

A Prospective Comparative Study of Endometrium by Transvaginal Sonogram and its Correlation with Histopathology in Peri-Menopausal Women with Abnormal Uterine Bleeding

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Abstract

Introduction: Abnormal uterine bleeding (AUB) is the most common reason for gynecological visits for perimenopausal bleeding and may account for more than 25% of all hysterectomies. The perimenopause is often characterized by irregularities in the menstrual cycle in volume and frequency. This is due to fluctuating estrogen levels. These changes are unique for each woman and are unpredictable. Although irregular bleeding patterns are normal and expected to be part of perimenopause, the incidence of uterine pathology and associated medical complications increase in this age group [3]. The more accurate diagnosis of endometrial pathology better the chances for alternative treatment and hysterectomies could be avoided. The accuracy or the superiority of the relatively non-invasive methods like TVS, Hysteroscopy, and SIS over histopathology have not been clearly established. Thus this study was undertaken to compare the diagnostic efficiency of TVS over the histopathology study of the endometrium and to test their agreement. **Materials & Methods:** 48 cases of perimenopausal women above 40 yrs. age not yet attained menopause. Patient with AUB in any other age group, any vaginal or cervical cause of bleeding, Patient with blood dyscrasias, Pregnancy related causes of bleeding, Patient with h/o of drug intake (Anticoagulant & hormone replacement therapy) has been excluded. The cases were studied for a period of 11 months in Noble hospital & research Centre. Detailed history & clinical examination including per vaginal and per speculum examination carried out. All the patient then subjected to transvaginal ultrasound & endometrial sampling. Results were correlated between transvaginal ultrasound & histopathology in these patients. **Results:** In this study, 72.4% of women with normal endometrium had an endometrial thickness of less than 12mm below which there was no endometrial pathology. Above this cut off level of 12mm, 88.6 % were found to be associated with endometrial pathology. The sensitivity and specificity were found to be 61.9% and 77.8%. Distribution of histopathology findings differ significantly between groups of cases with less than 12mm and more than 12 mm endometrial thickness (P -value < 0.048). **Conclusion:** Transvaginal sonogram is a simple, non-invasive convenient way to indirectly visualize the endometrium & endometrial cavity. The vaginal probe examination if incorporated into the gynecologist office setting and when combined with bimanual pelvic examination can enhance our anatomic diagnosis. Transvaginal sonography is useful as a first step diagnostic procedure in the evaluation of perimenopausal bleeding. When combined with dilatation and curettage it can supplement the shortcomings of dilatation and curettage. **Keywords:** Abnormal Uterine Bleeding, Perimenopause, PALM-COEIN, Histopathology, Trans-Vaginal Ultrasound, Endometrial Thickness.

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INTRODUCTION

Perimenopause or the recently preferred term “menopausal transition”, is defined by the WHO as the period in time beginning 2-8 years before the final menstrual period (FMP) and lasting up to 12 months after the FMP. The endocrinological, biological and clinical features of approaching menopause to

commence during this period [1]. Abnormal uterine bleeding (AUB) is the most common reason for gynecological visits for perimenopausal bleeding and may account for more than 25% of all hysterectomies.

In the perimenopausal period, intermittent ovulation or even chronic anovulation take place,

therefore progesterone levels are low because there is no corpus luteum. The ovaries are still producing estrogen, which allows a continued proliferation of the endometrium; the thickened endometrium outgrows its blood supply, undergoes focal necrosis and shedding begins. The shedding is not uniform, bleeding tends to be irregular, prolonged and heavy. The chronic endogenous estrogen stimulation of the endometrium, unopposed by adequate progesterone levels can lead to endometrial hyperplasia and cancer [2].

The perimenopause is often characterized by irregularities in the menstrual cycle in volume and frequency. This is due to fluctuating estrogen levels. These changes are unique for each woman and are unpredictable. Although irregular bleeding patterns are normal and expected as part of perimenopause, the incidence of uterine pathology and associated medical complications increase in this age group [3].

