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Original Research Article

Correlation of histopathological findings with ultrasound imaging and hysteroscopic findings in perimenopausal and postmenopausal women with abnormal uterine bleeding

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ABSTRACT

Background: Heavy breakthrough bleeding is a very frequent complaint in gynecological practice, more common during perimenopause and can be associated with structural pathologies, and abnormalities. Proper diagnosis as well as treatment are very vital for enhancing quality of the lives of such individuals and also treating possible malignancies. This research paper discusses the correlation of clinical presentation, USG and histopathology in the diagnosis of AUB in women to determine the most effective course of action. To compare and describe clinical features of AUB in perimenopausal and postmenopausal women and to posit Association between ultrasound findings and histopathological examination of hysterectomy samples, as well as to identify types of causal pathology.
Methods: A cross-sectional study was carried out in the Obstetrics and Gynecology department of a tertiary teaching hospital. Finally, 200 women aged 45 and above with AUB were recruited over a three-year period. Information on clinical presentation was also obtained and ultrasonographic evaluation with regard to endometrial thickness and uterine abnormalities noted. Objective assessment of the findings obtained by USG was done by histopathological examination of hysterectomy specimens and statistical correlation was done.
Results: 200 patients diagnosed with AUB aged 45 years and above, 66% of the patients were aged between 45-49 years. The highest frequency of pain was reported during menstruation followed by postmenstrual and intermenstrual pain; heavy menstrual bleeding was most prevalent 60%, postmenopausal bleeding 12% and intermenstrual bleeding 11%. The detailed ultrasonographic changes were abnormal in 83% of patients; endometrial thickening was seen in 44%, and fibroids in 17%. Comparison between hysteroscopy, and histopathological findings showed abnormal endometrium had significant positive relation with each other p=0.02.
Conclusion: This study shows that USG offers value as the primary diagnostic modality, especially in diagnosing fibroid-associated AUB.

Keywords: Abnormal uterine bleeding, Histopathology, Polyp, Endometrium, Hysteroscopy

INTRODUCTION

Abnormal Uterine Bleeding, it is a common gynaecological complaint in any age of life, but it is most common during the perimenopausal period. AUB is any deviation from the usual menstrual pattern of the woman, whether in frequency, cycle length, cycle duration, or amount of blood loss. (1) This circumstance may have hormonal, structural, and organic bases as well as iatrogenic factors for its development. Worldwide, the International Federation of Gynaecology and Obstetrics (IFGO) has designed a system called PALM-COEIN to

divide the causes of AUB into structural and non-structural disorders: PALM for structural changes, polyp, adenomyosis, leiomyoma and malignant disorders, while COEIN for non-structural changes: coagulopathies, ovulatory disorders, endometrial disorders, iat this system has been found to play a significant role in increasing the efficiency of diagnosis of AUB by practitioners.[2,3] An elevated risk is evident with age and the peri-menopausal period which places women over 45 at a considerably higher risk.

To many a lady, we interrupt their normal lives and the symptoms include anxiety, fatigue and even iron deficient anemia.[4,5] It may occasionally signal pathologic conditions: benign, including fibroids or polyps; potentially malignant or pre-malignant changes in the endometrial tissue. Heavy menstrual bleeding is the primary complaint that many women with AUB present and is the reason that brings them to a doctor.[6] Nevertheless, there are differences in terms of symptoms: intermenstrual bleeding is significantly different from postmenopausal bleeding, even though both indicate pathologic changes in the female reproductive system.[7]

An important characteristic of diagnostic strategies to AUB is that they are global, involving both clinical and investigational methods to arrive at a diagnosis. The first diagnostic test usually done is the CBC followed by thyroid function test to exclude any systemic processes.[8] Endometrial ultrasound continues to be a first-line imaging technique in the management of infertility, as it provides a safe and non-ionizing means of assessing endometrial, leiomyomas, and polyps and other anatomical lesions.

