

CORRELATION OF ULTRASONOGRAPHY AND HISTOPATHOLOGICAL FINDINGS IN PERIMENOPAUSAL WOMEN WITH ABNORMAL UTERINE BLEEDING

Dr. Trisha Arora^{1*}, Dr. Manisha Gupta², Dr. Neelima Agarwal³

¹Assistant Professor

^{2,3}Professor, Santosh Deemed to be University

Dr. Trisha Arora (Corresponding author) Email Id- arora.trisha@gmail.com

Background: Abnormal uterine bleeding is a frequently encountered gynecologic complaint in perimenopausal woman. The objective of the study was to correlate the ultrasonographic finding with histopathological examination in perimenopausal AUB.

Methods: This prospective study was carried out over 6 months in a teaching hospital. A total of 100 women in the age group of 40-51yrs who presented with AUB were included. After selecting the patient with eligibility criteria, detailed clinical history, systemic, gynecological examinations and investigations were done as per proforma. USG study of endometrial pattern and thickness was measured followed by dilatation and curettage and HPE was done. The data collected was entered in MS EXCEL spreadsheet and analysis was done using Statistical Package for Social Sciences (SPSS) version 21.0 (Trial Version)

Result: The commonest menstrual irregularity was heavy and prolonged menstrual bleeding (49%). Endometrial thickness >15 mm on USG was seen in (43%) patients, 9-15mm thickness(44%). On HPE, secretory phase endometrium(37%), proliferative phase (36%), endometrial hyperplasia(22%), disordered proliferative endometrium (2%) & endometrial carcinoma (3%) was seen.

Conclusion: USG should be the first diagnostic step in evaluation of AUB. HPE is done to confirm the diagnosis. Accurate diagnosis of the causative factor of AUB is imperative for appropriate management.

Keywords: Abnormal uterine bleeding, Heavy menstrual bleeding, Histopathological examination, Endometrial hyperplasia, Dilatation and Curettage

INTRODUCTION

Abnormal uterine bleeding (AUB) is any change seen in the frequency of menstruation, duration of the flow or amount of blood loss experienced by a woman. Perimenopause is defined as period of 2-8 yrs preceeding menopause & 1 yr after the final menses (WHO), literally means “around menopause”^{1,2} can last for up to 10 years.

AUB in perimenopausal women is associated with endometrial carcinoma in approximately 10 % of the total number of cases.³ In perimenopausal women, sonography should be included as the first choice of investigation. Endometrial biopsy including other methods of detecting endometrial hyperplasia or carcinoma must be considered early in the investigation workup.⁴

AUB in perimenopausal women accounts for almost 70 % of total gynaecological outpatient visits.⁵ This signifies that perimenopausal AUB may be the only clinical presentation

seen in endometrial cancer in most instances. Using a non-invasive and a convenient diagnostic technique such as USG is preferable at the first instance for studying the endometrial patterns and its thickness accurately and at the same time to exclude organic uterine pathology in AUB followed by the invasive technique of dilatation and curettage (D and C).^{6,7} Dilatation and curettage remain the standard diagnostic procedure for assessment of AUB and for early detection of atypical or typical endometrial hyperplasia, but it has a drawback of being a blind procedure with a chance of missing of a small or focal lesion.^{8,9}

Aim and objective of the present study was to study the various types of menstrual abnormalities prevalent in perimenopausal women and to correlate the ultrasonographic findings eg. endometrial thickness and pattern with histopathological examination as obtained from dilatation and curettage (D&C).

METHODS

The study was conducted on 100 perimenopausal patients with menstrual irregularity fulfilling the above criteria. Written informed consent was taken after explaining the complete procedure to the patient. After taking detailed history of the patients, thorough clinical examination and all routine hematological investigations were done. Ultrasonography was performed. D&C was done and endometrial curetting were sent for histopathological examination. Correlation of ultrasonography findings with the histopathological examination report was done.

