase	23	17	73.9	1	4.3	5	21.7	0	0.0	0.033*
Simple hyperplasia without atypia	10	5	50.0	3	30.0	1	10.0	1	10.0	0.747

Table 5 shows the association of HPE findings with age. Chronic endometritis was found more frequently in age group of 35-40 years. Simple hyperplasia was more commonly seen in the women of third and fourth decade but has no statistical significance. Secretory phase endometrium was found significantly high in patients of age 35-40 years (73.9%) with p-value of 0.03. Malignancy was also found more frequently in patients of age 51-55 years (75%) and is statistically significant with p-value of 0.05.

Table 6: Association of HPE with type of menstrual disorder

HPE findings	No. of patients	Type of menstrual disorder								p-value
		Menorrhagia		Metropathia haemorrhagica		Oligomenorrhea		Polymenorrhea		
		No.	%	No.	%	No.	%	No.	%	
Chronic endometritis	16	8	50.0	1	6.2	6	37.5	1	6.2	0.015*
Disordered proliferative endometrium	34	20	58.8	6	17.6	1	2.9	7	20.6	0.140
Malignancy	4	2	50.0	0	0.0	1	25.0	1	25.0	0.406
Menstrual phase	49	34	69.4	6	12.2	4	8.2	5	10.2	0.678
Proliferative phase	14	12	85.7	1	7.1	1	7.1	0	0.0	0.314
Secretory phase	23	12	52.2	3	13.0	4	17.4	4	17.4	0.569
Simple hyperplasia without atypia	10	5	50.0	3	30.0	0	0.0	2	20.0	0.237

Table-6 shows the association of HPE findings with type of menstrual disorder. Patients with disordered proliferative endometrium (58.8%) and Proliferative endometrium (85.7%) presented more commonly with menorrhagia and less frequently with oligomenorrhea. Patients with chronic endometritis presented more frequently with menorrhagia (50%) and is significantly high with p-value of 0.01. Patients with hyperplasia and malignancy presented more frequently with menorrhagia, but has no statistical significance.

Table 7: Association of HPE with Endometrial thickness

HPE findings	No. of patients	Endometrial thickness								p-value
		<4 mm		4-8 mm		9-15 mm		>15 mm		
		No.	%	No.	%	No.	%	No.	%	
Chronic endometritis	16	3	18.8	10	62.5	2	12.5	1	6.2	0.204
Disordered proliferative endometrium	34	1	2.9	20	58.8	11	32.4	2	5.9	0.632
Malignancy	4	1	25.0	0	0.0	2	50.0	1	25.0	0.020*
Menstrual phase	49	4	8.2	31	63.3	13	26.5	1	2.0	0.515
Proliferative phase	14	0	0.0	11	78.6	2	14.3	1	7.1	0.304
Secretory phase	23	3	13.0	12	52.2	8	34.8	0	0.0	0.501
Simple hyperplasia without atypia	10	1	10.0	1	10.0	5	50.0	3	30.0	0.001*

Table-7 shows the association of HPE findings with endometrial thickness. Proliferative phase HPE finding (78.6%) was found to be most common among patients whom endometrial thickness was 4-8 mm. Malignancy on HPE (75%) was found to be statistically significant in the patients having endometrial thickness>9mm with p-value being 0.02. Simple hyperplasia was found significantly high in patients with endometrial thickness of more than equal to 9mm (80%) with p- value of 0.001.

Discussion

The present study was conducted on 150 patients, we observed that more than half of the patients presented in third and fourth decade of their life. Our institute is situated in the outskirts of city, draining with rural population. Most of the patients of rural area have reluctant behavior towards their health thus presenting late to the hospital. In our study we found that majority of patients were multiparous (88%), as it may lead to alteration in hypothalamo pituitary ovarian axis. Thus, incidence of abnormal uterine bleeding increases with age and parity. This study showed that increasing BMI was accounted with increased incidence of AUB, due to the fact that obesity leads to excessive estrogen production which causes marked proliferation and thickening of endometrium resulting in abnormal uterine bleeding.

Menorrhagia was the most common type of menstrual disorder (62%) followed by metropathia haemorrhagica & polymenorrhea (13.3%) and oligomenorrhea (11.4%) in our study. This is in favour to the fact that in our study 105 out of 150 patients were in obese category, leading to the hormonal imbalance and alteration in the hypothalamo-pituitary ovarian axis. There is unopposed estrogenic stimulation of the endometrium, followed by estrogenic withdrawal bleeding which is heavy in amount due to proliferation and hyperplasia of the endometrium.