Moreover, hysteroscopy is often performed in order to visualize the uterine cavity, obtain a biopsy, and determine if the abnormality seen on imaging is present.[9] To confirm endometrial abnormality histopathologically, endometrial sampling or biopsy is advised commonly in women after 45 or those with symptoms suggestive of endometrial carcinoma. HPE offers indispensable information about the organizational structure of the tissue and can define such states as benign or hyperplastic reactions or, conversely, malignant transformations.[10]

Despite this array of diagnostic tools, the relationship between various diagnostic modalities for AUB has not been well explained. Though both ultrasound and hysteroscopy are minimally invasive with high diagnostic accuracy differences may exist between the findings noted on imaging, hysteroscopy and histopathology.[11] For example, endometrial thickness on ultrasound may be suggestive of hyperplasia or carcinoma, but accuracy of this sign is less accurate as compared to hysteroscopy and biopsy. In addition, there are lesions such as submucous fibroids and endometrial polyp that you may fail to diagnose if there is no direct view.[12]

This study seeks to assess and compare ultrasonography, hysteroscopy, and histopathology in assessing AUB. The achievement of this research is the goal of defining the relationships and gaps between these types of diagnosis in order to make studies more reliable and increase the effectiveness of such treatment. Therefore, this study is most informative in patients over 45 with AUB in whom early and accurate identification of underlying pathology is paramount to minimize lethality and malignancy. Greater harmonisation of diagnostic strategies may ultimately enable clinicians to make informed decisions in continuing to care for women with AUB.

METHODS

Study place

The present study was undertaken in Sri Ramachandra Medical College and Hospital.

Study duration

The study period was from 1st January 2024 to 30th June 2024.

Sample size

A purposive sampling technique was employed in choosing 200 postmenopausal women with abnormal uterine bleeding complaint.

Inclusion criteria

The women who consented to participate in the study were enrolled according to the following inclusion criteria includes the patient has completed child bearing age. Presence of abnormal TVS findings indicating a probable endometrial pathological state. Ability of patient to understand and communicate the results of hysteroscopy-guided biopsy. The main study criteria included all women older than 45 years with clear clinical diagnosis of AUB.

Excluded criteria

Patients who were either pregnant or had an IUCD, ovarian tumours that produce hormones, hyper or hypothyroidism, diabetes, adrenal diseases and altered prolactin levels were excluded from study. Further, patients with coagulopathy, liver or renal dysfunction, known cervical or uterine malignancy, on steroids, neuroleptics, anticoagulants, cytotoxic or similar agents were excluded.

Outpatient assessments during enrolment involved taking a detailed history of patient age, parity, chief complaints together with the detailed menstrual history including duration, interval, amount and type of bleeding and any associated symptom such as pain. Abdominal examinations were done to feel for any enlarged masses on the abdomen, speculum examination to feel for local pathology, vaginal examination was done with a view of feeling the size of the uterus, and any adnexal disease.

After PALM-COEIN classification and diagnosis of AUB, patients were advised to undergo transvaginal ultrasound. This imaging method gave the first glimpse of the pathology of the uterus and adnexae with regard to structural changes.

Further attention was paid to postmenopausal bleeding in patients, and according to the results of the control investigations, a decision was made about further examination and therapy. Routine preoperative investigations were conducted in all patients, and those who met the criteria for the procedure underwent hysteroscopy under strict aseptic measures.

While performing the procedure, both the cervix and vagina were visualized and the size and location of the uterus were checked before the hysteroscope was passed under direct vision. It included polyps, fibroids, vascularity changes among other structural pathologies. Punch biopsies were done at the areas of pathologic findings noted and the samples were submitted for histopathological evaluation (HPE) to either confirm or exclude the findings depicted on ultrasound or hysteroscopy.

Statistical analysis

All the patients included in the study provided written informed consent before their inclusion, and patient anonymity was preserved at all times. Records of patients' histories, clinical examination, radiology, hysteroscopy, and histopathology were used for research, and the data was processed using SPSS version 21. For the categorical data qualitative summary analysis, descriptive statistics like percentage and frequency were used. To evaluate the study results, statistical significance was determined by p value<0.05.

RESULTS

In this work, 200 patient of 45 years and more, with symptoms suggestive of abnormal uterine bleeding were considered. In Table 1, The participants in the 45-49 years age group reported the highest level of AUB, that is 132 (66%) followed by the 50-54 =42 (21%) 55-59=14 (7%) and 60-65=12 (6%).

Table 1: Distribution of age among patients with AUB.

Distribution of age among patients with AUB	Frequency (N)	%
45-49	132	66
50-54	42	21
55-59	14	7
60-65	12	6
Total	200	100

The chief complains of the patients as presented in Table 2 are as follows, of these 60% (n=120) complained of heavy menstrual bleeding. The next most common complaints were postmenopausal bleeding (12, n=24), intermenstrual bleeding (11, n=22), heavy and prolong and menstrual bleeding (10, n=20) and postcoital bleeding (7, n=14).