Long anovulatory periods with unopposed estrogen stimulation may result in endometrial hyperplasia thus increasing the risk of endometrial cancer. Therefore, AUB in the perimenopausal age group assumes great significance. Abnormal uterine bleeding is defined as any deviation from the normal menstrual cycle that includes change in regularity, the frequency of menses, duration or amount of bleeding during or in between periods [4].

The causes of abnormal uterine bleeding (AUB) in non-gravid women are standardized in the FIGO classification system (PALM-COEIN) [5]. The PALM group includes five entities with structural etiologies of AUB that can be diagnosed with imaging techniques and/or histopathology (polyp; adenomyosis; leiomyoma; malignancy, and hyperplasia). The COEIN group includes non-structural entities that are not diagnosed by imaging or histopathology: coagulopathy; ovulatory dysfunction; endometrial; iatrogenic; and not yet classified [5].

The major causes of perimenopausal bleeding are Adenomyosis (20-25%), Endometrial Hyperplasia (15-25%), Cancer Cervix (10-12%), Benign Lesion Of Uterus (~10%), Exogenous Estrogen Therapy (3-5%), Cancer Endometrium (2-4%), Endometrial Polyp, Cervical Polyp and rarely Pregnancy-Related causes.

Transvaginal Sonography (TVS) is an inexpensive, non-invasive and a convenient way to assess the uterine pathology. Therefore, it is recommended as a first line diagnostic tool for assessing uterine pathology in perimenopausal age women presenting with AUB. Transvaginal ultrasound can be a valuable aid in evaluating the woman presenting with complaints of abnormal vaginal bleeding by demonstrating anatomical abnormality. TVS also helps in evaluating the endometrium in terms of thickness and ovulatory and hormonal status of the

endometrium. The more accurate diagnosis of endometrial pathology better the chances for alternative treatment and hysterectomies could be avoided. The accuracy or the superiority of the relatively non-invasive methods like TVS, Hysteroscopy, and SIS over histopathology have not been clearly established.

AIMS & OBJECTIVE

To correlate the transvaginal ultrasonographic (TVUS) findings of endometrial thickness and pattern with the histopathological examination (HPE) of the Endometrium.

MATERIALS & METHODS

Study Design

A Prospective Comparative study

Place of Study

The study was “A Prospective Comparative study” carried out on cases that came in Gynae OPD of Noble Hospital Magarpatta City, Pune from December 2018 to October 2019 in collaboration with Pathology & Radiology Department of Noble Hospital.

Study Population

All cases of abnormal uterine bleeding in the perimenopausal age group that is 40 years and above and who have not attained menopause yet attending the Gynaecology Outpatient Department (OPD) at Noble Hospital for the check-up during the period of the Study.

Inclusion Criteria

All cases of abnormal uterine bleeding in the perimenopausal age group that is 40 years and above and who have not attained menopause.

Exclusion Criteria

1. Patient with AUB in any other age group other than the perimenopausal age group.
2. Any vaginal or cervical cause of bleeding
3. Patient with blood dyscrasias.
4. Pregnancy related causes of bleeding.
5. Patient with h/o of drug intake (Anticoagulant & hormone replacement therapy)

METHODOLOGY

The patients coming to OPD who fulfill the inclusion criteria are selected for the study. A detailed clinical history, obstetrical and gynecological history were taken for these patients. Further, a detailed clinical examination done as per designed proforma.

Obstetrical history includes parity and mode of delivery. Menstrual History was recorded for each patient’s menstrual cycle length, the number of days of menstruation, amount of blood loss and regularity of cycle.

Per speculum examination was performed on these patients under study to note abnormal discharge, erosion, cervical hypertrophy or cervical polyp to rule out any cervical cause of bleeding. Per vaginal examination was performed to know about the size of uterus, cervical and adnexal abnormality.

