Original Research Article

Correlation between ultrasonographic and histopathological findings of hysterectomy specimen in patients with abnormal uterine bleeding

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ABSTRACT

Background: AUB is a common and debilitating condition and it is one of the main gynaecological reasons for hysterectomy. Ultrasonography can be as good as histopathology (HPE) in the diagnosis of abnormal uterine bleeding. Hence, our study was conducted to validate the ultrasonographic findings with HPE findings in diagnosis of AUB.
Methods: A hospital based cross-sectional analytical study was conducted among 86 patients with abnormal uterine bleeding in the department of Obstetrics and Gynaecology in collaboration with department of Pathology, RIMS, Imphal from September 2017 to March 2019. The clinical history and socio demographic profile were collected using a pre-designed proforma. General physical examination, pelvic examination and ultrasonagraphy was carried out and the hysterectomy specimens were subjected to histopathological examination.
Results: Fibromyoma was diagnosed by ultrasound in 62.8% of the patients and it was the common diagnosis in this study. The sensitivity, specificity, positive predictive value, negative predictive value and kappa statistics of USG for diagnosing leiomyoma was 92.9%, 93.3%, 96.3%, 87.5% and 84.9% respectively. The sensitivity, specificity, positive predictive value, negative predictive value and kappa statistics of USG for diagnosing adenomyosis was 53.8%, 98.6%, 87.5%, 92.3% and 62.3% respectively.
Conclusions: The study provides an evidence that ultrasonography has good diagnostic accuracy as histopathology in the diagnosis of fibroid in patients with abnormal uterine bleeding. However, as with all the diagnostic procedures, the utility of ultrasound in the diagnosis of adenomyosis is questionable, since it has a low sensitivity amidst good specificity.

Keywords: Abnormal uterine bleeding, Cross-sectional analytical study, Diagnostic accuracy, Histopathology, Ultrasonagraphy

INTRODUCTION

Abnormal uterine bleeding (AUB) describes all abnormal patterns of menstrual bleeding that may result from a wide variety of causes including anovulation, pregnancy, uterine pathology and coagulopathies.[1] It occurs in various forms such as menorrhagia, polymenorrhea, polymenorrhagia, metorrhagia, and menometrorrhagia.[2] It accounts for more than 70% of all gynaecological consultations in the peri and post-menopausal age group.[3] Globally, the prevalence of AUB varies in different populations, with the overall prevalence fluctuating between 10% and 30%.[4] In India, the reported prevalence of AUB is around 17.9%.[5]

There are various causes of abnormal uterine bleeding. To standardize nomenclature of AUB, a new system known by the acronym PALM-COEIN, was introduced in

2011 by FIGO. The PALM-COEIN system is based on etiology and pathology of disorder, where PALM describing structural causes (polyp, adenomyosis, leiomyoma, malignancy and hyperplasia) and COEIN denoting non- structural causes of AUB (coagulopathy, ovulatory disorders, endometrial factors, iatrogenic and not classified).[7] Exogenous causes are foreign body, trauma and medications- sex steroids, anticoagulants, hyperprolactinemia inducing. Infective causes are sexually transmitted disease (STD), tuberculosis (TB), chronic endometritis etc.[6]

With ageing, risk of benign and malignant neoplastic growth increases. Even so, malignant neoplasms, especially endometrial carcinoma are found more often in this age group. Less commonly, oestrogen producing ovarian carcinoma may cause endometrial hyperplasia with uterine bleeding. Similarly, ulcerative vulvar, vaginal or cervical neoplasms can be sources. And rarely, serosanguinous discharge from a fallopian tube cancer may appear as uterine bleeding. Thus bleeding in this demographic usually prompts evaluation to exclude these cancers.[7]

The specific diagnostic approach depends on whether the patient is premenopausal, perimenopausal or postmenopausal. In premenopausal women with normal findings on physical examination the most likely diagnosis is dysfunctional uterine bleeding secondary to anovulation and the diagnostic investigation is targeted at identifying the etiology of anovulation.[8] Dysfunctional uterine bleeding is diagnosed by excluding pregnancy, iatrogenic causes, systemic conditions and genital tract pathology.

