

A RETROSPECTIVE STUDY TO EVALUATE THE DEGREE OF AGREEMENT BETWEEN THE ULTRASONOGRAPHIC AND HISTOPATHOLOGICAL FINDINGS IN WOMEN WITH THE PERIMENOPAUSAL AUB

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Abstract

Objective: The aim of the study was to evaluate the validity of Transvaginal sonography (TVS) in accurately diagnosing structural pathologies in patients with the perimenopausal AUB (PALM component of PALM COEIN classification) and to assess the degree of agreement between the Transvaginal ultrasonographic (TVS) and Histopathological (HPR) findings.

Material and Method: This retrospective study was conducted in 102 women with perimenopausal AUB attending the tertiary rural health center in North-west Maharashtra. Indoor case records of 102 perimenopausal women with AUB who were subjected to TVS and later diagnostic fractional curettage and /or hysterectomy as per institutional protocol, and in whom HPR examination reports were available were included in study. Data was collected and tabulated as per ethically approved format. Kappa Statistical test and Z test of difference between proportions was applied to assess the degree of agreement between the TVS and HPR findings

Results: In the present study 36% Leiomyoma, 24% Endometrial Hyperplasia & 10% Adenomyosis were diagnosed as cause of Perimenopausal AUB on TVS. However on HPR examination 41% Endometrial Hyperplasia, 33% Leiomyoma, 16% Adenomyosis & 5% malignancies were responsible for AUB. TVS had 97% specificity, 50% sensitivity & 92% Positive predictive value (PPV) in diagnosing Endometrial hyperplasia. TVS had 89%

specificity & sensitivity and 92% Negative predictive value (NPV) to diagnose Leiomyoma. Kappa test and Z test showed statistically good correlation over chance for leiomyoma and fair correlation over chance for diagnosing Endometrial Hyperplasia

Conclusion: Presence of endometrial hyperplasia on TVS in perimenopausal AUB confirms endometrial cause of AUB, However its absence on TVS still needs further evaluation by hysteroscopy/ curettage before going ahead with conservative line of management

Keywords:

Leiomyoma, Endometrial Hyperplasia, Perimenopause, ultrasonography, Dysfunctional uterine bleeding

Introduction

Perimenopause as defined by WHO is the period immediately prior to menopause when the endocrinological, biological and clinical features approaching menopause begin and the first year immediately after menopause.¹ In Indian woman the average age of menopause is 46.2 years which is found to be much less than their Western women approaching menopause (51 years).² In more than 70% of all gynecological consultations in the perimenopausal age group the most common complaint encountered is of abnormal uterine bleeding.³ The prevalence of abnormal uterine bleeding (AUB) worldwide ranges from 4% to 52%.⁴ In women between menarche and menopause 9% to 14% are reported to have AUB in India, with a prevalence of 17.9%.⁵

In 2018 FIGO developed a revised system classification for AUB called PALM COEIN classification to aid the clinician in systematically assessing the various causes of AUB and application of the investigations in order to interpret the results thus providing evidence based clinical care.⁶ Transvaginal ultrasound (TVS) is the most easily available, minimally invasive diagnostic method done for all AUB patients as a baseline investigation to study the endometrium and detect any organic or structural pathology causative for abnormal uterine bleeding. Histopathological (HPR) examination of uterus and cervix is done to diagnose the underlying structural aetiology causing AUB, however it is costly and requires invasive procedures to retrieve the required specimen. The present study is undertaken to evaluate the efficacy of transvaginal ultrasound in depicting endometrial pathologies with AUB and to assess the degree of agreement between the ultrasonographic and histopathological findings in women with the perimenopausal abnormal uterine bleeding.

Material & Methods

The present retrospective, observational and analytical study was conducted in department of Obstetrics & Gynecology at tertiary care rural hospital in Northern Maharashtra. Data for the study was extracted from indoor case records of perimenopausal women with AUB from 1st August 2018- 31st July 2020. The study population consists of 102 perimenopausal women⁷ in age group 40-50 yrs with abnormal uterine bleeding admitted to the hospital in whom TVS reports and HPR reports were available.

Inclusion criteria

All perimenopausal women aged 40-50 years with AUB subjected to TVS and underwent hysterectomy with HPR reports with both reports available between 1st August 2018- 31st July 2020

Exclusion criteria:

1. Patients with diagnosed bleeding disorders, Diabetes, thyroid disorders.
2. Diagnosed cases of carcinoma of the genital tract with inadequate reports

3. Pregnant women
4. Patient on oral or injectable hormonal contraceptives

The institutional ethical approval was taken for the study. After which data was extracted from indoor case records in the form of detailed history of the patient, clinical examination and routine blood investigations. As per our institutional protocol these perimenopausal women with AUB were previously subjected to TVS then women in whom hysterectomy was performed with available HPR reports were included in this study. Both TVS and HPR reports were confirmed to be reported by senior sonologists and pathologists. All this data was extracted and the tabulated for analysis. Case records where either data was not available were not included for the study.