The endometrium can be easily visualized by transvaginal sonography and its thickness can be used as a screening method. This study showed that endometrial thickness among more than half of the patients was 4-8 mm (56.7%) followed by 9-15 mm (28.7%), <4 mm (8.7%) and >15 mm (6%). Pillai (2014) showed similar results they studied on 88 women in the perimenopausal age 40-51 years (40%), 46.5% patients presented with menorrhagia and 46.5% of patients had endometrial thickness 5 to 9.9 mm. Choudhary *et al*. (2017) [4] showed that five out of 50 patients, three with frequent bleeding and two patient of irregular bleeding had endometrial thickness 6-9mm. Thus, this study showed different results to our study [5].

This study showed that menstural phase was the most common finding (32.7%) followed by disordered proliferative (22.6%) endometrium which is an exaggeration of the normal proliferative phase due to persistent oestrogen stimulation, without any significant increase in the overall ratio of glands to stroma.

The concern for presence of organic pathology increases with age and it is must to exclude it in the patient with AUB. In our study,chronic endometritis was found more frequently in age group of 35-40 years. Simple hyperplasia was more commonly seen in the women of third and fourth decade but has no statistical significance. Secretory phase endometrium was found significantly high in patients of age 35-40 years (73.9%) with p-value of 0.03. As premenstrual curettage was done in the patients with menorrhagia which accounts 47.46% of all the

bleeding pattern. Malignancy was also found more frequently in patients of age 51-55 years (75%) and is statistically significant with p-value of 0.05 this is in concordance with the literature that risk of malignancy increases with increasing age. Menstrual phase and proliferative phase was found in patients with perimenopausal age group. This may be due to the fact that most of curettages were performed early with the beginning of the cycle or during the menstrual phase.

In our study, we observed that with the estimation of endometrial thickness and the pattern of the endometrium on transvaginal sonography, we can reduce the number of patients requiring dilatation and curettage. In this study, only 2 patients had endometrial hyperplasia with ET < 8mm and only 1 patient had malignancy with ET <4mm. This finding is comparable with the Shobhitha *et al*. study (2015) [6]. The suggested cut off value of ET should be below which no pathology was found, but in this study as the sample size is small, further studies are needed to safely establish the endometrial thickness cutoff point for excluding endometrial abnormality.

Patient having ET between 9-15mm mostly had metropathica haemorrhagica (40%) and polymenorrhea (45%). Endometrial thickness is an indirect indicator of endometrial hyperplasia and amount of menstrual bleeding. Patient having ET >15mm presented with menorrhagia (6.4%),metropathica haemorrhagica (10%), and polymenorrhea(5%). No patient presented with oligomenorrhea. No statistical correlation was found between ET and menstrual disorder. The major challenge is to address the worries about the risk of malignancy with the advancing age in the patients with abnormal uterine bleeding. A visual assessment by the transvaginal sonography and histopathological assessment of the endometrium thus remains the cornerstone in the current practices.

Conclusion

More than half of the patients with AUB were in peri-menopausal age group with age of 41.35 ± 5.23 years. Majority of the patients were multiparous and overweight, who presented with menorrhagia. Malignancy was found more commonly in patients of age 51-55 years and in overweight group.

More common menstrual disorder among all recruited women is menorrhagia with endometrial thickness ranging between 4-8mm. Oligomenorrhoea was most common presentation seen in the patients with endometrial thickness <4mm. Simple hyperplasia and malignancy of endometrium was majorly seen among patients with endometrial thickness of >9 mm.

Our results showed that women with endometrial thickness of ≥ 8mm on TVS, can be further subjected for dilatation and curettage and remaining women having endometrial thickness ≤ 7.9 mm can be individualized for biopsy even in perimenopausal age, particularly with mean age of 41.35± 5.23.

Our study also support to the fact that in perimenopausal women with AUB, first investigation can be transvaginal sonogram. As transvaginal sonogram is a non invasive, easily acceptable by the patient and without any complication. Despite the phasic variation in endometrial thickness, endometrium can be easily visualized and its thickness can be used as a screening method to avoid unnecessary curettage. Hence, it is a better diagnostic tool for the evaluation of AUB as an initial procedure in perimenopausal women. We found that the histological examination of the endometrium is required so as to exclude the cases of hyperplasia, particularly atypical hyperplasia and endometrial cancer which may need surgical intervention.

Due to the small sample size of our study, further large randomized case control studies are needed to establish the endometrial thickness cut-off point for excluding endometrial abnormality in perimenopausal age group.

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