

DOI: <http://dx.doi.org/10.18203/2320-1770.ijrcog20183326>

Original Research Article

Correlation between ultrasonographic, hysteroscopic and histopathological findings in patients with abnormal uterine bleeding

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Received: 31 May 2018

Accepted: 28 June 2018

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ABSTRACT

Background: Menstrual disorders are common indication for medical visits among women of reproductive age and heavy menstrual bleeding affects up to 30% of women throughout their reproductive lifetime. This study aims at evaluating the different causes and, the clinical presentation of AUB and to compare the role of hysteroscopy, ultrasonography and histopathology in patients with AUB.

Methods: 100 women above 45 years of age, presenting with abnormal bleeding per vaginum were evaluated. All patients underwent transvaginal scan to note down the endometrial thickness and to rule out uterine and adnexal pathology. All the patients underwent diagnostic hysteroscopy, followed by a biopsy of the endometrium using a curette. The endometrium was sent to the pathologist. Findings of these diagnostic modalities then correlated.

Results: Incidence of AUB was present between the age groups of 45-49 years of age (66%). The commonest presenting complaint in this series was menorrhagia or heavy menstrual bleeding (60%). The finding of thickened endometrium as the most common abnormality on USG (44%) and also on hysteroscopy (45%). As per present study the sensitivity of hysteroscopy is 97.78% and specificity was 34.55%, the negative predictive value of the test is 95%.

Conclusions: TVS may be the first line of investigation while evaluating the endometrium in a perimenopausal AUB. It helps to triage the patients into high risk or low risk. Endometrial thickness > 4mm as per the present study needs further evaluation. Patients with endometrial thickness less than 4 mm can be reassured. Hysteroscopy is the gold standard in the diagnosis of focal pathology like sub mucous fibroid, polyps or anomalies. Histopathology probably is an indispensable tool specially to rule out premalignant and malignant conditions. Thus, all the modalities instead of being competitive to one another, are complimentary to each other. For complete evaluation of patient with AUB all the three modalities should be used together to come at exact diagnosis.

Keywords: Abnormal uterine bleeding, Hysteroscopy, Histopathology, Ultrasonography

INTRODUCTION

Abnormal uterine bleeding (AUB) refers to bleeding that is excessive or occurs outside of criteria of normal cyclic menstruation. AUB is described by a variety of terms and may be caused by number of gynecological conditions, systemic disorders, and medications. AUB was defined as 'bleeding from the uterine corpus that is abnormal in volume, regularity and/or timing that has been present for

the majority of the last 6 months.¹ AUB was redefined by Federation of International Gynaecology and Obstetrics (FIGO) in 2009 by the FIGO Menstrual Disorders Group (FMDG).^{1,2}

Menstrual disorders are common indication for medical visits among women of reproductive age and heavy menstrual bleeding affects up to 30% of women throughout their reproductive lifetime.³

About one third of gynaecological consultations in routine OPD and nearly two-thirds of hysterectomies are because of abnormal uterine bleeding. This problem further rises in perimenopausal and postmenopausal women.

Normal menstrual cycle is a physiological phenomenon for a woman in which woman bleeds every month with gap of 21 to 35 days average being 28 days and for duration of 3-5 days and amount being 25-30 ml per day. Menses is a suspension of blood and tissue derived solids within mixture of serum and cervicovaginal fluid; the blood content of menses varies over the days of bleeding.⁴

Bleeding in any of the following situations is abnormal intermenstrual. Postcoital, bleeding in excess of quantity, frequency or duration more than normal, Postmenopausal. AUB could be due to wide range of conditions like, endometrial hyperplasia, pregnancy and related condition, fibroids, ectopic pregnancy, adenomyosis, polyp, infection of the uterus or cervix and many more.

Patients with AUB can present in different ways such as menorrhagia, metrorrhagia, menometrorrhagia, polymenorrhea, postmenopausal bleeding. Most common presentation being menorrhagia.

