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Original Research Article

Comparative Diagnostic Accuracy of Tran-Vaginal Sonography and Hysteroscopy to Identify Intrauterine Pathology among Perimenopausal Women with Abnormal Uterine Bleeding

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Abstract

Background: Abnormal uterine bleeding (AUB) is any departure from a normal menstruation cycle pattern i.e., regularity, frequency, heaviness, and duration of flow.

Aim: To determine the diagnostic accuracy of transvaginal sonographic (TVS) and hysteroscopic in identifying the intrauterine pathologies among perimenopausal women presenting with abnormal uterine bleeding.

Material and Methods: This was a single-centre, hospital-based, cross-sectional observational study conducted in the Department of Obstetrics and Gynaecology, CARE Hospital, Hyderabad. A total of 100 perimenopausal women with AUB were enrolled. Thereafter, participants underwent clinical evaluation, transvaginal sonography, hysteroscopy, and histopathological examination of endometrial samples to evaluate intrauterine pathology. The following diagnostic characteristics viz. sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were calculated.

Results: The sensitivity, specificity, Positive Predictive Value, and Negative Predictive Value of Hysteroscopy for evaluation of endometrial pathology was greater than Trans-Vaginal Sonography. In addition, hysteroscopy had a good diagnostics agreement with histopathology for the evaluation of intrauterine pathologies. Individually, hysteroscopy has a substantial agreement with histopathology for endometrial hyperplasia [kappa=0.66 (95% CI- 0.49-0.84)] and almost perfect agreement [k=0.85 (95% CI- 0.70-0.99)] for detecting endometrial polyp.

Conclusion: In comparison to Trans vaginal sonography, Hysteroscopy is a more sensitive, specific, and accurate diagnostic investigation to evaluate intrauterine pathology associated with

AUB among perimenopausal women. Hysteroscopy with guided biopsy enhances the accuracy of endometrial sampling, thus providing an adequate diagnosis.

Keywords: Hysteroscopy, Perimenopausal Women, Abnormal Uterine Bleeding.

Introduction

Abnormal Uterine Bleeding (AUB) is defined as 'bleeding that is excessive or occurs outside of normal cyclic menstruation' [1]. Moreover, AUB accounts for two-thirds of hysterectomies[2]. International Federation of Gynaecology and Obstetrics (FIGO) classification for AUB is of 9 main categories, which are arranged according to the acronym PALM-COEIN: polyp, adenomyosis, leiomyoma, malignancy, hyperplasia, coagulopathy, ovulatory dysfunction, endometrial and iatrogenic[3]. The components of the PALM group are discrete (structural) entities whereas the COEIN group is related to entities that are not defined by imaging or on histopathology (non-structural)[4]. Evaluation of the intrauterine and endometrial pathologies as a cause of AUB is mainly by three modes[5].

1. Radiological investigation of intrauterine pathologies and pattern of the endometrium by transvaginal ultrasound (TVS).
2. Visual assessment by hysteroscopy.
3. Histopathological assessment by microscopic evaluation of endometrial samples.

In 2001, the Stages of reproduction ageing workshop (STRAW) defined perimenopause as the period beginning with early menopausal transition and ending 12 months after the final menstrual period i.e. a woman has not gone for 12 consecutive months of amenorrhoea and has not yet achieved menopause[5]. During the perimenopausal period, levels of the female reproductive hormones viz. oestrogen and progesterone may not follow their regular pattern[6]. Consequently, women may experience abnormal patterns of uterine bleeding. Accurate and prompt diagnosis is essential for the appropriate management of AUB in perimenopausal women[7]. Various diagnostic tests have evolved over time starting from TVS, blind dilatation, and curettage to the latest immunohistochemical marker with varied accuracy, to provide a precise diagnosis of causative pathologies of AUB[8,9]. Tran-vaginal Sonography is a quick, non-invasive procedure that does not expose the women to any radiation. Transvaginal sonography may assist in the detection of endometrial and other intrauterine pathologies[2]. It is a first-line diagnostic tool to assess intrauterine pathology in women presenting with AUB. Hysteroscopy provides direct visualization of the endometrial cavity[10]. Hysteroscopy is an eye inside the uterus. when combined with biopsy, hysteroscopy can establish an accurate diagnosis in most cases[11]. This study aimed to compare the diagnostic parameters, viz. sensitivity, specificity, Positive Predictive Value (PPV), and Negative Predictive Value (NPV) between the two diagnostic procedures viz. TVS, and Hysteroscopy against the gold standard Histopathology for the evaluation of the various endometrial pathologies among perimenopausal women presenting with AUB. The other objective of the present study was to evaluate the sonographic (TVS), hysteroscopic and histopathological spectrum of intrauterine pathologies and the degree of agreement between findings of hysteroscopic and histopathological findings.