Laboratory investigations including CBC, coagulation profile, random blood sugar, Urine analysis, liver and kidney function, thyroid profile & a urine pregnancy test were carried out for every patient in the study to rule out other causes of AUB.

All patients underwent transvaginal sonography (TVS). The patient's assessed during the premenstrual phase of the cycle. A 7.5 MHz transvaginal sector probe with phased array and end firing potential used.

The results of the transvaginal sonogram were interpreted as

1. Normal Endometrium
 - a. Endometrial Thickness < 12mm
 - b. Endometrium was seen as hypoechoic depicted as proliferative.
 - c. Endometrium was seen as echogenic depicted as secretory.
2. Thickened Endometrium
 - a. Endometrial Thickness (> 12 mm)
 - b. Thickening of the endometrial stripe and often appears homogeneously echogenic depicted as endometrial hyperplasia.
 - b. Echogenic endometrium with detectable small cysts depicted as Cystic Hyperplasia.
 - c. Inhomogeneous, Irregular endometrial stripe considered as Atypical Hyperplasia.

Endometrial biopsy was performed in all these patients as out-patient. Patients placed in lithotomy position. A routine per vaginal examination carried out. Endometrial tissue collected by MVA syringe. The sample was sent for histopathological examination. The biopsy reports were studied.

Sample Size: 48 cases.

Ethical approval: The study was approved by the institutional ethics committee.

Sampling Technique: Convenience Sampling Method.

Statistical Data Analysis

The data on categorical variables are presented as n (% of cases) and the values on continuous variables is presented as Mean \pm Standard deviation (SD). The significance of difference of distribution of prevalence of positivity of endometrial pathology across various groups of interest (such as age group, parity etc) is tested using Chi-Square test. Independent sample „t“

test was used to test the significance of difference in the continuous variables across two groups (presence or absence of endometrial pathology). The underlying assumption of normality is tested before subjecting the study variables to t test. In absence of normality appropriate nonparametric tests are used. Diagnostic efficacy indices such as sensitivity, specificity will be calculated for different cut-offs of TVS to detect the endometrial pathology. P-values less than 0.05 is considered to be statistically significant. All the hypotheses are formulated using two-tailed alternatives against each null hypothesis (hypothesis of no difference). The entire data will be statistically analyzed using Statistical Package for Social Sciences (SPSS ver 21.0, IBM Corporation; NY, USA) for MS Windows.

RESULTS AND OBSERVATION

The present study was a prospective comparative study between endometrium by transvaginal sonogram and its correlation with histopathological examination in peri-menopausal women with abnormal uterine bleeding. The study was carried out in the emergency department of Obstetrics and Gynecology of Noble Hospital, Pune during Dec 2018 to Oct 2019 and it included 48 cases of satisfying inclusion and exclusion criteria.

Out of 48 cases studied, 20 (41.7%) had their age between 40 – 44 years, 26 (54.2%) had age between 45 – 49 years and 2 (4.2%) had age more than or equal to 50 years. Mean \pm SD of age in the entire study group was 45.04 \pm 3.21 years and minimum – maximum age range was 40 – 51 years.

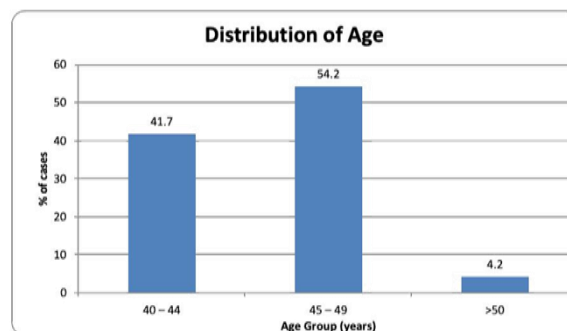


Fig-1: Distribution of age in study group

Out of 48 cases studied, 11 (22.9%) had parity 1, 15 (31.3%) had parity 2, 19 (31.3%) had parity 3 and 3 (6.3%) had parity 4.