46 AUB can be evaluated using different methods; most common are ultrasound, endometrial biopsy and hysteroscopy. Since dilatation and curettage is a blind procedure, it will only scrape less than 50% of the endometrial cavity in 60% of the patients, so becomes less accurate than hysteroscopy in diagnosing structural pathology such as polyps, fibroids, intrauterine adhesions and congenital malformations.⁵ It has a cancer detection failure rate of 0.9%.⁶ With limited resources, in developing countries like India, it is the most commonly used method of assessing AUB.⁷

Transvaginal scan is also less accurate than hysteroscopy in diagnosing exact pathology, but it can give fair idea about structural abnormalities intrauterine pathology.⁸

Transvaginal sonography is preferred over uniform biopsy of postmenopausal women with vaginal bleeding because it is a less invasive procedure, generally painless, has no complications and may be more sensitive for detecting carcinoma than blind biopsy.⁹

METHODS

Women above 45 years of age, presenting with abnormal bleeding per vaginum from August 2015 to July 2017 were included in the study. The study was conducted after obtaining ethical clearance and after fulfilling the exclusion and inclusion criteria. Informed written consent was obtained from them. A detailed history was taken, and a thorough clinical examination was done. Complete

blood count, bleeding time, clotting time, random Blood Sugar, urine analysis for protein, sugar and microscopy, HIV, HBsAg, VDRL, Blood grouping and Rh typing were done in all the patients. All patients underwent Transvaginal scan using 7.5MHz probe to note down the endometrial thickness and to rule out other uterine and adnexal pathology. Next all the patients underwent diagnostic hysteroscopy under short GA, using a 4mm hysteroscope. The hysteroscopy findings were documented. This was followed by a biopsy of the endometrium using a curette. The hysteroscopy findings were classified as atrophic endometrium, proliferative (dull pink relatively thin), secretory (bright pink uniform), and hyperplastic (Fluffy thick obscuring the view), and other findings like sub mucous fibroid, polyps, local unhealthy areas suggestive of malignancy were noted. Histopathology findings of atrophic, hyperplasia, secretory, proliferative and malignancy of the endometrium were noted. The sensitivity, specificity, positive predictive value and negative predictive values of TVS and hysteroscopy in relation to histopathology were calculated. To study the correlation between the findings Kappa coefficient was calculated and declared as poor, fair, moderate, substantial, almost perfect and perfect depending on the Kappa value. Following this conclusion were drawn.

Inclusion criteria

- Women above 45 years of age with history of abnormal uterine bleeding.

Exclusion criteria

- Pregnancy
- IUCD
- Hormone producing ovarian tumours
- Endocrine disorders like hyper- or hypothyroidism, diabetes, adrenal disease, prolactin disorders
- Coagulation disorders
- Liver/renal diseases
- Known cervical or uterine malignancy
- On medications like steroids, neuroleptics, anticoagulants and cytotoxic agents.

RESULTS

In present study authors found that the maximum incidence of AUB was present between the age groups of 45-49 years of age (66%).

Table 1: Distribution among the cases of -age.

Age (years)	No.	Percentage
45 to 49	66	66.0
50 to 54	21	21.0
55 to 59	7	7.0
60 to 65	6	6.0
Total	100	100.0

The commonest presenting complaint in this series was menorrhagia or heavy menstrual bleeding (60%). Most of the patients coming to OPD usually seek medical attention within 6 months of menstrual complains (75%). The finding of thickened endometrium as the most common abnormality on USG (44%) and also on hysteroscopy (45%). As per present study the sensitivity of hysteroscopy was 97.78% and specificity was 34.55%, the negative predictive value of the test was 95% hence there was a fair correlation between the hysteroscopic findings and HPE report to find out true negative cases. In present study sensitivity of ultrasonography in diagnosing the cause of AUB was 84.44%, specificity was 18.18%, positive predictive value was 45.78% and negative predictive value is 58.82%.

Table 2: Distribution among the cases of -chief complaints.

Chief complaints	No.	Percentage
Heavy menstrual bleeding	60	60.0
Postmenopausal bleeding	12	12.0
Intermenstrual bleeding	11	11.0
Heavy and prolonged menstrual bleeding	10	10.0
Postcoital bleeding	7	7.0
Total	100	100.0

Table 3: Distribution among the cases of duration of chief complaints.