INCLUSION CRITERIA:-

1. Perimenopausal patients with abnormal uterine bleeding (age group 40-51 years).

EXCLUSION CRITERIA:-

1. Age less than 40 or more than 51 years of age.
2. Women who have attained menopause.
3. Women on hormonal treatment at the time of first presentation.
4. Women with intrauterine device in situ.
5. Women with endocrine disorders.
6. Women with bleeding disorders.
7. Women opting for medical management for abnormal uterine bleeding.
8. Women with adnexal pathology.
9. Pregnancy and related causes of bleeding per vaginum.

Detailed menstrual, contraceptive, obstetric, medical and surgical history of the eligible candidates were taken along with H/O presenting complains and general, physical, systemic and gynecological examination was done as per proforma. Every patient was subjected to following laboratory investigations including CBC, blood group, RBS, coagulation profile, liver and kidney function tests, urine routine and microscopy and UPT. All the eligible candidates were subjected to USG, various sonographic parameters such as endometrial thickness, uterine pathology, adnexal and any other pelvic pathology was noted.

TABLE 1:-The endometrial thickness in different phases of the menstrual cycle is described as follows

Menstrual Phase	Endometrial thickness (full thickness) in mm(ET)
Menstrual (Late)	0.5 - 1
Proliferative (follicular phase)	4 – 8

Peri-ovulatory phase	6 – 10
Secretory (Luteal phase)	10 – 12
Post Menopausal	1 - 3

TABLE 2:-Correlation of normal menstrual cycle anatomy and physiology with ultrasound endometrial patterns

Menstrual Cycle Phase	Ultrasound Pattern
Menses (Early)	Hyper echoic: Resembles a luteal phase endometrium with anechoic areas indicating endometrial breakdown.
Mid Menses	Mixed pattern with hyperechoic and anechoic areas indicating blood and tissue endometrium per se noted
Late	As two thin hyperechoic lines outlining the endometrial cavity. Single line: Thin line representing the endometrial cavity
Early Follicular phase	Three line: The two outer hyperechoic lines represent the endometrial myometrial junction. The central line is the endometrial cavity.
Late Follicular phase	Three line: Thickening of the anechoic endometrial layer between the hyperechoic three lines.
Early Luteal phase	Transitional: Thickening of the hyperechoic three lines and irregular hyper echoic filling of the previously anechoic endometrial layers
Late Luteal phase	Hyperechoic: Uniform hyperechoic (White) endometrium
Premenstrual	Hyperechoic: With small anechoic collections.

TABLE 3:- Atypical endometrium patterns and corresponding sonographic findings

Atypical Patterns	Sonographic findings
Atrophic endometrium	Uniform thin echogenic line
Cystic atrophic endometrium	Abnormally thickened endometrium with multiple small cystic spaces (Swiss cheese endometrium)

Endometrial Hyperplasia Focal, Diffuse	Thickening of the endometrial stripe and often appears homogeneously echogenic
Cystic hyperplasia	Echogenic endometrium with detectable small cysts
Atypical hyperplasia	Inhomogenous, Irregular endometrial stripe

Endometrial carcinoma	Thick, Solid, Heterogenous ill defined endometrial tissue. Enlarged uterus from 2-5 cm (AP Uterine Diameter) to 9-14 cm (cervico- fundal uterine diameter) Distended Uterine Cavity -Lobular uterus, loss of incomplete central hyperechoic line, Hypo or hyper echogenic uterine body, preservation of endometrial halo indicates superficial invasion, absence of halo indicates deep invasion.
-----------------------	---

The D and C procedure performed under short general anesthesia in OT. The endometrial tissue sample for histopathological examination was fixed in 10% formalin and sent to the college pathology department for analysis.

STATISTICAL ANALYSIS

Categorical variables were presented in number and percentage (%) and continuous variables were presented as mean $\pm$ SD and median. Normality of data was tested by Kolmogorov-Smirnov test. If the normality was rejected then non parametric test was used. Statistical tests were applied as follows-

1. Quantitative variables were compared using ANOVA/Kruskal Wallis test (when the data sets were not normally distributed) between HPE of endometrial biopsy.
2. Qualitative variables were correlated using Chi-Square test.

A p value of ≤ 0.05 was considered statistically significant.