Statistical analysis

The efficacy of ultrasonography was assessed by calculating the sensitivity, specificity, positive predictive value and negative predictive value while comparing with the gold standard such as histopathology in the tabulated form. The degree of agreement between ultrasonography and histopathology were assessed by Kappa test. Kappa ratio is a proportion that can take values from -1 (indicating perfect disagreement) through 0 to +1 (indicating perfect agreement). The results are expressed in percentage as follows: less than 20% is negligible improvement over chance, 20%-40% is minimal, 40% to 60% is fair, 60% to 80% is good and greater than 80% is excellent. The statistical significance was assessed by applying Z test of difference between two proportions i.e the agreement by chance to the total agreement and actual agreement to the total agreement. All analysis was done using SPSS software version 20.0.0. Statistical significance was calculated at $p=0.05$ confidence level.

Results

Data of one hundred and two number of patients with perimenopausal AUB was included in the study. USG reports of all 102 perimenopausal women with AUB was noted and the diagnosis obtained on USG was tabulated to understand the most commonly encountered diagnosis. Table 1 reveals that on the ultrasonography, most of the patients were of leiomyoma uteri. i.e 37 cases (36.2%), while only 2 cases each were of endometrial carcinoma and cervical carcinoma.

Table 1: Diagnosis on Ultrasonography

Table 2- Histopathology correlation with Ultrasonography diagnosis

The Table 2 shows the relation between cases diagnosed on ultrasound and confirmed with histopathology. The table reveals that, ultrasonography detected leiomyoma in 37 (36%) cases out of which 30 (81%) were confirmed on histopathology. In the remaining 7 cases, 4 cases were of adenomyomas which were confused with leiomyomas on USG depending on their location and need histopathological confirmation while the remaining 3 cases had a normal uterus on HPR which can be explained by overdiagnosis as well as localized contractions of myometrium in perimenopausal women with heavy menstrual bleeding in AUB.

Out of the 10 (9.8%) cases who underwent hysterectomy for adenomyosis, 8 (80%) were confirmed on histopathology report while the remaining two cases were diagnosed leiomyomas on HPR, this can be due to the location of the leiomyoma which can be confused with adenomyomas.

4 cases of polyp were detected on ultrasonography out of which 3 were confirmed on histopathology and one was diagnosed as endometrial hyperplasia. Localized endometrial hyperplasia mimics polyp on USG.

Cervical carcinoma was detected on ultrasonography in 2 cases, both were operable and underwent Radical hysterectomy after confirmed diagnosis on histopathology report of cervical biopsy.

25(24.5%) cases of AUB had endometrial hyperplasia on TVS of these 23(92%) cases were confirmed endometrial hyperplasia on HPR and 1 case (4%) was diagnosed to have carcinoma endometrium, only 1 case(4%) was found to have normal secretory endometrium. On histopathology of the endometrium amongst all 102 cases of hysterectomy, the most common finding was endometrial hyperplasia seen in 42 cases(41.17%).Out of these, 37(36.9%) cases were diagnosed as endometrial hyperplasia without atypia and rest 5(4.9%) cases were of endometrial hyperplasia with atypia.17 more cases of endometrial hyperplasia were diagnosed on HPR amongst the AUB patients, these patients were of Leiomyoma (4) , adenomyoma,(3) and bulky uterus (7) , one each from normal uterus, ca cervix & polyp ,. In our study USG correctly identify 96% cases of endometrial hyperplasia on scanning. Hyperestrogenic states including Leiomyoma, Adenomyoma& Bulky enlarged uteri were diagnosed correctly on TVS but the endometrial hyperplasia was absent. The other various types of endometrium encountered in cases of AUB were secretory-(30%), proliferative– (15%) inflammatory-(5%)

Out of the 2 cases of endometrial carcinoma, 1 was confirmed on histopathology other was diagnosed as Endocervical adenocarcinoma having access to spread to endometrium by direct spread.

2% cases of AUB were diagnosed to have CIN and Ca- cervix on HPR and 96% cases had a normal or inflammatory report of cervix on HPR. Both cases of carcinoma cervix were diagnosed on TVS & had underwent a cervical biopsy prior to Radical hysterectomy and bilateral lymphnode removal.