Duration of chief complaint (months)	No.	Percentage
One	13	13.0
2	12	12.0
3	10	10.0
4	19	19.0
5	5	5.0
6	16	16.0
8	5	5.0
12	12	12.0
18	1	1.0
24	7	7.0
Total	100	100.0

In present study sensitivity of ultrasonography in diagnosing the cause of AUB was 84.44%, specificity was 18.18%, positive predictive value was 45.78% and negative predictive value is 58.82%.

In the present study, by comparing the TVUS results against hysteroscopy authors found that hysteroscopy has significantly high sensitivity but comparable specificity with TVUS in diagnosing intrauterine pathology like endometrial polyp and submucous fibroid. Comparable sensitivity and specificity in diagnosing endometrial hyperplasia.

Table 4: Distribution among the cases of-comorbidities.

Comorbidities	No.	Percentage
Hypertension	9	9.0
Diabetes	5	5.0
Hypertension and DM	4	4.0
Tuberculosis	3	3.0
Hypothyroid	3	3.0
DM+Hyperthyroid	1	1.0
Galactorrhea	1	1.0
Hypothyroid+Tuberculosis	1	1.0
Megaloblastic anaemia	1	1.0
Rheumatoid Arthritis+DVT+Hypothyroid	1	1.0
No comorbidity	71	71.0
Total	100	100.0

Table 5: Distribution among the cases of-pathology in ultrasonography.

Pathology in ultrasonography	No.	Percentage
Thickened endometrium	44	44.0
Submucous fibroid	17	17.0
Adenomyosis	13	13.0
Endometrial polyp	8	8.0
Endocervical polyp	1	1.0
No abnormality detected	17	17.0
Total	100	100.0

Table 6: Distribution among the cases of-hysteroscopic finding.

Hysteroscopic finding	No.	Percentage
Thickened endometrium	45	45.0
Endometrial polyp	15	15.0
Atrophic endometrium	12	12.0
Submucous fibroid	7	7.0
Septate uterus	1	1.0
No abnormality detected	20	20.0
Total	100	100.0

Table 7: Distribution among the cases of- HPR report.

HPE Report	No.	Percentage
Endometrial hyperplasia with atypia	2	2.0
Secretory phase endometrium	39	39.0
Proliferative phase endometrium	16	16.0
Disordered proliferative endometrium	14	14.0
Endometrial polyp	14	14.0
Endometrial hyperplasia without atypia	14	14.0
Leiomyoma	1	1.0
Total	100	100.0

Table 8: HPE report by hysteroscopic findings.

Hysteroscopic finding	HPE Report			Total		
		Abnormal	Normal			
Abnormal	No.	44	36	80		
	%	55.00%	45.00%	100.00%		
Normal	No.	1	19	20		
	%	5.00%	95.00%	100.00%		
Total	No.	45	55	100		
	%	45.00%	55.00%	100.00%		
Sensitivity	97.78%	88.23%	99.94%			
Specificity	34.55%	22.24%	48.58%			
Predictive value of positive test	55.00%	43.47%	66.15%			
Predictive value of negative test	95.00%	75.13%	99.87%			
Likelihood ratio of positive test	1.4938	1.2267	1.8191			
Likelihood ratio of negative test	0.0643	0.0090	0.4622			
Youden's index	0.3232	0.1904	0.4561			
Measure of Agreement	Kappa	Value	Approx. T	p-value	Agreement is-	
		0.302	4.020	5.8200E-05	Fair	
Pathology in ultrasonography	HPE Report			Total		
		Abnormal	Normal			
Abnormal	No.	38	45	83		
	%	45.80%	54.20%	100.00%		
Normal	No.	7	10	17		
	%	41.20%	58.80%	100.00%		
Total	No.	45	55	100		
	%	45.00%	55.00%	100.00%		
Sensitivity	84.44%	70.54%	93.51%			
Specificity	18.18%	9.08%	30.90%			
Predictive value of positive test	45.78%	34.79%	57.08%			
Predictive value of negative test	58.82%	32.92%	81.56%			
Likelihood ratio of positive test	1.0321	0.8649	1.2317			
Likelihood ratio of negative test	0.8556	0.3542	2.0665			
Youden's index	0.0263	-0.1207	0.1732			
Measure of Agreement	Kappa	Value	Approx. T	p-value	Agreement is-	
		0.024	0.348	0.728	Slight Fair	

Table 8: Association among the cases between pathology in ultrasonography * HPE report.