Table 2: Distribution of chief complaints.

Distribution of chief complaints	Frequency (N)	%
Heavy menstrual bleeding	120	60
Post menopausal bleeding	24	12
Intermenstrual lebeding	22	11
Heavy and prolonged Menstrual bleeding	20	10
Postcoital bleeding	14	7
Total	200	100

Table 3: Pathology in ultrasonography.

Pathology in Ultrasonography	Frequency (N)	%
Thickened endometrium	88	44
Submucous fibroid	34	17
Adenomyosis	26	13
Endometrial polyp	16	8
Endocervical polyp	2	1
No abnormality detected	34	17
Total	200	100

In Table 3, thirty-seven of the patients had Ultrasonography done, of which 83% (n=166) had abnormalities noted, the most frequent of which was thickened endometrium, seen in 44% (n=88) of the cases. Among the studied cases 17% (34) had submucous fibroids, 13% (26) adenomyosis, 8% (16) endometrial polyp and 1% (2) endocervical polyp. Ultrasonography was performed in 134 patients: There were no abnormal findings in 17% (n=34).

Table 4: Hysteroscopic findings.

Hysteroscopic findings	Frequency (N)	%
Thickened endometrium	90	45
Endometrial polyp	30	15
Atrophic endometrium	24	12
Submucous fibroid	14	7
Septate uterus	2	1
No abnormality detected	40	20
Total	200	100

In Table 4, the results obtained by Hysteroscopy also flagged out diseases in 80% (n=160) patients. The endometrial pathologies encountered most frequently were thickened endometrium in 45% (n=90) of patients, endometrial polyps diagnosed in 15% (n=30) patients, followed by cases of atrophic endometrium in 12% (n=24), and submucous fibroids in 7% (n=14). Septate uterus was observed in 1 percent (2) of the study population. In 20%

(n=40) of the patients there were no distinguishing characteristics. The findings revealed high degree of agreement with ultrasonography especially on diagnosis of thickened endometrium.

Table 5: Distribution of HPE report findings.

Distribution of HPE report findings	Frequency (N)	%
Secretory phase endometrium	70	35
Proliferative phase endometrium	30	15
Disordered proliferative endometrium	28	14
Endometrial polyp	28	14
Endometrial hyperplasia without atypia	20	10
Endometrial carcinoma	20	10
Endometrial hyperplasia with atypia	4	2
Total	200	100

As shown in Table 5, histopathological examination (HPE) was carried out on all patients. The overall most common endometrial pattern was therefore secretory phase in 35% (n=70) and least common was disordered proliferative 14% (n=28). Normal endometrium was found in 30% (n=60), endometrial hyperplasia without atypia in 10% (n=20), endometrial carcinoma in 10% (n=20), and endometrial hyperplasia with atypia 2% (n=4).

Table 6, As regards the hysteroscopic findings the 88 patients out of 160 had abnormally on HPE and out of these 160 patients 72 had a normal HPE. On the other hand, only 5% (n=2) of the patients with normal hysteroscopic features had abnormal HPE findings while 95% (n=38) had a normal HPE finding.

In ultrasonography, 166 patients had an abnormal finding and of these 45.8% (76) had an abnormal HPE result and 54.2% (90) had a normal HPE result. Among patients with normal ultrasonography the tissue diagnosis was normal by HPE in 20 patients (58.8%) and abnormal in 14 patients (41.2%). Hysteroscopy appeared to be more sensitive than ultrasonography when used to diagnose intrauterine pathology.