Material and Methods

Study Type: A single-centre, hospital-based, cross-sectional, observational study(12).

Study Duration: 12 months - from March 2016 to February 2017.

Study settings: Department of Obstetrics and Gynecology CARE Hospital, Hyderabad, India. The institutional ethical committee approved this study for biomedical research.

Sample Size: A total of 100 participants were enrolled in the present study(13).

Study Participants: Perimenopausal women presenting with complaints of Abnormal Uterine Bleeding and fulfilling the following inclusion criteria-

Inclusion Criteria: Perimenopausal women (>40 years old but not achieved clinical menopause i.e., not yet gone for 12 consecutive months of amenorrhoea) with abnormal uterine bleeding and those agreeing to consent for the study.

Exclusion Criteria: Postmenopausal women, pregnant women, women of age <40 years, women with uterine size >12 weeks, having known genital tract malignancies, cervical and vaginal causes of bleeding, with coagulation disorder, with a thyroid disorder, with intrauterine contraceptive device, with pelvic inflammatory disease, with recent uterine perforation, on medications like neuroleptics, anticoagulants, and cytotoxic agents, hormone therapy, hemodynamically unstable patients and those who did not give consent were excluded.

Following the rules and guidelines recommended for researching human subjects, a consent form was prepared in the English language (and later translated into Hindi and Telugu). Everyone who participated was provided with a copy of the consent form to read. Following that, the contents of the consent form were explained to every potential participant in easy-to-understand language. It was made clear to the participants, both verbally and in writing, that they are free to discontinue their participation in the research at any moment. After that, those participants who were willing to take part were asked to sign the consent form.

After obtaining informed written consent, each patient who fulfilled the selection criteria underwent a preliminary assessment by detailed clinical history, examinations, and investigations-Complete haemogram, blood grouping and Rh typing, bleeding and clotting time, complete urine examination, urinary pregnancy test, serum TSH, blood sugar, viral markers, and PAP smear. After that, all women underwent transvaginal sonography, hysteroscopy, and histopathological examination (HPE) of an endometrial sample. TVS was performed using an endovaginal probe of 7.5MHz after emptying the bladder. Uterine size, any uterine or adnexal pathology, endometrial thickness, and echo pattern at the endometrial and myometrial junction were noted. 12 millimetres of endometrial thickness is considered as an upper limit of normal endometrium in perimenopausal women, beyond which it was taken as thickened endometrium. Thickened endometrium on TVS is expected to correlate with endometrial hyperplasia. After transvaginal sonography and pre-aesthetic check-ups, patients were posted for hysteroscopy. Hysteroscopy was performed under short general anaesthesia (laryngeal mask airway) using a 4mm telescope with a 30-degree fore-oblique lens with a 5mm sheath. The distension media used was 0.9% normal saline. Hysteroscopy was performed in lithotomy after emptying the bladder. After measuring the length of the uterine cavity, the internal os was dilated with Hegar's dilator whenever necessary. The distension media flow was started as the hysteroscope was introduced into the external os of the cervix.

As the telescope was advanced through the external os, distension media separated the wall of the endocervix to allow an excellent view of endocervical folds and crypts. The internal os was identified as a narrow constrictive opening at the end of the cervical canal and the hysteroscope was manipulated under vision into the uterine cavity. The flow rate might need adjustment after entering the uterine cavity. The following observations were recorded on hysteroscopic examination.

1. Panoramic view of the uterine cavity
2. The character of the endometrium
3. Fundus, Tubal ostia and bilateral cornua
4. Any other abnormalities
5. Endocervical canal

After a thorough examination, any suspicious area visualized by hysteroscope was biopsied followed by curetting of the whole of the endometrium. The tissue obtained was sent for histopathological examinations. After the procedure patients were observed for any complications and were discharged on the same day.

Data Collection:

The data were collected in a paper-based proforma. The proforma had 4 parts as follows:

1. Part 1: Demographic details, clinical history and examination.
2. Part 2: Findings of Trans Vaginal Sonography.
3. Part 3: Findings of Hysteroscopy.
4. Part 4: Findings of Histopathology

Statistical Analysis

All dependent and independent variables with necessary explanations were first defined by the research team. All the data were collected in a paper-based data collection form. Thereafter, the data were coded and entered in Microsoft Excel. The coded data were imported into Stata 17.1 version for analysis. The continuous data were expressed in terms of mean, median, mode, and standard deviation whereas the discrete data were expressed as frequency, proportion, and percentage. Diagnostic characteristics (Sensitivity, specificity, PPV, NPV, Accuracy) and Kappa's statistics were calculated as per recommended formulas(14). For calculating diagnostic parameters of the TVS and Hysteroscopy, the clinical diagnosis arrived at by Histopathology was considered as Gold Standard i.e., either true positive or true negative.