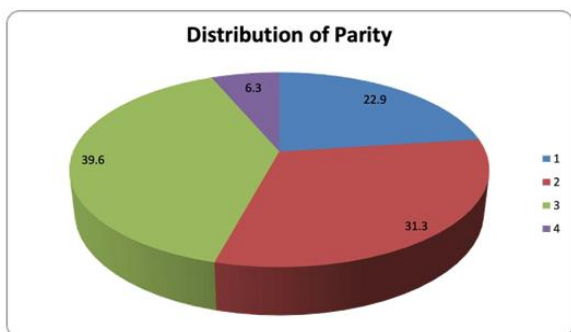


Fig-2: Parity distribution of cases

Out of 48 cases studied, 25 (52.1%) did not have any risk factor, 8 (16.7%) had anemia, 5 (10.4%) had obesity, 3 (6.3%) had diabetes, 6 (12.5%) had hypertension and 1 (2.1%) had diabetes with hypertension.

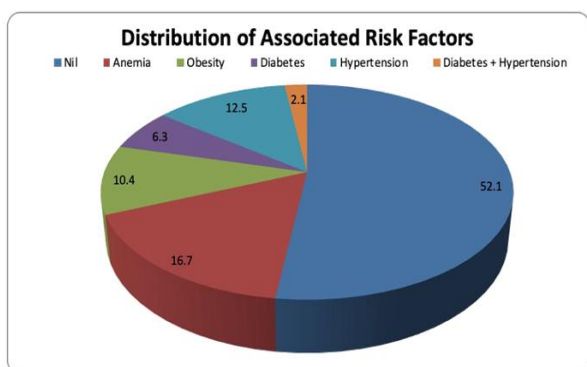


Fig-3: Distribution of cases with Associated Risk Factors

Out of 48 cases studied 24 (50%) presented with heavy menstrual bleeding, 3 (1.38%) with intermenstrual bleeding, 4 (8.33%) with frequent menstrual bleeding, 13(27.08%) with heavy prolonged bleeding, 4(8.33%) with irregular menstrual bleeding.

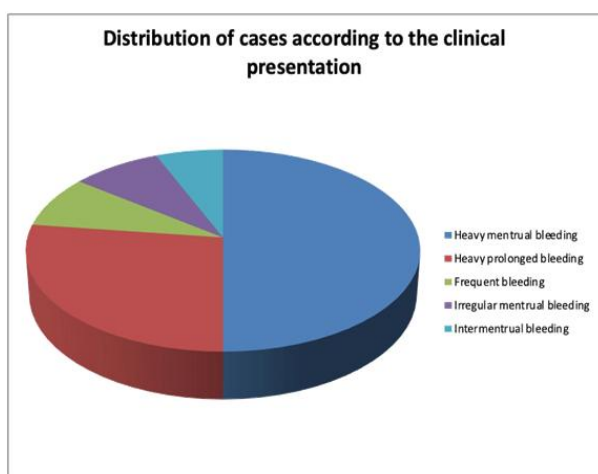


Fig-4: Distribution of cases according to clinical presentation

Out of 48 cases studied, 29 (60.4%) had endometrial thickness less than 12 mm and 19 (39.6%) had endometrial thickness more than 12 mm.

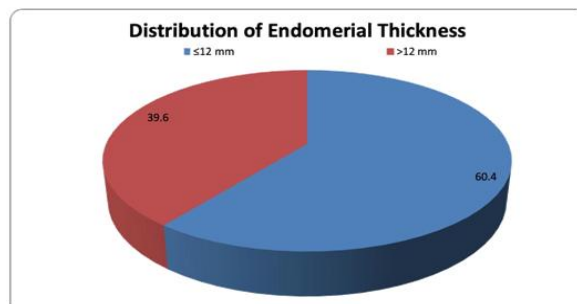


Fig-6: Distribution of endometrial thickness in the study group

Out of 48 cases studied, 14 (29.2%) had proliferative endometrium, 13 (27.1%) had secretory endometrium, 7 (14.6%) had Cystic Glandular Hyperplasia, 6 (12.5%) had Simple Hyperplasia without Atypia, 1 (2.1%) had Simple Hyperplasia with Atypia, 2 (4.2%) had Complex Hyperplasia Without Atypia, 4 (8.3%) had Complex Hyperplasia With Atypia and 1 (2.1%) had Endometrial carcinoma.