In perimenopausal women endometrial biopsy and other methods of detecting endometrial hyperplasia or carcinoma must be considered early in investigation. An international expert consensus from the FIGO Menstrual Disorders working group has proposed a standardized classification system for AUB to facilitate greater appreciation of the complexities of this clinical entity. The PALM side of the classification refers to structural causes that could be evaluated and diagnosed on imaging and or biopsy. The COEIN side allows consideration of underlying medical disturbances that could result in AUB. Imaging studies are indicated when examination suggests structural causes for bleeding or when conservative management has failed or when there is a risk of malignancy [obesity, diabetes, nulliparity, history of PCOS, family history of hereditary non-polyposis colorectal cancer (HNPCC)].[9]

In post-menopausal women with AUB, uterine pathology, particularly endometrial carcinoma is common. Thus, in this age group; endometrial biopsy or transvaginal sonography is included in the initial investigation. If imaging is indicated, transvaginal ultrasound should the first one of imaging modality for AUB.[10] Saline infusion sonography and diagnostic hysteroscopy could be used in the diagnosis and characterization of discrete intrauterine abnormalities such as sub mucosal fibroid.[11]

Ultrasonography can be as good as histopathology in the diagnosis of abnormal uterine bleeding. Studies have been conducted across the different parts of the world to correlate the ultrasonographic findings with histopathology in the diagnosis of abnormal uterine bleeding. However, very few studies are conducted in our country in this regard, in particular, in Manipur. Hence, our study was conducted to determine the causes of abnormal uterine bleeding and to correlate and validate the ultrasonographic findings with HPE findings in diagnosis of AUB among women who underwent hysterectomy for AUB.

METHODS

A hospital based cross-sectional analytical study was conducted among patients with abnormal uterine bleeding who underwent abdominal hysterectomy from September 2017 to August, 2019 in the department of Obstetrics and Gynaecology in collaboration with department of Pathology, Regional Institute of Medical Sciences, Imphal. Patients with gestational bleeding genital prolapse, bleeding diathesis and trauma induced bleeding were excluded. The study was conducted after obtaining permission from the Institutional Ethics Committee, RIMS, Imphal.

Sample size and sampling

Assuming the specificity of ultrasound as 89% and prevalence of AUB as 10%, the sample size was estimated to be 85 at 95% confidence level and a precision of 7%, using the formula for diagnostic tests.[12] All the patients who underwent abdominal hysterectomy were included in the study until the sample size was reached.

Study procedure

After obtaining informed consent was obtained from the participants, the detailed clinical history including age, parity, the chief presenting complaints, menstrual, contraceptive, medical history (age of patient, patterns of abnormal uterine bleeding, severity, associated pain, family history, and use of medication) and socio demographic profile were then recorded. Following the socio demographic and clinical characteristics, general physical examination (pallor, oedema, neck glands, thyroid and systemic examination and pelvic examination (per speculum, pap-smear, bimanual examination) was carried out for the participants.

All the routine investigations including complete haemogram, urine routine examination, liver and kidney function tests, ABO grouping and Rh typing, blood sugar estimation, thyroid profile along with necessary investigations like ultrasonogrzphy (trans-vaginal) and

coagulation profile, fundoscopy, MRI (if neurological damage suspected) were also performed. Data was recorded in a pre-designed proforma.

Ultrasonography was performed using MODEL SONOACE X8 (Samsung Medison Co. Ltd, Korea), Curvilinear probe (5-7 MHZ) and power/NETZ/ ALIMENTATION- 100 to 120/200 to 240v. Hysterectomy specimens were subjected to histopathological examination. Histopathological examination was carried out using automated tissue processor (Leica, China), binocular light microscope (India, model no- CH2OiB1MF), rotary microtone (Leica, China) and heamatoxylin and eosin stain.

Statistical analysis

Data was analysed using SPSS version 21.0 IBM. Categorical variables like parity; menstrual complaints etc. we re expressed as frequency and percentages. Continuous variables like age, duration of complaints etc. are expressed as mean (standard deviation) or median (inter quartile range) depending upon the type of distribution. The validity of ultrasonagraphic findings is presented in terms of sensitivity, specificity, positive predictive value and negative predictive value.

