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ULTRASOUND DIAGNOSIS OF DYSFUNCTIONAL UTERINE BLEEDING WITH HISTOPATHOLOGICAL CORRELATION

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ABSTRACT

Background: Abnormal uterine bleeding may be defined as bleeding pattern that differs in frequency, duration and amount from a pattern observed during a normal menstrual cycle or after menopause.

Aims : To study accuracy of Transvaginal Sonography in relation to endometrial biopsy in depicting endometrial changes in DUB and to formulate an effective protocol for the first line evaluation of all cases of DUB at the out-patient level.

Materials and methods: This study on ultrasound diagnosis of DUB with histopathological correlation in 50 patients between 18-45 yrs. The study was aimed to study accuracy of TVS in relation to endometrial biopsy in depicting endometrial changes in DUB. TVS and endometrial sampling was done as outpatient procedure 2-3‘days prior to date of menstruation or on day of menstruation. The relevant clinical findings and investigations were recorded in the proforma which is enclosed. A master sheet showing all details of the cases is also enclosed.

Results: The incidence of DUB in age groups of 18-45 years is high. Menorrhagia was noted in 44% , Polymenorrhagia in 20% by histopathology. In cases of normal endometrium, proliferative endometrium noted in 52%, secretory endometrium in 12% , menstrual endometrium in 12% .Simple hyperplasia was noted in 14%, Cystoglandular hyperplasia in 6%. Out of 6 patients with ET 1 – 4.9 mm , endometrial parenchyma is menstrual on TVS and HPE . Out of 4 patients with ET 15 and above endometrium show hyperplasia on TVS and HPE . The sensitivity , specificity ,PPV and NPV of TVS findings in comparision to Histopathology as Proliferative phase :- 88.8% , 100% , 100% , 88.46% . Secretory phase :- 100% , 86%, 53% , 93% . Menstrual phase :-100% , 100% ,100%, 100%. Hyperplasia :- 70% , 100% ,100% ,93.02% . Surgery is done in 22% of cases , all are above 35 years.

Conclusions: Endo-vaginal scan when combined with endometrial sampling is an valuable tool for the preliminary screening, diagnosis, management all cases of DUB. Therefore, we strongly

recommend the routine use of endovaginal scan with endometrial sampling in the clinical and laboratory evaluation of all cases.

Keywords: Abnormal uterine bleeding, proliferative endometrium Menorrhagia, endovaginal scan.

INTRODUCTION

Dysfunctional uterine bleeding (DUB) can be defined as 'excessive uterine bleeding' (excessively heavy, prolonged or frequent), which is not due to demonstrable pelvic disease, complications of pregnancy or systemic disease. It is therefore a diagnosis of exclusion and includes both ovulatory and anovulatory bleeding. The majority of cases of DUB are secondary to hormonal dysfunction, and occur in perimenopausal women or after the menarche .[1] In adolescence, this is usually of hypothalamic-pituitary origin, whilst in the perimenopause, it is related to unstable and reducing ovarian function. A wealth of observational data supports the idea of increasing variability of the menstrual pattern as women approach the menopause. This may make the detection of underlying pathology particularly challenging in this age group.[2]

Clinical management aims at obtaining an accurate diagnosis and charting out the correct line of treatment. Clinical history, physical and pelvic examination attempts to determine the site and source of the bleeding. Conventional interventions consist of ultrasonography (USG), followed by a diagnostic dilation and curettage (D&C). USG only shows the uterine contour and the status of the ovary, but fails to provide adequate information regarding the endometrium. D&C is a blind procedure and the endometrium has to be sent to the pathologist to study. It also requires skill so as to obtain an adequate sample of the endometrial tissue. Complications like perforations, cervical tears and injuries, scar tissue formation and intrauterine adhesions are common. Hysteroscopy in this new era is increasingly becoming a prime investigation of choice for the evaluation of AUB. Owing to the direct visualization of the uterine cavity, it is able to pinpoint the etiology in most of the cases.[3]

Therefore, it becomes mandatory that for an accurate diagnosis of DUB a combination of two modalities Ultrasound & Histopathology will not only arrive at correct diagnosis but also help us to compare the relative efficiency, merits & demerits of these two procedures.

MATERIALS AND METHODS

This study was carried out in the department of Obstetrics and Gynaecology in 50 patients of dysfunctional uterine bleeding were studied during the period from December 2020 to November 2021 at Kakatiya Medical College. The diagnosis of DUB was established on basis of history, clinical examination findings, blood investigations and TVS findings.