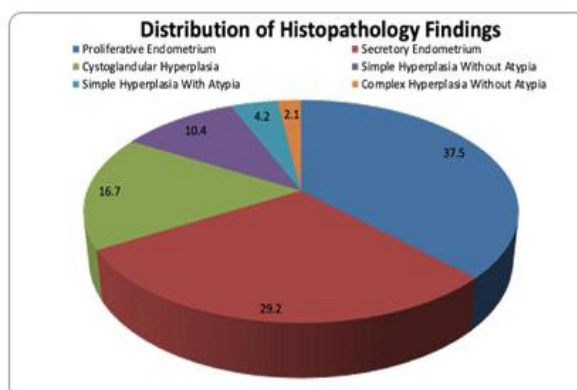


Fig-7: Distribution of Histopathology in the study group

Out of 29 cases with endometrial thickness less than 12 mm, 11 (37.9%) had Proliferative Endometrium, 10 (34.5%) had Secretory Endometrium, 3 (10.3%) had Cystic Glandular Hyperplasia, 4 (13.8%) had Simple Hyperplasia without Atypia, none had Simple Hyperplasia with Atypia, 1 (3.4%) had Complex Hyperplasia without Atypia, none had Complex Hyperplasia with Atypia and none had Endometrial Carcinoma.

Out of 19 cases with endometrial thickness more than 12 mm, 3 (15.8%) had Proliferative Endometrium, 3 (15.8%) had Secretory Endometrium, 4 (21.1%) had Cystic Glandular Hyperplasia, 2 (10.5%)

had Simple Hyperplasia without Atypia, 1 (5.3%) had Simple Hyperplasia with Atypia, 1 (5.3%) had Complex Hyperplasia without Atypia, 4 (21.1%) had Complex

Hyperplasia With Atypia and 1 (5.3%) had Endometrial Carcinoma.