RESULTS

A total of 86 patients with abnormal uterine bleeding who underwent abdominal hysterectomy were included. The mean age of the patients was 41.9 (9.1) years with a minimum of 28 years and a maximum of 66 years.

Table 1: Socio-demographic characteristics of the patients with abnormal uterine bleeding who underwent abdominal hysterectomy in a tertiary care centre, Imphal (N=86).

Characteristics	Frequency (n)	Percentage
Age category (years)		
≤45	63	73.2
45-60	19	22.1
≥61	4	4.7
Parity		
0	3	3.5
1	5	5.8
2	31	36.0
3	29	33.8
4 and above	18	20.9

Table 1 shows nearly 3/4th (73.2%) of the participants were in less than or equal to 45 years followed by 45-60 years age group (22.1%) and 3.5% of the participants were nulliparous, 5.8% were primipara. and the remaining participants were multiparous women.

Table 2: Clinical profile of patients with abnormal uterine bleeding who underwent abdominal hysterectomy in a tertiary care centre, Imphal (N=86).

	Frequency (n)	Percentage
Anaemia		
No anaemia (≥12 mg/dl)	0	0
Mild anaemia (11.0-11.9 mg/dl)	8	9.3
Moderate anaemia (8.0-10.9 mg/dl)	75	87.2
Severe anaemia (<8 mg/dl)	3	3.5
Menstrual complaints		
Menorrhagia	34	39.5
Metrorrhagia	18	20.9
Menometorrhagia	12	14.0
Polymenorrhagia	9	10.5
Postmenopausal bleeding	13	15.1
Duration of symptoms (months)		
1-3	24	27.9
4-6	43	50.0
7-12	13	15.1
>12	6	7.0
Co-morbidities		
No co-morbidity	57	66.3
Diabetes	9	10.5
Hypertension	7	8.1
Diabetes + hypertension	3	3.5
Heart disease	5	5.8
Others*	5	5.8

*Others include thyroid disorders, asthma etc.

Table 2 shows majority (87.2%) of the patients had moderate anaemia. None of the patients were normal with respect to the haemoglobin level. The most common menstrual complaint was menorrhagia (39.5%) followed by metrorrhagia (20.9%). Postmenopausal bleeding was present in 15.1% of the patients. The mean duration of the symptoms was 5.2 (3.3) months with a minimum of one month and a maximum of 14 months. About half of the patients (50.0%) were having symptoms for 4-6 months duration. Only six patients presented with the symptoms for more than 12 months. About 2/3rd of the patients were without any comorbidity. Diabetes was present in 10.5% of the patients and hypertension was present in 8.1% of the patients.

Table 3 shows ultrasonagraphically 54 (62.8%) cases were fibroid uterus, 8 (9.3%) cases were adenomyosis, 6 (7.0%) cases were thickened endometrium and one case was endometrial polyp. Seventeen (19.7%) cases were bulky uterus. Table 4 shows nearly 2/3rd (65.1%) of the patients had leomyomatous changes on histopathological examination. The myometrium was normal in 19.8% cases. Of the 17 cases diagnosed as bulky uterus on USG, 11 cases had normal endometrium, two cases had leomyomatous changes and four cases had

adenomyomatous changes. Endometrium was hyperplastic (53.5%) in majority followed by secretory (22.1%) and proliferative (10.5%). Two patients were found to have carcinoma on histopathological examination. Cervix was normal in 38.4% cases. Cervix was inflammatory type in 58.1% cases and CIN1 was observed in three cases. Simple typical hyperplasia was present in 82.6% cases who showed hyperplastic endometrium in histopathological examination. Simple atypical, complex typical and complex atypical hyperplasia was present in 2.2%, 8.7% and 6.5% cases.

Table 3: Ultrasonagraphic diagnosis of the patients with abnormal uterine bleeding who underwent abdominal hysterectomy in a tertiary care centre, Imphal (N=86).

Ultrsonagraphic diagnosis	Frequency (n)	Percentage
Fibroid	54	62.8
Bulky uterus	17	19.7
Adenomyosis	8	9.3
Thickened endometrium	6	7.0
Endometrial polyp	1	1.2

Table 4: Histopathological findings among patients with abnormal uterine bleeding who underwent abdominal hysterectomy in a tertiary care centre, Imphal (N=86).