The data was entered in MS EXCEL spreadsheet and analysis was done using Statistical Package for Social Sciences (SPSS) version 21.0 (Trial Version)

RESULTS

Most women were in the age group of 46-50 years (53%) with Maximum patients were with parity 3 and above (60%).

TABLE 4

Age Group	Cases	
	Frequency	Percentage(%)
41-45	47	47.00
46-50	53	53.00
Mean $\pm$ SD	46.2 $\pm$ 1.3	
Parity		
≤ 3	73	73.00
≥ 4	27	27.00

Maximum patients had heavy and prolonged menstrual bleeding (HPMB) that is (49%) followed by intermenstrual bleeding (IMB) in 33% cases. Heavy menstrual bleeding was observed in 18% cases.

TABLE 5

Bleeding patterns	Frequency	Percentage
Heavy and prolonged	49	49.00

menstrual bleeding		
Intermenstrual bleeding	33	33.00
Heavy menstrual bleeding	18	18.00

Irregular bleeding pattern was observed in 52% of cases. Dysmennorhoea was associated in 40% of the total.

The most common ultrasonographic findings were of uterus normal in size shape and echotexture, followed by bulky uterus and endometrial thickening.

In this study, 43% patients had endometrial thickness >15 mm on USG and 57% had <15mm of endometrial thickness on USG.

TABLE 6a Ultrasonography Finding (Uterus)

ULTRASONOGRAPHY FINDING	Frequency	Percentage (%)
Uterus		
Normal in size, shape and echotexture	62	62.00
Endometrial thickening	13	13.00
Bulky	25	25.00

TABLE 6b

Endometrial Thickness	Cases	Frequency
≥16mm	43	43.00
9-15mm	44	44.00
5-8mm	12	12.00
≥4mm	1	1.00

On histopathological reports as obtained from D&C, 37% patients had secretory phase endometrium, 36% were in the proliferative phase, 22 % had endometrial hyperplasia, 2 % had disordered proliferative endometrium & 3% had endometrial carcinoma (adenocarcinoma).

TABLE 7 Histopathology of Endometrial Biopsy

HISTOPATHOLGY	Frequency	Percentage(%)
ENDOMETRIAL PATTERN		

Secretory phase endometrium	37	37.00
Proliferative phase endometrium	36	36.00
Disordered proliferative endometrium	2	2.00
ENDOMETRIAL HYPERPLASIA		
Simple hyperplasia	14	14.00

Complex hyperplasia	5	5.00
Simple atypical hyperplasia	2	2.00
Complex atypical hyperplasia	1	1.00
ENDOMETRIAL CARCINOMA (Adenocarcinoma)	3	3.00
Total	100	100.00

Ultrasonographic finding of normal uterus or bulky uterus without any endometrial thickening showed proliferative and secretory endometrial patterns on histopathology. Complex typical and complex atypical hyperplasia was also seen only in cases with endometrial thickness >15 mm (5 and 1 cases respectively). Endometrial carcinoma (Adenocarcinoma) was seen only in cases with endometrial thickness >15 mm (3 cases). Endometrial cancer was seen only in cases with bulky uterus (2 cases) or uterus with asymmetrical endometrial thickening (1 case). There was a strong significant correlation between uterine findings on USG and Endometrial biopsy findings ($p < 0.0001$). There was a very significant correlation between endometrial thickness (USG) and endometrial biopsy findings from D & C. ($p < 0.0002$)