Results

Of the 100 enrolled participants, 4 women could not complete the study and hence the data of only 96 participants were analysed as a part of this study. Out of 96 cases, 61.45% of women were in the age group of 40-45 years, 35.41% of women in 45-50 years, and only 3.12% of women were in 50-52 years. The mean age of women was 44.64 (±3.16) years. Most (52.8%) of the participants had a parity of 2 followed parity of 3 (30.20%), while (7.29%) cases were of parity 1 and only one woman was nulliparous.

On transvaginal sonography, out of 96 cases normal endometrium was observed in 48 (50%) cases, thickened endometrium (ET>12mm) i.e., suspected hyperplasia (33.3%) was the commonest abnormal finding followed by endometrial polyp (13.5%) and submucous myoma 3 (3.12%). Out of 96 cases, histopathology diagnosed (37.5%) proliferative, (12.5%) secretory, (25%) hyperplasia, (14.58%) endometrial polyp, (1.04%) submucous myoma and (1.04%) of carcinoma endometrium against hysteroscopic findings of (41.6%), (10.4%), (25%), (18.75%), (3.12%) and (1.04%) respectively. Histopathology also diagnosed (7.29%) of cases of disordered proliferative endometrium and (1.04%) of chronic endometritis which were not diagnosed by hysteroscopy (Table 1)

Table1: Diagnosis based on TVS, Hysteroscopy, and Histopathology

Findings (parameter)	TVS findings	Hysteroscopic findings	Histopathological findings
Proliferative endometrium	Normal endometrium (ET<12mm) 48(50.0%)	40 (41.6%)	36 (37.5%)
Secretory endometrium		10 (10.4%)	12(12.5%)
Disordered proliferative endometrium	-	-	7 (7.29%)
Endometrial hyperplasia	(ET>12mm) 32 (33.3%)	24(25%)	24 (25.0%)
Endometrial polyp	13(13.5%)	18(18.75%)	14 (14.58%)
Submucous myoma	3(3.12%)	3(3.12%)	1(1.04%)
Carcinoma endometrium	-	1(1.04%)	1(1.04%)
Chronic endometritis	-	-	1(1.04%)

Table 2 and Table 3 compare the 96 participants based on the diagnosis suggested by TVS and Hysteroscopy and compares them against the diagnosis confirmed by the histopathology. On TVS 32 women were diagnosed to have endometrial hyperplasia, 13 women had an endometrial polyp, and there were 3 cases of submucous myoma while histopathology confirmed 24 women to have endometrial hyperplasia, 14 women had an endometrial polyp, 7 women had disordered proliferative endometrium and 1 woman each had myoma, carcinoma endometrium, and chronic endometritis.

Table 2: Comparison of findings on Trans Vaginal Sonography and Histopathology

Histopathology findings	Normal Endometrium	Endo. Hyperplasia	Endo. Polyp	Sub. Myoma	Disordered proliferative endometrium	Ch. endometritis	Ca endometrium
TVS findings							
Normal endometrium	24	13	3	0	7	0	1
Thickened endometrium	17	11	3	0	0	1	0
Endo. polyp	5	0	8	0	0	0	0
Sub. myoma	2	0	0	1	0	0	0
Disordered proliferative endometrium	0	0	0	0	0	0	0
Ch. Endometritis	0	0	0	0	0	0	0
Ca endometrium	0	0	0	0	0	0	0
Total	48	24	14	1	7	1	1

On comparing the findings of hysteroscopy diagnosed proliferative endometrium in 40 (41.6%), secretory endometrium in 10 (10.4%), hyperplasia in 24(25%), endometrial polyp in 18 (18.75%) and submucous myoma in 3(3.12%), carcinoma endometrium 1 (1.04%), while histopathology diagnosed 36(37.5%),12(12.5%),24 (25.0%), 14(14.6%), 1(1.04%) and 1 (1.04%) case

respectively. Histopathology also detected 7 (7.29%) cases of disordered proliferative endometrium and one case of chronic endometritis which were not seen by hysteroscopic.