Discussion

The study included the data of 102 perimenopausal women of AUB fulfilling the inclusion criteria. The most commonly affected age group was between 44-47 years (62.74%) and Para 4 and more had a higher incidence of AUB. The most common menstrual problem encountered was heavy menstrual bleeding(46.02%). This was comparable with the study of Shobha et al⁹(46.60%), Talukdar et al¹⁰(43.69%) and Kumari G et al¹¹(42.00%).

Our study documents 88.23% sensitivity, 89.70% specificity, 81.08% PPV and 93.84% NPV of leiomyoma detection on USG respectively. This was in concordance with the study of Talukdar et al¹⁰ where sensitivity, specificity, PPV and NPV was found to be 89.13%, 89.47%, 87.23% and 91.07% respectively. Kappa test when applied showed the result of 76.00% thus indicating that there is good improvement over the chance expectation while using USG as a diagnostic tool. After applying the Z test of significance between two proportions, the calculated p value was <0.001 which reveals that it is statistically very significant.

Table 3: Sensitivity, Specificity, PPV & NPV of TVS in diagnosing AUB

Table 4: Kappa test correlation and Z test statistical significance

Kappa results interpretation less than 20% is negligible correlation over chance, 20%-40% is minimal correlation over chance, 40% to 60% is fair correlation over chance, 60% to 80% is good correlation over chance and greater than 80% is excellent correlation over chance.

As per table 5 , TVS detected Adenomyosis with the sensitivity(50.00%), specificity(97.67%), PPV (80.00%) and NPV (91.30%) respectively. Kappa test had a result of 56.00% indicating that there is fair improvement over the chance expectation. After applying the Z test of significance

between two proportions, the calculated p value was 0.0132 and it proved to be statistically significant.

Table 5:-Sensitivity, Specificity, PPV and NPV of this study with other studies in diagnosing Adenomyosis on TVS

In this study, out of the 25 cases diagnosed as endometrial hyperplasia on ultrasonography, 23 were confirmed on histopathology while one had secretory endometrium on USG & one was diagnosed as endometrial carcinoma on. Table 6 shows the comparison of sensitivity, specificity, PPV and NPV of this study with the previous studies. The sensitivity in this study is higher as compared to those of Wankhade et al⁷ and Talukdar et al¹⁰ lower as compared to those of Jain M et al¹³. However the specificity is in concordance with the other studies. Kappa test showed the result of 54.76% indicating that there is fair improvement over the chance expectation. After applying the Z test of significance between two proportions, the calculated p value was 0.002 and it was statistically significant.

Table 6:-Sensitivity, Specificity, PPV and NPV of this study with other studies in diagnosing Endometrial hyperplasia on TVS

The present study stated that the endometrial carcinoma had the sensitivity, specificity, PPV and NPV of 50.00%, 99.00%, 50.00% and 99.00% respectively on USG. A study conducted by Wankhade et al⁷ showed the similar results of endometrial carcinoma with 50.00% sensitivity, 99.15% specificity, 50.00% PPV and 99.15% NPV respectively. Kappa test showed the result of 49.00% indicating that there is fair improvement over the chance expectation. After applying the Z test of significance between two proportions, the calculated p value was 0.418 and it was not significant statistically.

Both the sensitivity and specificity of cervical carcinoma was 100% in a present study which was in concordance with the study done by Talukdar et al¹⁰. Kappa test showed the result of 100% indicating that there is perfect agreement between the two variables. After applying the Z test of significance between two proportions, the calculated p value was 0.0434 and it was statistically significant. However as the sample size was less and only 2 cases of cervical carcinoma were positive it should not be considered as the reliable result.

Conclusion: Presence of endometrial hyperplasia on TVS (PPV 92%) in Perimenopausal AUB confirms Endometrial Hyperplasia in AUB, However its absence on TVS (NPV 75%) needs further evaluation by HPR before going ahead with conservative line of management (Kappa 56%). Presence of leiomyoma/Adenomyosis on TVS (Kappa 76%) has good correlation with HPR as a cause of Perimenopausal AUB.

In our study, kappa test and Z test showed that ultrasonography and histopathological findings correlated well to diagnose fibroids, adenomyosis and endometrial hyperplasia and showed statistically significant results. TVS is an easily available, cheap, noninvasive tool and which can be used effectively in the initial screening for ascertaining the cause of abnormal uterine bleeding in perimenopausal women rural hospitals it correlates well with histopathology.

Limitation:

The only limitation to our study was that it was a retrospective study and hence we were dependant on the Indoor papers for the data.