FIGURE 1 DISTRIBUTION OF MENSTRUAL IRREGULARITY

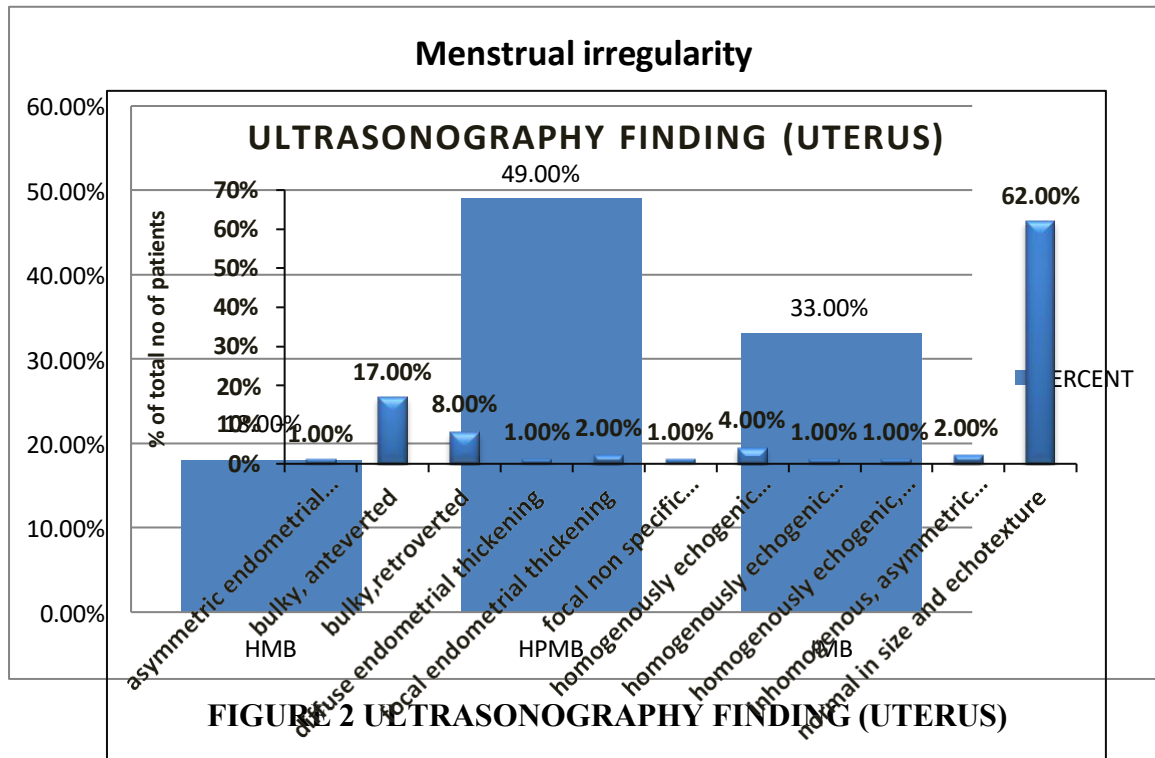


FIGURE 3 ENDOMETRIAL THICKNESS ON ULTRASONOGRAPHY

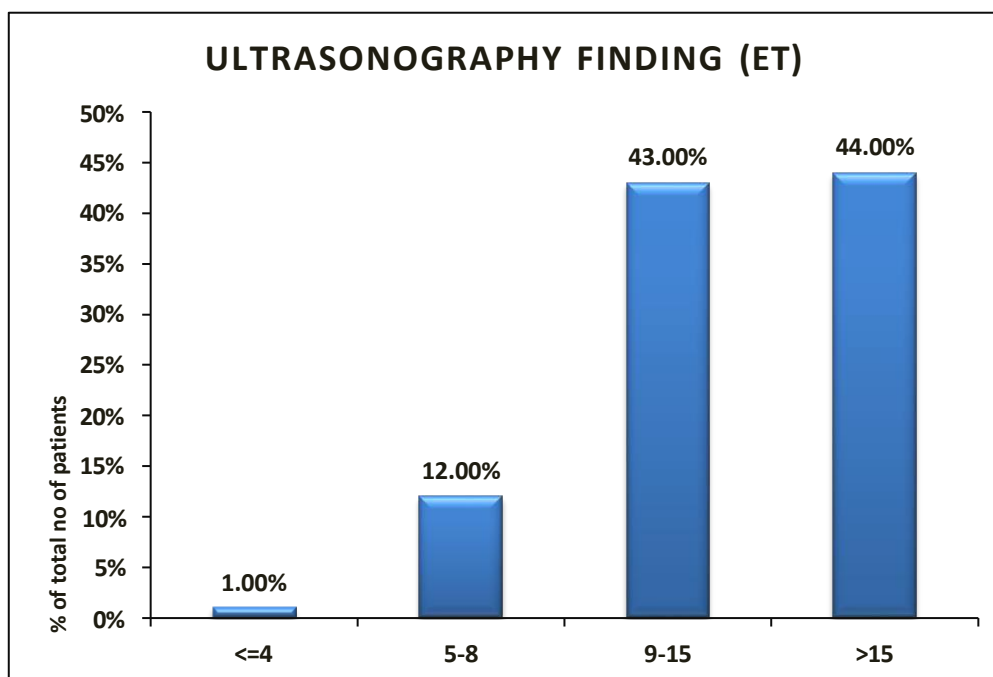
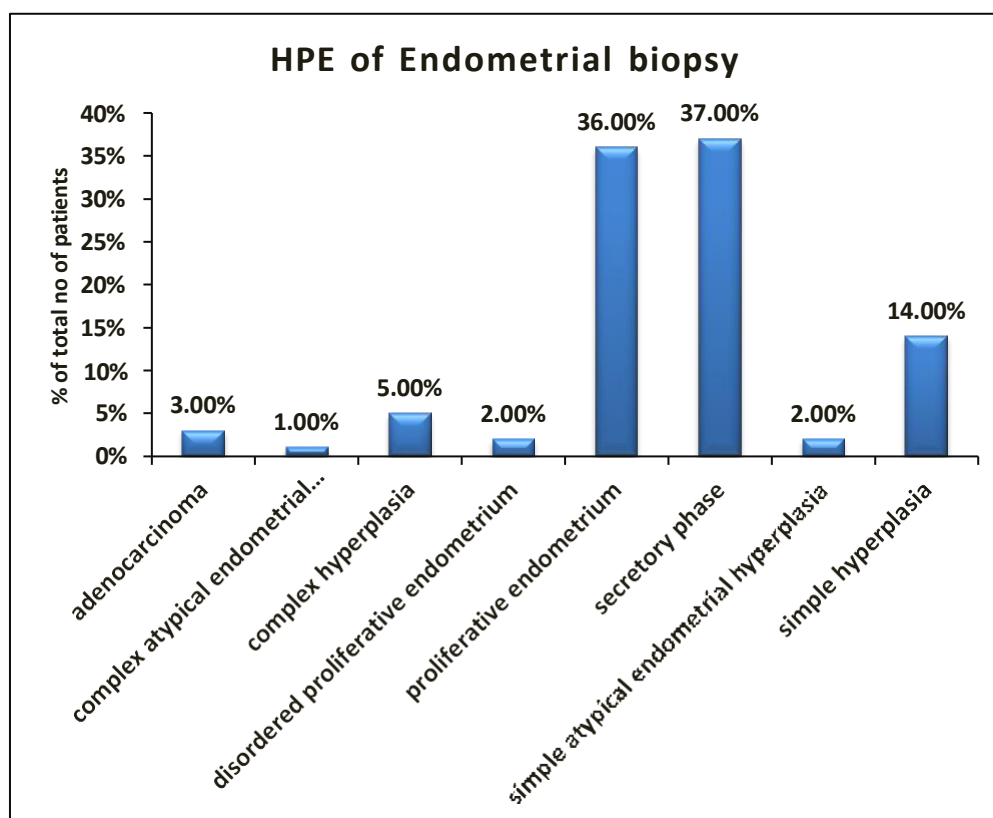


FIGURE 4 HPE OF ENDOMETRIAL BIOPSY



In our study, adenocarcinoma was seen only in cases with bulky uterus (2 cases) and uterus with asymmetric endometrial thickening (single case). Complex atypical hyperplasia was seen only in bulky anteverted uterus (single case). Simple atypical hyperplasia was seen only in inhomogenous asymmetric endometrial thickening (2 cases). Proliferative and Secretory endometrium were observed in normal uterus or bulky uterus without any endometrial thickening. There was a strong significant correlation between uterine findings on USG and Endometrial biopsy findings. ($p < 0.0001$) as has been shown in Table 5.