Table 3: Comparison of findings on Hysteroscopy and Histopathology

Histopathology findings	Proliferative	Secretory	Endo. Hyperplasia	Endo. Polyp	Sub. Myoma	Disordered proliferative	Ca. Endometrium	Ch. Endometritis
Hysteroscopic findings								
Proliferative endometrium	28	2	2	0	0	7	0	1
Secretory endometrium	0	7	3	0	0	0	0	0
Endo. hyperplasia	3	3	18	0	0	0	0	0
Endo. polyp	3	0	1	14	0	0	0	0
Sub. myoma	2	0	0	0	1	0	0	0
Disordered proliferative endometrium	0	0	0	0	0	0	0	0
Ca endometrium	0	0	0	0	0	0	1	0
Ch. endometritis	0	0	0	0	0	0	0	0

*Endo=endometrial, Ca=carcinoma, Ch=chronic

Table 4: Diagnostic parameters of the Trans-vaginal Sonography and Hysteroscopy

Diagnostic Parameters	Sensitivity*		Specificity*		PPV*		NPV*		Accuracy*	
Intrauterine pathologies	TVS	Hysteroscopy	TVS	Hysteroscopy	TVS	Hysteroscopy	TVS	Hysteroscopy	TVS	Hysteroscopy
Endometrial hyperplasia	45.8	75	70.8	91.6	34.3	75	79.7	91.6	64.5	87.5
Endometrial polyp	42.8	100	93.9	95	61.5	77.7	92.8	100	88.5	95.8
Submucous myoma	100	100	97.8	97.8	25	33.3	100	100	97.9	97.9
Carcinoma endometrium	-	100	-	100	-	100	-	100	-	100
*- Rounded off to nearest integer										

Table 5: Degree of agreement between hysteroscopy and histopathology

Findings	Agreement	Disagreement	Kappa coefficient(k) (95%CI)
Endometrial hyperplasia	18	6	0.66(0.49-0.84)
Endometrial polyp	14	4	0.85(0.70-0.99)
Submucous myoma	1	2	0.49(0-1)

Discussion

Abnormal uterine bleeding (AUB) is a common problem among perimenopausal women, and it refers to any bleeding that occurs outside of the normal menstrual cycle[6]. During perimenopause, women may experience irregular menstrual periods, heavy bleeding, or bleeding between periods[6]. Other causes of AUB in perimenopausal women may include hormonal imbalances, fibroids, polyps, endometrial hyperplasia, and certain medications. It is important for women experiencing AUB during perimenopause to consult their healthcare provider to determine the cause of the bleeding and to rule out any serious conditions, such as endometrial cancer. Early detection and treatment can help prevent complications and improve quality of life.

Transvaginal sonography (TVS) and hysteroscopy are two commonly used diagnostic tools for evaluating abnormal uterine bleeding (AUB) in women[15]. While both procedures are effective, they have some key differences that make them better suited for different situations. TVS is a non-invasive procedure that can be used to detect a variety of abnormalities, such as fibroids, polyps, and thickening of the endometrial lining[15]. TVS is generally considered the first-line imaging modality for AUB due to its relatively low cost and accessibility. However, it has some limitations. Hysteroscopy, on the other hand, is a minimally invasive procedure that allows to directly visualize the inside of the uterus using [11]. It can be used to detect and treat a variety of abnormalities, including polyps, fibroids, and adhesions. Hysteroscopy is generally considered more accurate than TVS for diagnosing certain conditions, such as endometrial hyperplasia and endometrial cancer[11]. However, it is a more invasive procedure that requires anaesthesia, and it may not be as readily available as TVS[11]. In summary, both TVS and hysteroscopy have their advantages and limitations in the evaluation of AUB in perimenopausal women.

In the present study, the mean age of the patient presenting with AUB was 44.6 (40-52) years. Like our findings, Jetley S *et al*. also reported that the mean age of perimenopausal women presenting with AUB was 44.8 years (40-50 years)[16]. Most participants in the present study were in 40-45 years of age (61.45%), followed by 46-50 years (35.41%) and (3.12%) of 51-52 years. Gandotra N *et al*. also reported the majority of patients (69%) with AUB were of 40-50 years[17]. In this study, the majority (82.2%) of the affected cases were of parity 2 (52.08%) may be because of modern trends of family size, followed by 3 (30.20%) and the least affected were with parity 1 (1.04%) and nulliparous (1.04%). Similar findings were reported by Goyal BK *et al*. [18].