Pathology in ultrasonography	HPE Report			Total		
		Abnormal	Normal			
Abnormal	No.	38	45	83		
	%	45.80%	54.20%	100.00%		
Normal	No.	7	10	17		
	%	41.20%	58.80%	100.00%		
Total	No.	45	55	100		
	%	45.00%	55.00%	100.00%		
Sensitivity	84.44%	70.54%	93.51%			
Specificity	18.18%	9.08%	30.90%			
Predictive value of positive test	45.78%	34.79%	57.08%			
Predictive value of negative test	58.82%	32.92%	81.56%			
Likelihood ratio of positive test	1.0321	0.8649	1.2317			
Likelihood ratio of negative test	0.8556	0.3542	2.0665			
Youden's index	0.0263	-0.1207	0.1732			
Measure of agreement	Kappa	Value	Approx. T	p-value	Agreement is-	
		0.024	0.348	0.728	Slight	

Structural abnormalities of endometrial cavity such as polyps, submucous fibroid can be better diagnosed with hysteroscopy. Likelihood ratio of positive test with hysteroscopy was 1.4938 and it was more than that of ultrasonography (1.0321) again proving that hysteroscopy was better investigation as compared to ultrasonography as there is more possibility of having abnormality on HPE report if hysteroscopy was showing some abnormality.

DISCUSSION

Clinical management of AUB aims at obtaining an accurate diagnosis and charting out correct line of management. On USG the uterine contour and morphology of ovary can be found but it fails to provide adequate information regarding the pathology of the endometrium. Hysteroscopy in this new era is increasingly becoming a valuable investigation for the evaluation of AUB.

In this study we evaluated 100 patients of AUB above the age of 45 who presented to OPD. In present study authors found that the maximum incidence of AUB was present between the age groups of 45-49 years of age (66%). In a study conducted by Patil et al a total of 100 patients of age more than 18 years with AUB were evaluated and found that Abnormal uterine bleeding was most prevalent among women of two age groups, 26-30 years and 41-45 years (22%).¹⁰ In another study conducted by Kathuria et al evaluating 50 patients between age group of 20-60 years and found to maximum incidence between the age group of 30-39 years (44%).¹¹ Present study showed a different prevalence profile than the above studies as we have considered patients above 45 years of age as study population.

The commonest presenting complaint was menorrhagia or heavy menstrual bleeding (60%) followed by post-menopausal bleeding (12%) followed by intermenstrual bleeding (11%) and heavy and prolonged menstrual bleeding (10%) in that order. This was in consistence with many other studies like in a study by Shyam et al, the most common symptom in patients with abnormal uterine bleeding was menorrhagia (40%), metrorrhagia (18%), menometrorrhagia (14%), and polymenorrhea (14%).¹² In Kathuria et al series the commonest presenting complaint was menorrhagia 46%, followed by polymenorrhea (30%) and metrorrhagia (18%) and post-menopausal bleeding in 6%.¹¹ Shrinivas concluded that 46% of patients presented with heavy menstrual bleeding, 34% had increased cycle frequency (Past terminology of polymenorrhea) and 20% of them had presented with continuous bleeding.¹³

Most of the patients coming to OPD usually seek medical attention within 6 months of menstrual complains (75%). In study by Kathuria et al found that most of the patients seek medical attention after suffering for 3-6 months time (50%).¹¹ In another study conducted by Kulkarni S et al,

it was found that 54% patients presents within 6 months of complaints.¹⁴ Patients do not seek medical attention early because menstrual complaints are usually neglected in our country and also may be because females feel awkward discussing these complaints and most of the time they are not aware that this can cause serious problem in future.

Out of 100 patients in present study most of them (71%) presented with isolated complaints of menstrual abnormality and had no other associated medical comorbidities while the remaining patients had some or the other associated morbid conditions. Among these hypertension was seen in 9% patients, diabetics in 5% patients and hypothyroidism in 3% patients and tuberculosis in 3%. In a study conducted by Patil et al 14% of the patients were hypertensive, 6% had history of tuberculosis, 5% were diabetic and 5% of the patients were having sickle cell disease.¹⁰

Ultrasonography being easily available and more feasible as compared to hysteroscopy, done first. In present study ultrasonography showed some abnormality in 83% of the patients while in 17% patients it was normal. Among the detected abnormalities, thickened endometrium was the most common (44%) followed by fibroid in 17%, adenomyosis in 13%, endometrial polyp 8% and endocervical polyp in 1%. This finding of thickened endometrium as the most common abnormality on USG is in concordance with many other studies.