Criteria for selection of cases:

1. All cases diagnosed to have dysfunctional uterine bleeding in age group between 18 -45 years were selected.
2. All patients had major complaint of menstrual disturbances e.g., Polymenorrhoea, menorrhagia, polymenorrhagia, continuous bleeding.
3. Patients with Pelvic Inflammatory Disease, Uterine Fibroids, Adenomyosis, Endometriosis, Thyroid dysfunction, genital Tuberculosis were excluded.

Method:

- A detailed history was obtained with special relevance to age, bleeding pattern.
- Onset, duration, amount of bleeding was noted in detail.
- Detailed contraceptive, obstetric, medical and surgical history of patients were taken. A thorough clinical examination including general systemic and gynaecological examination was carried out.
- All these 50 women after excluding other disorders by pelvic examination and investigations were diagnosed as "Dysfunctional Uterine Bleeding". TVS was done on the day of biopsy, phase of endometrium noted, followed by biopsy. HPE report obtained after 7^{th} day was correlated with sonographic findings and results analysed.

This was undertaken in office setting as it does not require a full bladder. An examination table with cushion inserted below the pelvis after elevating the head end which allows free movement of examiner's hand in fitting the transducer in vertical plane to achieve maximum angle is used. Trendelenburg position was avoided since minimal amount of pelvic fluid often present may help in out lining the pelvic organs. Patients were briefed about the procedure to prevent anxiety. Endovaginally transducer of 5 MHz frequency was used in the study. The tip of the transducer was smeared with transducer gel and covered with condom which was pulled firmly over the tip of the probe to avoid air trapping. The covered transducer probe was dipped in to the gel which facilitate the vaginal penetration. After the probe is inserted contact is made with the anterior wall of the vagina. The first structure in the path of vaginal probe is cervix. For scanning cervix, the probe was introduced 2.5 to 3 cm into the vagina.

Four types of probe movements are required:

(1) pushing and pulling,

(2) rotation,

(3) rocking or upwards and downwards,

(4) side-to-side or 'Panning'.

The most prominent landmark in the pelvis is usually the uterus. Uterus was scanned from back to front first in horizontal plane followed by vertical scanning to reveal entire uterus with its endometrial lining. The size of uterus, type of endometrium, thickness of endometrium, Endo-myometrial junction are noted. After uterus, pouch of Douglas was sought which may contain minimal fluid which outlines the posterior wall of uterus and the ovaries along with it.

Technique of endometrial biopsy

With all aseptic precautions each patient was examined again just before procedure bimanually to confirm the pelvic findings.

Sims speculum was used to retract the posterior vaginal wall. Cervix was held with vulsellum uterine sound was passed to determine the length and direction of uterocervical canal. Cervical dilatation was done up to 10 Hegar. Endometrial biopsy done using endometrial biopsy curette.

Endometrium in each case was submitted for histopathological examination in 10% formalin bottle. Paraffin section of the endometrium was stained by haematoxylin and eosin stain and thoroughly studied. The details noted were Surface epithelium, glands-their shape, size lining epithelium and stroma.

RESULTS

Table-1: Incidence of demographic patterns in cases of DUB.

Age in years	**No. of Cases**	**Percentage**
18-25 yrs	3	6%
26-30 yrs	11	22%
31-35 yrs	15	30%
36-40 yrs	15	30%
41-45 yrs	6	12%
Clinical Symptoms		
Polymenorrhoea	10	20%
Menorrhagia	22	44%
Polymenorrhagia	10	20%
Continuous bleeding	8	16%
Size of Uterus		
Normal	35	70%
Bulky	15	30%
Condition of Ovaries		
Normal	45	90%
Follicular cysts	5	10%

Mean age in study is 34.12 years and maximum number of cases of DUB were in age group of 31-40 yrs. (60%). Commonest menstrual irregularity observed was Menorrhagia (44%) followed Polymenorrhoea (20%) and Polymenorrhagia (20%). 90% of patients had normal ovaries. 10% had Follicular cysts.

Table-2: Thickness of endometrium as measured by TVS

Thickness of endometrium	No. of Cases	Percentage
1 – 4.9 mm	6	12%
5 – 9.9 mm	24	48%
10 – 14.9 mm	16	32%
>15 mm	4	8%
Type of endometrium		
Type-I: Endometrium in menstrual phase	6	12%
Type-II: Endometrium in early proliferative phase	14	28%
Type-III: Endometrium in late proliferative phase	10	20%
Type-IV: Endometrium in peri ovulatory phase	0	0
Type-V: Endometrium in early	7	14%

secretory phase		
Type-VI: Endometrium in late secretory phase	6	12%
Type-VII: Endometrial hyperplasia	7	14%

Majority of cases had endometrial thickness between 5 – 9.9 mm. 8% cases had thickness >15mm, which were labelled as hyperplasia. There is predominance of proliferative phase of endometrium. Type-II endometrium was most frequent finding in 28%, while type-III 20%. Type-I, Type-V, Type-VI, Type-VII were found to be 12% ,14% ,12%, 14% respectively.