In the present study, it was observed that on TVS, 53.12% of participants had normal endometrium (ET<12mm), 34.3% cases had thickened endometrium (ET>12mm) i.e., endometrial hyperplasia followed by endometrial polyp (9.37%). Submucous myoma was found in (3.12%) of cases. Katke RD *et al*. reported that on ultrasonography endometrial hyperplasia was detected in 65.2% and endometrial polyp in 4.5% of cases[19]. Verma U *et al*. in their study reported on ultrasonography endometrial hyperplasia was detected in 14%, endometrial polyp in 9%, and submucous myoma in 3% of cases[20]. Swathi GR *et al*. in their study reported normal endometrium in 59% of cases, endometrial hyperplasia in 24%, endometrial polyp in 8%, submucous Myoma in 1%, and atrophic endometrium in 8% of cases respectively[21]. Sensitivity, specificity, PPV and NPV of TVS for endometrial hyperplasia were

45.8%,70.8%,34.3%, and 79.7%, for endometrial polyp were 42.8%, 93.9%, 61.5%, 92.8% respectively and for submucous myoma 100%,97.8%,25% and 100% respectively.

Hysteroscopy provides direct visualization of the endometrial cavity. On hysteroscopy, dominant findings were normal endometrium inclusive of proliferative 41.61% and secretory 10.4%, and among abnormal findings, the most common finding was hyperplasia 25% followed by endometrial polyp 18.75%, submucous myoma 3.12% and carcinoma endometrium in 1.04%. One case of chronic endometritis was missed by hysteroscopy while diagnosed by histopathology in this study. Katke RD *et al*. their study reported 43.9% normal endometrium, 28.8% hyperplasia, and 22.7% endometrial polyp[19]. Verma U *et al*., reported 44% normal endometrium, 11% hyperplasia, 13% endometrial polyp, 8% submucous myoma and 2% endometrial malignancy on hysteroscopy[20]. Swathi GR *et al*. reported that 37% of participants had normal endometrium, 20% had endometrial hyperplasia, 18% had endometrium polyp, 9% had submucous myoma, 11% had atrophic endometrium, and 3% cases of endometrial malignancies[21].

In this study sensitivity, specificity, PPV and NPV of hysteroscopy for hyperplasia were 75%, 91.6%, 75%, and 91.6% respectively. Mukhopadhyay *et al*. reported sensitivity, specificity, PPV and NPV 50%, 95.78%, 70%, and 90.36% respectively[22]. Patil SG *et al*. reported sensitivity, specificity, PPV and NPV of hysteroscopy for detecting endometrial hyperplasia at 75%, 92.5%, 71.4%, and 93.6% respectively[23]. In the current study, the endometrial polyp was diagnosed by hysteroscopy in 18 cases and was confirmed by histopathology in 14 cases. Sensitivity, specificity, PPV, and NPV of hysteroscopy for endometrial polyp were 100%, 95.12%,77.7%, and 100% respectively. Similar findings are reported by other studies. Das S *et al*., reported sensitivity, specificity, PPV, and NPV of 92.6%,96.7%,86.2%, and 98.3% respectively [24]. Patil SG *et al*. reported 100%, 95.78%, 55.55%, and 100% respectively for detecting endometrial polyps by hysteroscopy[23]. Hysteroscopy in the current study has sensitivity, specificity, PPV, and NPV of 100%,97.8%,33.3%and 100% respectively for detecting cases of submucous myoma.

In this study, hysteroscopy detected one case of endometrial malignancy and it was confirmed by histopathology as carcinoma endometrium but missed by TVS showing 100% accuracy of hysteroscopy in diagnosing endometrial carcinoma. Hysteroscopy showed substantial agreement (k=0.66) with histopathology for detecting endometrial hyperplasia, almost perfect agreement (k=0.85) for detecting endometrial polyp, and moderate agreement (k=0.49) for detecting submucous myoma. Mukhopadhayay *et al*. reported kappa agreement of hysteroscopy with histopathology (k=0.51) for detecting hyperplasia and (k=0.81) for an endometrial polyp in perimenopausal women with AUB [22].

Conclusion

Perimenopausal women have one or multiple causes of AUB that need a thorough evaluation. Endometrial hyperplasia a risk factor for malignancy was the most frequently observed abnormal endometrial pathologies in these women. By differentiating benign from malignant pathologies appropriate management can be offered to avoid unnecessary hysterectomy. TVS provides a preliminary diagnosis of endometrial pathologies that should be used as a first-line imaging modality. Hysteroscopy is a safe, easy, simple, and quick procedure that provides direct visualization and has more sensitivity,

specificity and accuracy than TVS for detecting endometrial pathologies. Hysteroscopy with biopsy is efficient to characterize endometrial abnormalities accurately and by differentiating benign pathologies from malignant pathologies avoids unnecessary hysterectomies thereby lowering the cost and hospital stay.

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