In a study done by Karlsson et al, they found that 39 out of 51 patients in their studies had thickened endometrium as abnormal finding on USG.¹⁵ In a study by Patil S, et al. endometrial hyperplasia (15%) was the most commonly detected pathology, followed by fibroid uterus (13%), on ultrasonography.¹⁰ In a study by El-Ihyat W et al it was 32%.¹⁶ In a study by Sharma et al (66%) had abnormal finding in which most common finding of hyperplastic endometrium.¹³ USG as a diagnostic modality overestimates the actual number of abnormalities as found in present study.

Patients with either abnormal or normal findings on USG were then evaluated with hysteroscopy followed by endometrial biopsy sampling in the same setting. Hysteroscopy provides direct visualization of the endometrial cavity. In present study, out of 100 patients, 80% patients were found to have abnormal findings (thickened endometrium, polyp, fibroid, scarring, atrophy, septum) rest 20% found to have no detectable cause of AUB on hysteroscopy. Out of these 80% abnormal findings, thickened endometrium was found in 45% patients which was similar to USG findings. This was similar to many other studies. In present study, the most common finding was thickened endometrium (45%), followed by endometrial polyp 15%, atrophic endometrium 12%, submucous fibroid 7% and an incidental finding of septate uterus in one patient. On contrast in a study done by El-Ihyat et al, on

hysteroscopy the commonest lesion diagnosed was endometrial polyp which was found in 28% of cases, while endometrial hyperplasia found only in 20%.¹⁶

In present study endometrial sampling was done for all 100 patients in same setting when patient was posted for Dilatation and curettage with hysteroscopy. On HPE report the most common histopathological finding was Secretory phase endometrium in 39 patients followed by proliferative phase endometrium in 16 patients. Finding of disordered proliferative endometrium was noted in 14 patients, endometrial polyp in 14 patients, endometrial hyperplasia without atypia in 14 patients, endometrial hyperplasia with atypia in 2 patients and leiomyoma in 1 patient. In present study histopathology report revealed abnormality in 43% patients while rest 57% patients were found to have normal histopathological report. This almost similar to study done by Kathuria R et al where 40% patients have some or the other abnormality while 60% patients have normal HPE report.¹¹ In a study by Patil S et al they found proliferative phase endometrium as most common finding which is contrary to present study finding of secretory endometrium as most common histopathological report.¹⁰

Among the 100 patients that were evaluated with hysteroscopy 80% of the patients found to have abnormality whereas 20% patients had normal hysteroscopic findings. Among the patients with abnormal hysteroscopic findings 44 cases (55%) were also have abnormality on HPE report while 36 cases (45%) were normal on HPE report. Among the 20 hysteroscopically normal patients 19 cases (95%) had normal HPE report, and only 1 case (5%) found to have abnormality.

As per present study the sensitivity of hysteroscopy was 97.78% and specificity were 34.55%, the negative predictive value of the test is 95% hence there is a fair correlation between the hysteroscopic findings and HPE report to find out true negative cases. Because of high sensitivity (97.78%) of hysteroscopy, there were higher chances to detect cases with true abnormality but due to low specificity the test was not appropriate to diagnose cases with no abnormality and hence HPE is needed to come to confirm the diagnosis. Though HPE will be required for final diagnosis but there is fair correlation between hysteroscopic findings and actual HPE report and hence hysteroscopy can be used as initial investigation while evaluating the patients with AUB.

Structural abnormalities of endometrial cavity such as polyps, submucous fibroid can be better diagnosed with hysteroscopy. Likelihood ratio of positive test with hysteroscopy was 1.4938 and it was more than that of ultrasonography (1.0321) again proving that hysteroscopy was better investigation as compared to ultrasonography as there is more possibility of having abnormality on HPE report if hysteroscopy is showing some abnormality.