Histopathological findings	Frequency (n)	Percentage
Myometrium		
Normal	17	19.8
Leomyomatous changes	56	65.1
Adenomyomatous changes	13	15.1
Endometrium		
Hyperplastic	46	53.5
Secretory	19	22.1
Proliferative	9	10.5
Atrophic	6	7.0
Inflammatory	3	3.4
Carcinoma	2	2.3
Polyp	1	1.2
Cervix		
Normal	33	38.4
Inflammatory	50	58.1
CIN1	3	3.5
Type of endometria hyperplasia (N=46)		
Simple typical	38	82.6
Simple atypical	1	2.2
Complex typical	4	8.7
Complex atypical	3	6.5

Table 5 shows the validity of ultrasonography in diagnosing leiomyoma and adenomyosis. The sensitivity, specificity, positive predictive value, negative predictive value and kappa statistics of USG for diagnosing

leiomyoma was 92.9%, 93.3%, 96.3%, 87.5% and 84.9% respectively. The sensitivity, specificity, positive predictive value, negative predictive value and kappa statistics of USG for diagnosing adenomyosis was 53.8%, 98.6%, 87.5%, 92.3% and 62.3% respectively.

Table 5: Summary of validity of ultrasonagraphy with histopathology for diagnosis of leiomyoma and adenomyosis (N=86).

	Leiomyoma (%)	Adenomyosis (%)
Sensitivity	92.9	53.8
Specificity	93.3	98.6
Positive predictive value	96.3	87.5
Negative predictive value	87.5	92.3
Kappa statistics	84.9	62.3

Figure 1 shows that majority of patients who were diagnosed as fibroid in USG had presented with menorrhagia (61.1%). Menometrorrhagia (29.4%) was the common presentation in patients with bulky uterus. None of the patient presented with menorrhagia that had diagnosis of adenomyosis, thickened endometrium and endometrial polyp. Among six patients with thickened endometrium on USG, three patients presented with postmenopausal bleeding and 2 patients presented with Metrorrhagia and one patient with polymenorrhagia.
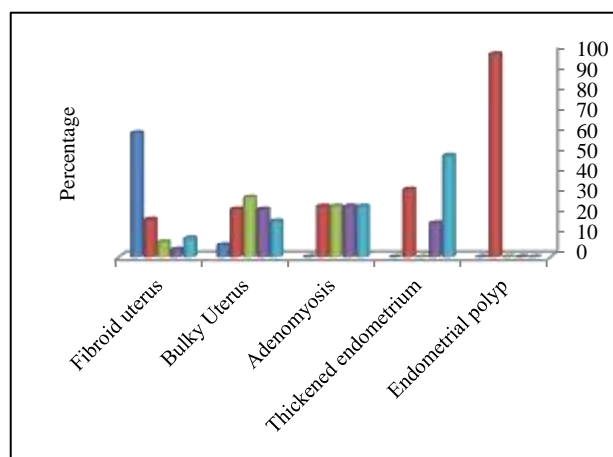

Figure 1: Patient distribution with respect to bleeding pattern and ultrasonography findings (N=86).

DISCUSSION

Histopathological diagnosis has been considered as the gold standard in the diagnosis of abnormal uterine bleeding. This is one of the fewer studies conducted across the country to decipher the utility of ultrasound in the diagnosis of abnormal uterine bleeding.

In our study, most number of patients (44.2%) were in the age group of 36-45 years with majority of them above 40

years. This observation is comparable to studies conducted by Talukdar et al, Pillai et al and Jetley et al where the most common age group of abnormal uterine bleeding was 40-45 years.[12-14] This might be due to the fact that perimenopause, also called the menopausal transition, is the interval in which a woman's body makes a natural shift from more-or-less regular cycles of ovulation and menstruation toward permanent infertility, or menopause. This phase generally occurs at around 40-50 years of age. This result is also consistent with numerous studies conducted across our country.[15-20] in which AUB was most common in peri-menopausal age group.