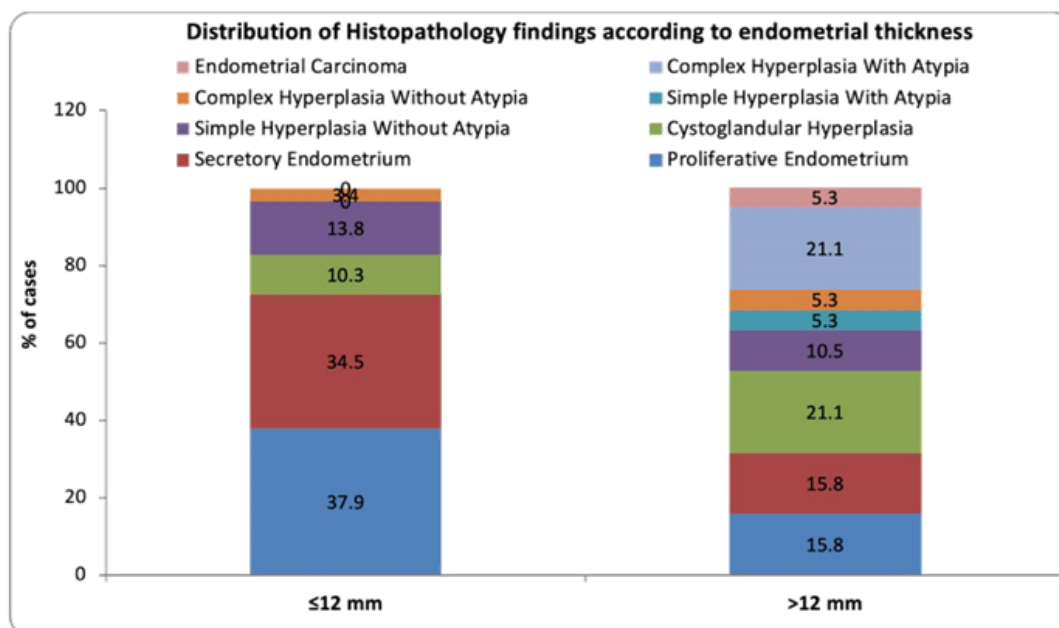


Fig-8: Distribution of Histopathology Findings according to endometrial thickness

Diagnostic efficacy indices of TVS against histopathology for Proliferative Endometrium findings

Diagnostic efficacy indices such as sensitivity, specificity, PPV, NPV and accuracy of TVS against Histopathology as a Gold standard is 21.4%, 52.9%, 15.8%, 62.1% and 43.7% respectively.

Diagnostic efficacy indices of TVS against histopathology for Secretory Endometrium findings

Diagnostic efficacy indices such as sensitivity, specificity, PPV, NPV and accuracy of TVS against Histopathology as a Gold standard is 23.1%, 54.3%, 15.8%, 65.5% and 45.8% respectively.

Diagnostic efficacy indices of TVS against histopathology for Cystic Glandular Hyperplasia findings

Diagnostic efficacy indices such as sensitivity, specificity, PPV, NPV and accuracy of TVS against Histopathology as a Gold standard is 57.1%, 63.4%, 21.0%, 89.6% and 62.5% respectively.

Diagnostic efficacy indices of TVS against histopathology for Simple Hyperplasia Without Atypia findings

Diagnostic efficacy indices such as sensitivity, specificity, PPV, NPV and accuracy of TVS against Histopathology as a Gold standard is 33.3%, 59.5%, 10.5%, 86.2% and 56.2% respectively.

Diagnostic efficacy indices of TVS against histopathology for Simple Hyperplasia With Atypia findings

Diagnostic efficacy indices such as sensitivity, specificity, PPV, NPV and accuracy of TVS against Histopathology as a Gold standard is 100.0%, 61.7%, 5.3%, 100.0% and 62.5% respectively.

Diagnostic efficacy indices of TVS against histopathology for Complex Hyperplasia Without Atypia findings

Diagnostic efficacy indices such as sensitivity, specificity, PPV, NPV and accuracy of TVS against Histopathology as a Gold standard is 50.0%, 60.9%, 5.3%, 96.5% and 60.4% respectively.

Diagnostic efficacy indices of TVS against histopathology for Complex Hyperplasia With Atypia findings

Diagnostic efficacy indices such as sensitivity, specificity, PPV, NPV and accuracy of TVS against Histopathology as a Gold standard is 100.0%, 65.9%, 21.0%, 100.0% and 68.7% respectively.

Diagnostic efficacy indices of TVS against histopathology for Endometrial Carcinoma findings

Diagnostic efficacy indices such as sensitivity, specificity, PPV, NPV and accuracy of TVS against Histopathology as a Gold standard is 100.0%, 61.7%, 5.3%, 100.0% and 62.5% respectively.

Diagnostic efficacy indices of TVS against histopathology for findings (Overall)

Diagnostic efficacy indices such as sensitivity, specificity, PPV, NPV and accuracy of TVS against Histopathology as a Gold standard is 61.9%, 77.8%, 68.4%, 72.4% and 70.8% respectively.