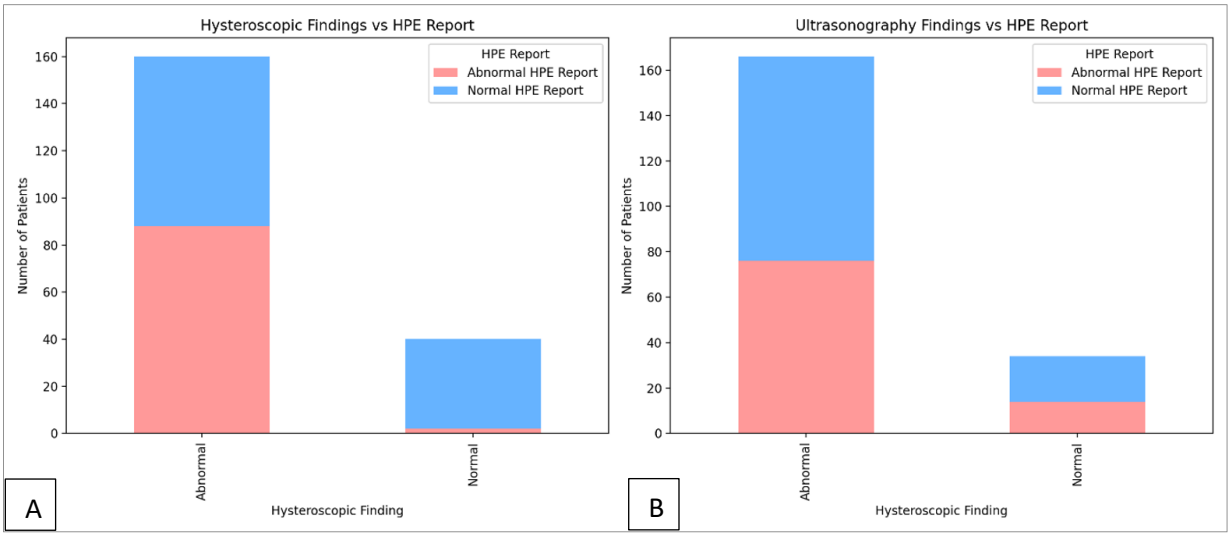

Figure 1 (A and B): Hysteroscopic findings vs HPE report.

Table 6: Association between HPE report and hysteroscopic findings.

Association between HPE report and hysteroscopic findings	HPE report abnormal (N)	HPE report normal (N)	Total (N)	Percentage abnormal	P value
Hysteroscopy: Abnormal	88	72	160	55	0.02
Hysteroscopy: Normal	2	38	40	5	
Total	90	110	200		

Table 7: Association between pathology in ultrasonography and HPE report.

Association between pathology in ultrasonography and HPE report	HPE report abnormal (N)	HPE report normal (N)	Total (N)	Percentage abnormal	P value
Ultrasonography: Abnormal	76	90	166	45.80	0.06
Ultrasonography: Normal	14	20	34	41.20	
Total	90	110	200		

DISCUSSION

This study focuses on the possibility of diagnosing AUB, during the perimenopausal and postmenopausal periods, by using hysteroscopy in combination with TVS and histopathology. The high rate of thickened endometrium observed in women in the current age group through hysteroscopy, TVS and histopathology indicates that it is probably a major contributor to AUB. TVS provides more accuracy than hysteroscopy in diagnosing intrauterine pathology in terms of accuracy, sensitivity of hysteroscopy is higher than TVS in biopsies, Specificity of hysteroscopy and TVS is nearly equal. The PALM COEIN classification system also helps to sort AUB into new subgroups and systematically approach differential diagnosis depending on the imaging findings and histology.

According to the results presented in the current study, it can be hypothesized that due to its non-invasive procedure, TVS may be used as an initial assessment of structural abnormalities. However, occasionally the findings on TVS may be inconclusive and the use of hysteroscopy provide added diagnostic input in order to perform biopsies on the lesions. The strong association between hysteroscopy finding and histopathological evidence indicates hysteroscopy may be can improve the diagnostic yield for AUB particularly in cases involving polyps, endometrial hyperplasia and malignancies.

These findings emphasise the significance, of having a standardized process for approaching AUB where TVS can be used as the screening method, then hysteroscopy and histopathology results to conclusively determine AUB and offer individualised management plans.

In our study, the distribution of presenting complaints, USG findings, and histopathological examination in patients with AUB and the comparative analysis matches well with the findings of other study and is relevant to number of clinical considerations. The study by Zia et al, also noted that in perimenopausal women who underwent hysterectomy for AUB, the most common complaint was HMB. The most frequent sonographic and histopathological findings were fibroids (41%) among patients. Similarly in the present research, HMB also presented itself as one of the key complaints. This strengthens the argument of the authors that ultrasonographic examination should be used as an initial approach to diagnosing fibroids in patients with AUB because although it fails to be specific as histopathological analysis, it is highly sensitive.[13]