Recommendation: Presence of endometrial hyperplasia on TVS in perimenopausal AUB confirms endometrial cause of AUB, However its absence on TVS still needs further evaluation by hysteroscopy/ curettage before going ahead with conservative line of management

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Table 1: Diagnosis on Ultrasonography

Diagnosis	Cases
Leiomyoma	37 (36.2%)
Adenomyosis	10 (9.8%)

Polyp	4(3.9%)
Endometrial hyperplasia	25 (24.5)
Endometrial carcinoma	2 (1.9%)
Cervical carcinoma	2 (1.9%)
Bulky uterus	15 (14.7%)
Normal sized uterus	7(6.8%)

Table 2- Histopathology correlation with Ultrasonography diagnosis

		Ultra-sonography	Leiomyoma 37 (36.2%)	Adenomyosis 10 (9.8%)	Polyp 4 (3.9%)	Endo-Hyperplasia 25 (24.5%)	Ca-Endo 2 (1.9%)	Ca-Cx 2 (1.9%)	Bulky uterus 15 (14.7%)	Normal uterus 7 (6.8%)	Total 102 (100%)
HISTOPATHOLOGY	ENDOMETRIUM	Proliferative	12	2	0	0	0	0	0	1	15 (14.7%)
		Secretory	16	5	0	1	0	0	7	2	31 (30.3%)
		Endometrial hyperplasia without atypia	4	3	1	20 (80%)	0	1	6 (40%)	2	37 (36.2%)
		Endometrial Hyperplasia with atypia	0	0	0	3 (12%)	0	1	1	0	5 (4.9%)
		Polyp		0	3	0	0	0	1	0	4 (3.9%)
		Inflammatory	3	0	0	0	0	0	0	2	5 (4.9%)
		Endometrial carcinoma	0	0	0	1	1	0	0	0	2 (1.9%)
		Atropic	2	0	0	0		0	0	0	2 (1.9%)
		Endocervical carcinoma	0	0	0	0		1	0	0	1 (0.98%)
		MYOMETRIUM	CERVIX	Normal	3	0	4	22	2	2	13
Leiomyoma	30 (81%)			2	0	1	0	0	1	0	34 (33.3%)
Adeno myomatous	4			8 (80%)	0	2	0	0	1	1	16 (15.6%)
Normal	34			9	3	21	0	0	10	7	84 (82.3%)
		Inflammatory	3	1	0	4	1	0	5	0	14 (13.7%)
		CIN	0	0	1	0	1	0	0	0	2 (1.9%)
		Cervical carcinoma	0	0	0	0	0	2	0	0	2 (1.9%)

Table 3: Sensitivity, Specificity, PPV & NPV of TVS in diagnosing AUB

Pathology	Sensitivity	Specificity	PPV	NPV
Lieomyoma	88.23%	89.70%	81.08%	93.84%
Adenomyosis	50.00%	97.67%	80.00%	91.30%
Endometrial Hyperplasia	54.76%	96.66%	92.00%	75.32%
Endometrial carcinoma	50%	99%	50%	99%
Cervical carcinoma	100%	100%	Low sample size for Ca cervix & Ca endometrium	

Table 4: Kappa test coorelation and Z test statistical significance

Pathology	Kappa result	P Value	Statistical Significance
Lieomyoma	76 %	<0.001 %	Significant
Adenomyosis	56%	0.0132	Significant
Endometrial Hyperplasia	54.76%	0.002	Significant
Endometrial carcinoma	49%	0.418	Not significant
Cervical carcinoma	100%	0.0434	Significant

Table 5:-Sensitivity, Specificity, PPV and NPV of this study with other studies in diagnosing Adenomyosis on TVS

References	Sensitivity	Specificity	PPV	NPV
Wankhade et al ⁷	23.53%	100%	100.00%	82.75%
Talukdar et al ¹⁰	47.62%	98.78%	90.91%	80.04%
Ascher et al ¹²	52.90%	66.60%	90.00%	20.00%
Present study	50.00%	97.67%	80.00%	91.30%

Table 6:-Sensitivity, Specificity, PPV and NPV of this study with other studies in diagnosing Endometrial hyperplasia on TVS

References	Sensitivity	Specificity	PPV	NPV
Wankhade et al ⁷	36.00%	98.95%	90.00%	85.45%
Talukdar et al ¹⁰	17.24%	95.55%	83.33%	47.25%
Jain M et al ¹³	81.81%	92.30%	75.00%	94.73%
Present study	54.76%	96.66%	92.00%	75.32%