The most common menstrual complaint was menorrhagia which was observed in 39.5% of the cases. This finding is comparable to studies conducted by Taludkar et al where menorrhagia was the common menstrual problem in 43.69% of the patients.[12] Same results were observed by studies conducted by Jetley et al, Goyal et al, Gupta et al, Bolde et al, Verma et al and Rani et al in which clinical presentation as menorrhagia in AUB evaluation revealed 46.4%, 58%, 53%, 46.86%, 57% and 48% respectively.[14,21-25] Majority of patients (50%) who attended the hospital for treatment were suffering for 4-6 months which is comparable to studies conducted by Taludkar et al (54.37%) and Kathuria et al (50%).[12,26]

Fibromyoma was diagnosed by ultrasound in 62.8% of the patients and it was the common diagnosis in this study. The study result is consistent with many other studies conducted across the globe, where fibroid uterus was the common condition associated with abnormal uterine bleeding.[12,20,21,27-29] Unless uterine polyp, uterine fibroid develops during the reproductive age group, which would have contributed to the above finding, since majority of patients in this study were in the reproductive age group. Adenomyosis was the next common condition diagnosed by ultrasound which is also comparable with other studies.

The sensitivity, specificity, positive predictive value and negative predictive value of USG for diagnosing leiomyoma was 92.9%, 93.3%, 96.3% and 87.5% respectively. Study conducted by Talukdar et al showed the similar results in which sensitivity and specificity was 89.13% and 89.47% respectively.[12] The results were consistent with numerous studies, where the ultrasound was as good as histopathology in the diagnosis of uterine fibroid in patients with abnormal uterine bleeding. [21,27,30-32] However a study conducted by Hunter et al showed a sensitivity of 75% for USG in diagnosing uterine fibroid, even though it showed a specificity of 90%.[33] Similarly, a study conducted by Erdem et al showed a specificity of 100%.[34] The agreement (kappa) between USG and histopathology in the diagnosis of uterine fibroid was 0.849 which is similar to studies conducted by Shobitha et al[31] and Goyal et al[21] which showed an excellent agreement of 0.72 and 0.898 respectively.[21,31]

Contradictory to diagnosing fibroid, the USG had a lesser sensitivity in diagnosing adenomyosis, although it had a good specificity. The sensitivity and specificity for diagnosing adenomyosis was found to be 53.8% and 98.6% respectively which is similar to results of Talukdar et al, in which the sensitivity and specificity was found to be 47.62% and 98.78% respectively.[12] Similarly, Nicula et al reported a sensitivity of 8% for diagnosing adenomyosis.[27] Hence, USG has a limitation in tissue characterization in diagnosis of adenomyosis. The agreement (kappa) between USG and histopathology was 0.623.

Out of 86 patients those who has presented as AUB and underwent Hysterectomy, we got two carcinoma endometrium cases (2.3%) in HPE and out of these two HPE confirmed carcinoma endometrium cases, USG detected thickened endometrium 1 case and bulky uterus in other case. This finding is comparable to studies conducted by Taludkar et al where ca endometrium found in 2.8% cases.[12] So USG detected thickened endometrium and bulky uterus in postmenopausal woman presents as a postmenopausal bleeding is a good indicator of endometrial carcinoma.

The major strength of the study is that it is one of the fewer studies conducted in this part of the country with adequate sample size, which ensured its generalisability to the similar setting. The selection bias was kept to minimum by including all the patients of all ages who underwent hysterectomy for abnormal uterine bleeding.

The limitation of the study is that the number of patients for pathologies other than fibroid and adenomyosis were very less and comparability was not possible.

CONCLUSION

Uterine fibroid was the leading cause of abnormal uterine bleeding for which hysterectomy was done. The study provides a concrete evidence that ultrasonagraphy has good diagnostic accuracy as histopathology in the diagnosis of fibroid in patients with abnormal uterine bleeding. However, as with all the diagnostic procedures, the utility of ultrasound in the diagnosis of adenomyosis is questionable, since it has a low sensitivity amidst good specificity. The low sensitivity might be due to lesser patients with adenomyosis. In addition to that, the combination of procedures viz. ultrasound/hysteroscopy and endometrial biopsy with hysteroscopy can aid in a better diagnosis rather than a single procedure.

Recommendations

Further studies are recommended with combination of all the procedures viz. ultrasound/hysteroscopy and endometrial biopsy with hysteroscopy to look into the diagnostic utility of the combination of procedures in a cost-effective way.

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