Table-3: Histopathological types of endometrium **in DUB**

HPER	**No. of Patients**	**% of Patients**
Proliferative	26	52%
Secretary	6	12%
Menstrual	6	12%
Hyperplasia		
Simple hyperplasia	7	14%
Cystic glandular hyperplasia	3	6%
Irregular shedding	1	2%
Irregular Ripening	1	2%

By this table, proliferative endometrium is seen in 52 %, secretory endometrium is seen in 12 %, menstrual endometrium is seen in 12 %, simple hyperplasia in 14 %, cystic glandular hyperplasia 6%, irregular shedding in 2%, irregular ripening in 2 %.

The Table shows that in a majority of cases there has no pathology in endometrium proving the hypothesis that there is only a derangement of hypothalamo- pituitary axis.

Table-4: Correlation between TVS findings and HPE findings at different endometrial thickness

Endometrial thickness (in mm)	**No. of cases**	**TVS**	**HPE**
1- 4.9	6	6- Menstural	6-Menstural
5 - 9.9	24	22- Proliiferative 2- Secretory	21- Proliferative 1-Secretory 2-Hyperplastic
10 -14.9	16	2- Proliiferative 11-Secretory 3- Hyperplastic	6- Proliferative 6-Secretory 4-Hyperplastic
>15	4	4- Hyperplastic	4 –Hyperplastic

Out of 6 patients with ET 1 – 4.9 mm, endometrial parrern is menstrual on TVS and HPE. Out of 24 patients with ET 5 – 9.9 mm 22 patients have proliferative endometrium and 2 have secretory endometrium on TVS. And findings on HPE are 21 have proliferative endometrium, 1 have secretory endometrium, 2 have hyperplastic.

Out of 16 patients with ET 10 – 14.9 mm 2 patients have proliferative, 11 have secretory, 3 have hyperplastic endometrium on TVS. And findings of these patients on HPE are 6 have proliferative endometrium, 6 have secretory endometrium, 4 have hyperplasia.

Out of 4 patients with ET 15 and above endometrium show hyperplasia on TVS and HPE.

Mean ET in proliferative phase - 6.75 mm .

Mean ET in secretory phase - 10 mm

Patients with normal histology has mean ET – 6.8 mm and endometrial hyperplasia has mean ET 16.4 mm

Table-5: Sensitivity, specificity, PPV, NPV of TVS findings in comparison to histopathology

Findings	No. of cases	HPE	TVS				Sensitivity	Specificity	PPV	NPV
			True		False					
	TVS		+ ve	- ve	+ ve	- ve				
Proliferative	24	27	24	23	0	3	88.8	100	100	88.46
Secretory	13	7	7	37	6	0	100	86	53	93
Menstrual	6	6	6	44	0	0	100	100	100	100
Hyperplasia	7	10	7	40	0	3	70	100	100	93.02

The sensitivity, specificity, PPV and NPV are as follows:

Proliferative phase: - 88.8%, 100%, 100%, 88.46%.

Secretory phase: - 100%, 86%, 53%, 93%.

Menstrual phase: -100%, 100%,100%, 100%.

Hyperplasia: - 70%, 100%, 100%, 93.02%.

Proliferative phase: - Chi – square -42.4, P < 0.0001

Secretory phase: Chi- square -22.703, P < 0.0001

Menstrual phase: Chi –square – 49, p < 0.0001

Hyperplasia: Chi – square -31.907, p <0.0001

Table -6: Clinical response to different types of treatment.

Age	Medical	Surgical
Upto 25	3	-
25-30 Yrs.	11	-
31-35 Yrs.	15	-
36-40 Yrs.	10	5
41-45 Yrs.	-	6

22%% of patients Surgery was done (Total Abdominal Hysterectomy) for management of DUB. All the patients were above 35 years. TAH was done because of endometrial hyperplasia in 8 cases and because of failure to respond to hormones in 3 cases. This goes to prove that in

perimenopausal age group surgical management is more effective as compared to medical. It is observed that patients between 18 to 35 years responded well to NSAIDS, Ethamsylate and hormones. Medical management is much better because hysterectomy may lead to pre-mature ovarian failure.