Our results are also in concordance with Mahapatra et al. (2022) who compared endometrial lesions in postmenopausal bleeders and insisted on the hysteroscopic and histopathological correlation. In Mahapatra's study hysteroscopy indicated that majority of women had an atrophic endometrium and endometrial hyperplasia confirmed histopathologically. Our study also demonstrated high consistency between the clinical diagnosis, ultrasound findings and histopathological assessment where biopsy served as the gold standard having conclusive pathology in cases where the non-invasive modalities were not conclusive. This paper adds to the growing body of evidence that, although ultrasonography may offer preliminary data on endometrial thickness and pathology, histopathology remains imperative in discerning between benign and potentially malignant causes of AUB and especially in postmenopausal women.[14]

They also showed a significant relationship between enhanced endometrial thickness, which was assessed by transvaginal sonography (TVS), and the risk of abnormal endometrial histopathology in perimenopausal women with AUB as proved in the study done by Modak et al. Our study supported these observations where we also found a comparable trend of endometrial thickness and histopathological oddity of hyperplasia. Modak's study found that TVS had a high sensitivity in identifying endometrial hyperplasia where thickness was above 12-15 mm; a fact that was in harmony with our finding that the use of ultrasonography in predicting hyperplasia may be helpful but not conclusive. This emphasizes the importance of a clinician to follow any abnormal ultrasonographic appearance with histopathological assessment especially in women with thick endometrial measurements.[15]

Similarly, Upadhyay et al, confirmed the diagnostic value of hysteroscopy compared to ultrasonography by comparing the sensitivity and specificity of the hysteroscopy in assessment of different abnormalities in AUB patients. The correlation coefficient of our study comparing hysteroscopic and histopathological findings was statistically significant which supports Upadhyay's findings and establishes hysteroscopy as a second step after non-invasive imaging but before histopathological confirmation. Although ultrasonography is a valuable screening examination, hysteroscopy is preferred since it allows direct visualisation and biopsy in case of solitary lesions, or in cases when ultrasonic findings are equivocal or suspicious, resulting in decreased rate of false negative results and increased diagnostic certainty.[16]

Thomas et al, also stressed that AUB is a leading complaint among perimenopausal and postmenopausal females, and menorrhagia is the clinical sign that is most frequently reported. This can be well explained by the fact that our study population comprised of women with high prevalence rates of menorrhagia.

Thomas et al also pointed out that in their study of ultrasonographic findings in reproductive woman, fibroid uterus was also common, which was evident in our study too. This is consistent with other studies pointing to the typical presentation of AUB and brings to forefront the value of ultrasound in identifying structural pathology like fibroids. However, Thomas et al. also reported an extensive range of cases with proliferative or hyperplastic

endometrial patterns on histopathology, which also called for histopathology to understand the etiology H of AUB.[17]

Coming to postmenopausal bleeding (PMB), Vempalli et al, gave clues about the subject and stressed how endometrial thickness should be considered when looking for malignant origins. The authors used an endometrial thickness measurement of 4 mm as the cut-off with high sensitivity for malignant pathology although they observed a disproportionally low endometrial lesion detection rate for benign diseases, compared to histopathological examination.

This insight is relevant to postmenopausal patient's sample investigated in the study as endometrial atrophy was a histopathological characteristic identified. Despite the fact that Vempallis study challenges the ability of ultrasonographic findings alone to accurately predict the benign pathologies, the results of the study endorse the standard utilization of the ultrasonography in the initial evaluation for the risk of malignancy, particularly in cases of PMB.[18]

Accordingly, our study, as well as the referenced studies, seem to stress on the complexity of the diagnostic approach to AUB. Ultrasonography remains as the first investigation tool of choic, however due to the shortcomings found in the use of the modality, histopathological biopsy or hysteroscopy has to be used to make a definitive diagnosis.

The sample size thus power of the study may be limited to produce more conclusive results. Moreover, there may be inter-clinician variability in the ultrasonographic examination and the accuracy of sample collection and subsequent histopathological assessment. The study therefore only partly relates to the specific target group of perimenopausal and postmenopausal women and can therefore also only allow limited generalization on young women with abnormal uterine bleeding.

CONCLUSION

It is evident that performing a combination of TVS with hysteroscopy and subsequent histopathological examination will provide more efficient diagnosis of AUB in perimenopausal and postmenopausal females. TVS and hysteroscopy results were also compared to histopathological confirmation of the pathologies such as endometrial polyps and fibroid. The present work highlights the need to employ a multimodal approach to increase diagnostic precision when diagnosing AUB, which would contribute to improving the clinical management of this disease and patients' quality of life in this group.

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