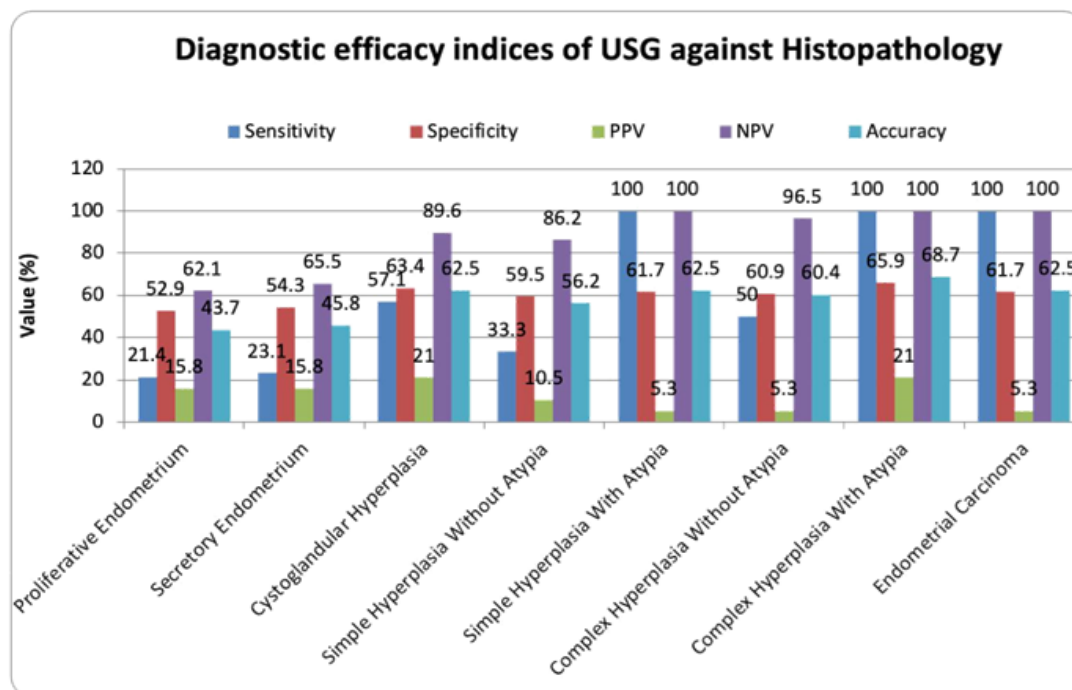


Fig-9: Diagnostic efficacy indices of TVS against Histopathology

DISCUSSION

Abnormal uterine bleeding is one of the most common problems in perimenopausal age accounting for 10-15 % of the cases in everyday gynecology OPD. An optimal management of endometrial disease requires an accurate and timely diagnosis. This study aims to compare the accuracy and predictive values of TVS and HPE in diagnosing AUB in an outpatient setting. In this study, 48 patients who underwent TVS and D&C, There HPE were studied.

Among perimenopausal women, the average at presentation is 45.04 ± 3.21 years with an age group varying between 40 and 51 years. This is similar to the average age at presentation of 46.2 in a study Gupta et al [7]. Most women (54.2%) belonged to the age group of 45-49 years in our study. This is similar to another Indian study by Shobha et al [6] where 40 % of the study population were between 48 and 51 years.

In present study 77.2 % of the study population is multiparous with most being triparous (39.6%). In the study by Gupta et al [7] a similar proportion (88.5%) were multiparous. The parity of our study population is significantly higher than the study population of a similar study in Shobha et al [6]. Only 29.5% of their study population had a parity of 3 or more compared to 39.6% in our study population.

The most common presenting symptom is heavy menstrual bleeding (50%) followed by heavy prolonged menstrual bleeding (27.1%). This is similar to other studies where heavy menstrual bleeding was the most common presenting complaint ranging between 46.5 % to 73% in other studies.

Most of the women (52.1%), had no associated comorbidity. The most common comorbidity seen was anemia (16.7%) followed by hypertension and diabetes mellitus at 12.5% each. A high percentage of the population was also overweight (10.4%)

Most women who underwent TVS for AUB in the perimenopausal age group had normal findings (37.5%). The most common abnormal finding seen is a thickened endometrium in (29.2%) of the population. Adenomyosis (10.4%), Fibroid (16.7%) and Endometrial carcinoma (2.1%) were the next most common diagnosis. Polyps were also rarely picked up by TVS in 4.2% of the study population.