DISCUSSION

Abnormal uterine bleeding is the main reason women referred to gynaecologists and accounts for two thirds of hysterectomies. Evaluation of patients with abnormal uterine bleeding and identifying those with Dysfunctional uterine bleeding is achieved with combination of the following: history, physical examination, ultrasound and histopathological evaluation.

Awwad et al [2]described DUB as a common debilitating problem amongst women in all age groups and accounting for 20% of gynecology OPD visits and may account for 25% of all hysterectomies In present study maximum number of cases were recorded in the age group of 31-40 years (60%). . Bhoomika[4] et al study maximum cases were recorded in age group of 41-50 years (40.66%). DUB may present at any age between puberty and menopause and may occur with any type of endometrium.

Menorrhagia which was predominant bleeding pattern in this study, was consistent with studies conducted by Veena M[5] et al 41.30%. Polymenorrhagia 20% had slightly higher incidence when compared to Veena M et al [5] 12.50%. In our study Polymenorrhoea was 20% which was same when compared to studies. Veena M et al[5] 13.50%. Incidence of continuous bleeding in present study was 16% which was slightly higher when compared to studies of Veena M et al [5]7.70%.

Table-8: Comparison of spectrum of endometrial pattern by HPER in different studies

Type of endometrium	**Veena M et al[5]**	**Varsha D et al[6]**	**Present study**
Proliferative	30.8%	62%	52%
Secretory	25.8%	20%	12%
Menstrual	-	-	12%
Endometrial Hyperplasia • Simple. • Cystic glandular hyperplasia	-	12% -	14% 6%
Irregular shedding	-	1%	2%
Irregular ripening	-	1%	2%

In present study proliferative phase of endometrium (52%) was predominant, other studies of Varsha D et al[6] 62%, Veena M et al[5] 30.8% had lower incidence. In proliferative phase menorrhagia was observed due to prolonged and unopposed action of oestrogens. This represents anovulatory type of DUB. In study by Dr. S. Babu et al [7], Anjali singh et al[8], Acharya Veena et al[9] the most common HPER finding was proliferative endometrium which again points towards anovulatory type of dysfunctional uterine bleeding.

Secretory endometrium was found in 12% of cases which was slightly lower when compared to studies of Varsha D et al[6] 20%, Veena M et al[5] 25.8%. Simple hyperplasia was 14% which was consistent with study of Varsha D et al[5] (12%). Some case of endometrial hyperplasia can be

associated with thin endometrium. Increased ovarian follicular activity which presents as cystic ovaries is also associated with endometrial hyperplasia. Therefore, endometrial hyperplasia can ‘t be ruled out in absence of abnormal endometrial thickness. Present study irregular shedding 2% and irregular ripening 2% which are consistent with study of Varsha D et al[6] 1% and 1%.

Table-8: Comparison of mean ET in different studies

Mean ET	**Varsha D et al[6]**	**Acharya Veena et al[9]**	**Present study**
Proliferative phase	6.9mm	7.3mm	6.75mm
Secretory phase	12.3mm	9.7mm	10mm
Endometrial hyperplasia	22.8mm	11.5mm	16.4 mm

Mean ET in proliferative phase in present study is 6.75 mm, slightly low when compared to studies of Varsha D et al[6] 6.9mm, Acharya Veena et al[9] 7.3 mm. Mean ET in secretory phase in present study is 10 mm, slightly low when compared to studies of Varsha D et al[6] 12.3mm, Acharya Veena et al9 9.7 mm.

Mean ET in endometrial hyperplasia in present study is 16.4mm which favourably compares study of Margit Deuholm et al[10] 11.5mm, Varsha D et al[6] had higher mean ET of 22.8mm. Study by Aliya Aslam and Ghazala[11], it was found that at ET < 14mm, no major endometrial pathology is detected. Study by Chatapavit Getpook[12], states that endometrial thickness of 8mm or less is less likely to the associated with malignant pathologies in premenopausal uterine bleeding.

Study by Mechado Lovina S.et al[13] no statistically significant association was found between endometrial thickness and cycle days with histopathology. None of the women with endometrial thickness < 5 mm had atypia or malignancy.