Among the 100 patients that were evaluated with ultrasonography 83% of the patients found to have abnormality whereas 17% patients had normal ultrasonography findings. Amongst the patients with abnormal ultrasonography findings 38 cases (45.80%) were also having abnormality on HPE report while 45 cases (54.20%) were normal on HPE report.

Among the 17 ultrasonographically normal patients 10 cases (58.80%) had normal HPE report, and 7 cases (41.20%) cases found to have abnormality. In present study sensitivity of ultrasonography in diagnosing the cause of AUB is 84.44%, specificity is 18.18%, positive predictive value is 45.78% and negative predictive value is 58.82%.

While comparing the findings of ultrasonography and hysteroscopy, among the 100 patients, on ultrasonography 83 patients found to have abnormality whereas 17 patients had normal ultrasonography findings. Amongst the patients with abnormal ultrasonography findings 65 cases (78.30%) were also having abnormality on hysteroscopy. Among the 17 patients with normal ultrasonographic findings only 2 patients (11.80%) were also normal on hysteroscopy. This means that it is possible to over diagnose an abnormality on ultrasonography.

The sensitivity, specificity and negative predictive value, all the modalities of good screening test are higher with hysteroscopy as compared to USG. Hence it was not possible to diagnose true negatives or positives as accurately on ultrasonography as hysteroscopy, when the actual histopathological correlation is kept in mind. This was further confirmed by the later observations and analysis between USG and hysteroscopy where it shows that USG overestimates the disease burden probably due to interobserver variability. Though the experience of the surgeon doing the hysteroscopy is also a factor to be considered, but usually it is negated by the direct observation and cross confirmation with the experienced surgeons during procedure. Also, the hysteroscopic findings pathognomonic of septate uterus, small submucous fibroid etc. are easy to be missed on USG but can be picked up in hysteroscopy with ease.

Of the 100 patients in present study, 66% were in the age group of 45-49 years of age, followed by 21% between age group of 50-54 years, 7% between 55-59 years and 6% between 60-65 years. 60% of them presented with the complaints of heavy menstrual bleeding. The transvaginal scan assessment showed that 3 patients showed an endometrial thickness of less than 4 mm, 60 patients showed an endometrial thickness between 4-8 mm, 25 between 8-12 mm, 9 of them between 12-16mm, 3 of them >16 mm.

Diagnostic hysteroscopy revealed the appearance of thickened endometrium in 45%, atrophic in 12%. No case of endometrial carcinoma was diagnosed. Focal lesions

like sub mucous fibroid was diagnosed in 7%, Polyp in 15% and a septate uterus was noted in 1% cases. Histopathology reports showed proliferative endometrium in 16 patients, secretory in 39 patients, endometrial polyp in 14 and disorder proliferative endometrium in 14. Incidence of hyperplasia with atypia was 2% and 14% without atypia. Diagnostic value of hysteroscopy in comparison to histopathology gave an average sensitivity and specificity of 97.78% and 34.55% respectively, which is different for different findings on histopathology report.

Using kappa coefficient an agreement test was done between hysteroscopy and histopathology and again between TVS and histopathology. TVS showed a moderate agreement with histopathology for proliferative and secretory endometrium whereas the agreement was fair for hyperplastic endometrium but was poor for polyp. Hysteroscopy showed a substantial agreement for proliferative, secretory and hyperplastic endometrium and almost perfect agreement for focal lesions like polyp. For focal lesions TVS showed a low sensitivity which is in accordance with the report by Shrinivas K et al, who concluded that TVS was a preferred modality for endometrial thickness but not sensitive enough to rule out pathology.¹⁴

Pyari JS et al, too have concluded that hysteroscopy has a better sensitivity and specificity compared to TVS.¹² Focal abnormalities were detected in the present study in a small number in contrast to other studies. This was probably due to the fact that the age group considered here is only perimenopausal whereas other studies have included women in reproductive age group, which could explain this.

ACKNOWLEDGMENTS

Authors would like to thank Dr Meenakshi Mathur for her support and encouragement.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Bhatiyani BR, Dhumale S, Pandeewari, Bashani D. Correlation between ultrasonographic, hysteroscopic and histopathological findings in patients with abnormal uterine bleeding. *Int J Reprod Contracept Obstet Gynecol* 2018;7:3250-6.