Histopathologic examination was performed on the entire study population. One- third (29.2%) of the study population showed proliferative phase and almost another one third (27.1%) showed secretory phase. This is similar to Shobha et al [6] where the most

common histopathological finding was proliferative. Endometrial malignancy is seen in 2.1% of the population, as compared to 4% in other Indian studies. The reason for a decreased incidence compared to the international population is attributed to very little use of hormone replacement therapy.

The maximum endometrial thickness (TVS- 21 mm) was seen in a woman diagnosed with adenocarcinoma. The average endometrial thickness for women with a proliferative histopathology is 10 mm on TVS, which is marginally more than women with a secretory histopathology 8mm. No women with proliferative or secretory phase had an endometrial thickness > 18mm.

In 48 women with normal pelvic examination adenomyosis was diagnosed in 5 cases, fibroid was diagnosed in 8 cases and endometrial polyp diagnosed in 2 cases. Endometrial carcinoma was correctly diagnosed in 1 case. The ultrasonographic findings correlated well with the pathological report of the hysterectomy specimen giving a sensitivity and specificity of 53% & 100% with 100% PPV & 36.55% NPV. Dilatation and curettage missed the diagnosis of adenomyosis, uterine fibroid and endometrial polyps.

In this study, 72.4% of women with normal endometrium had an endometrial thickness of less than 12mm below which there was no endometrial pathology. Above this cut off level of 12mm 88.6% were found to be associated with endometrial pathology. The sensitivity and specificity was found to be 61.9% and 77.8%.

Distribution of histopathology findings differ significantly between groups of cases with less than 12mm and more than 12 mm endometrial thickness (P-value < 0.048)

Towbin, March *et al* (1996) [8] had found that in their analysis of 131 patients with perimenopausal bleeding, a thick endometrial stripe of ≥ 15 mm were found to correlate strongly with the presence of intrauterine pathology and endometrial abnormalities. Sensitivity 100%, specificity 86%, positive predictive value 91.7% and negative predictive value 94%. Emanuel *et al* [9] in their analysis of 279 women with perimenopausal bleeding have found a cut off value of 12 mm for endometrial thickness below which the report was normal endometrium and above which it was associated with endometrial pathology. Emanuel *et al* [9] have also stated that though in the literature, normal cutoff levels for premenopausal endometrial thickness were not available, he concludes from his study that such a cutoff level can be assigned to the premenopausal patients for exclusion of endometrial abnormalities as is available in postmenopausal women. Mathew, *et al.*, (2000) [10] in their study, found that sensitivity of TVS in detection of these abnormalities was 54%, whereas the specificity was 100%. Positive

predictive value was 100% and negative predictive value was 81.1%. TVS and HYS were in agreement in 84.5% cases. The percentage of abnormal findings detected by HYS and TVS was 33.6% and 18.2%, respectively. This difference is statistically significant. Based on the above results, they concluded that HYS is superior to TVS for the exclusion of intrauterine abnormalities in premenopausal women.

CONCLUSION

Transvaginal sonogram is a simple, non-invasive convenient way to indirectly visualize the endometrium & endometrial cavity. The vaginal probe examination if incorporated into the gynecology office setting and when combined with bimanual pelvic examination can enhance our anatomic diagnosis. Transvaginal sonography is useful as a first step diagnostic procedure in the evaluation of perimenopausal bleeding. When combined with dilatation and curettage it can supplement the shortcomings of dilatation and curettage. This study proves that this diagnostic tool correlates well with the histopathology findings. Intrauterine pathology of the endometrium and myometrium were well delineated and endometrial carcinoma detected with precision. In the future it appears that ultrasonography will continue to take the role of a stethoscope for the gynecologist. To be able to see the lining of the uterine cavity and the information obtained seems worthwhile.

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