Table-9. Comparision of sensitivity, specificity, PPV AND NPV of TVS

TVS for proliferative phase	**Sensitivity**	**Specificity**	**PPV**	**NPV**
Varsha D et al [6]	92.64	100	100	88.09
Acharya Veena et al[9]	89.41%	100%	100%	62.50%
Present study	88.8	100	100	88.46
TVS for secretory phase				
Varsha D et al [6]	100	89.77	70	100
Acharya Veena et al[9]	100%	100%	100%	100%
Present study	100	86	53	93
TVS for menstrual phase				
Varsha D et al [6]	100	100	100	100
Present study	100	100	100	100
TVS for endometrial				

hyperplasia				
Varsha D et al [6]	76	100	100	95.60
Acharya Veena et al [9]	100%	91.49%	42.86%	100%
Present study	70	100	100	93.02

Sensitivity is 88.8%, specificity is 100%, PPV is 100%, NPV is 88.09% which is consistent with Varsha D et al[6] study. In present study sensitivity is 100 %, specificity is 86%, PPV is 53%, NPV is 93% which are consistent with Varsha D et al[6] study 100% ,89.77% ,70% ,100%. Present study sensitivity, specificity, PPV and NPV of TVS in menstrual phase are in consistent with Varsha D et al[6] study. Present study sensitivity, specificity, PPV and NPV of TVS 70%, 100%, 100%, 93.02% are consistent with Varsha D et al[6] study 76%, 100%, 100%, 95.60%

Present study sensitivity, specificity, PPV, NPV of TVS in proliferative phase are 88.8%, 100%, 100%, 88.4% which are consistent with Acharya Veena et al[9] study. Present study sensitivity, specificity, PPV, NPV of TVS in secretory phase are 100% ,83.7%, 53.8%, 100% which are consistent with Acharya Veena et al[9] study. Present study sensitivity, specificity, PPV, NPV of TVS in Hyperplastic endometrium are 70%, 100%, 100%, 93.02% which are consistent with Acharya Veena et al[9] study

Present study endometrial hyperplasia is 20% which is consistent with study of Anjali singh et al [8] 28%. In present study Histopathological findings were well correlated with TVS findings in almost all cases except in 11 cases. In Anjali singh et al[8] study Histopathological findings were well correlated with TVS findings in almost all cases except in 4 cases. In Karlsson B et al[14] study the sensitivity and specificity using transvaginal sonography to diagnose an endometrial abnormality were 100% and 75%, respectively. In Aslam M et al[15] study sensitivity and specificity of TVS is 71.4% and 67.7% in endometrial hyperplasia. Mathew *et al*[16]., in their study, found that sensitivity of TVS in detection of endometrium was 54%, whereas the specificity was 100%. Positive predictive value was 100% and negative predictive value was 81.1% Endometrial thickness reflects oestrogen levels. TVS gives indirect evidence about hormone status. TVS also gives information about length of cervix, size of uterus, ovaries, free fluid in pouch of Douglas. Therefore, TVS has replaced D and C for all practical purposes. It is a diagnostic tool in case of DUB and has greater patient compliance and is a non –invasive OPD procedure. Surgery was done in 22% of patients, 78% were managed conservatively. The indication for surgery was endometrial hyperplasia, failure of medical therapy. The follow up of patients on medical treatment is easy using TVS and compliance is good. TVS with histopathology is not only a diagnostic use but guides in treatment and follow-up of patient.

CONCLUSION

TVS scan which is a simple non-invasive OPD procedure can be utilized as a screening test for the diagnosis of endometrial patterns in DUB cases as a preliminary procedure. Regarding the role of histopathology in diagnosis of abnormal endometrium (endometrial hyperplasia), it is established by our study and other studies that because of its objectivity it has got more diagnostic accuracy when compared to endo-vaginal scan alone. Endo-vaginal scan can ‘t differentiate between cystoglandular hyperplasia or atypical hyperplasia for which histopathological diagnosis is definitive and imperative. Therefore, trans-endo-vaginal scan when combined with endometrial sampling (HPE) is the best combination for diagnosing cystoglandular hyperplasia, Adenomatous hyperplasia.

Our study proves that endo-vaginal scan is a useful adjuvant for endometrial sampling but at the same time it can‘t substitute for the same. There is greater patient compliance with both these procedures as compared to DD&C which is having its own morbidity and complication rate. TVS scan also excludes the organic causes of abnormal uterine bleeding like fibroids, adenomyosis and ovarian cysts (benign or malignant).

Endo-vaginal scan when combined with endometrial sampling is an valuable tool for the preliminary screening, diagnosis, management and follow-up of all cases of DUB. Therefore, we strongly recommend the routine use of endovaginal scan with endometrial sampling in the clinical and laboratory evaluation of all cases of DUB in all teaching hospital and for all consultant gynaecologists.

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