Table 5 Correlation of Ultrasonographic finding of Uterus and HPE of endometrial biopsy

Uterus on USG	HPE of Endometrial biopsy								Total	χ ² , p, value
Asymmetric endometrial thickening	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	1 (33.33)	1 (1.00)	<.0001
Bulky, anteverted	7 (18.92)	2 (5.56)	4 (28.57)	0 (0.00)	2 (40.00)	1 (100.00)	0 (0.00)	1 (33.33)	17 (17.00)	
Bulky, retroverted	3 (8.11)	1 (2.78)	3 (21.43)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	1 (33.33)	8 (8.00)	
Diffuse endometrial thickening	0 (0.00)	0 (0.00)	1 (7.14)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	1 (1.00)	
Focal endometrial thickening	0 (0.00)	0 (0.00)	1 (7.14)	0 (0.00)	1 (20.00)	0 (0.00)	0 (0.00)	0 (0.00)	2 (2.00)	
Focal non specific endometrial thickening	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	1 (20.00)	0 (0.00)	0 (0.00)	0 (0.00)	1 (1.00)	
Homogenously echogenic asymmetric endometrial	0 (0.00)	0 (0.00)	4 (28.57)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	4 (4.00)	

thickening										
Homogenously echogenic focal endometrial thickening	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	1 (20.00)	0 (0.00)	0 (0.00)	0 (0.00)	1 (1.00)	
Homogenously echogenic, diffuse endmetrial thickening	0 (0.00)	0 (0.00)	1 (7.14)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	1 (1.00)	
Inhomogenousasymmetric endometrial thickening	0 (0.00)	0 (0.00)	0 (0.00)	2 (100.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	2 (2.00)	
Normal in size and echotexture	27 (72.97)	33 (91.67)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	2 (100.00)	0 (0.00)	62 (62.00)	
Total	37 (100.00)	36 (100.00)	14 (100.00)	2 (100.00)	5 (100.00)	1 (100.00)	2 (100.00)	3 (100.00)	100 (100.00)	

In our study, adenocarcinoma was seen only in cases with endometrial thickness >15 mm (3 cases). Complex typical and atypical hyperplasia was also seen only in cases with endometrial thickness >15 mm (5 and 1 cases respectively). Simple atypical hyperplasia was also seen only in cases with endometrial thickness >15 mm (2 cases). Proliferative endometrium was seen with all endometrial thickenings ranging from ≤4 to >15 mm and Secretory endometrium was seen in endometrial thickenings ranging from >4 to >15 mm. There was a strong significant correlation between endometrial thickness (USG FINDING) and endometrial biopsy findings. (P=0.0002) It has been shown in Table 6.

Table 6 Correlation of Endometrial thickness and HPE of endometrial biopsy

Endometrial thickness (mm)	HPE of Endometrial biopsy								Total	p value
	Secretory Endometrium	Proliferative Endometrium	Simple Hyperplasia	Atypical Endometrial Hyperplasia	Complex Hyperplasia	Complex Atypical Endometrial Hyperplasia	Atypical Proliferative Endometrium	Adenocarcinoma		
≤ 4	0 (0.00)	1(2.78)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	1(1.00)	0.0002
5-8	1(2.70)	8 (22.22)	1 (7.14)	0 (0.00)	0 (0.00)	0 (0.00)	2 (100.00)	0 (0.00)	12 (12.00)	
9-15	16 (43.24)	23 (63.89)	4 (28.57)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	43 (43.00)	
> 15	20 (54.05)	4 (11.11)	9 (64.29)	2 (100.00)	5 (100.00)	1 (100.00)	0 (0.00)	3(100.00)	44 (44.00)	

Total	37 (100.00)	36 (100.00)	14 (100.00)	2 (100.00)	5 (100.00)	1 (100.00)	2 (100.00)	3 (100.00)
-------	-------------	-------------	-------------	------------	------------	------------	------------	------------

CONCLUSION

Accurate diagnosis of the causative factor of abnormal uterine bleeding is imperative in the initiation of the appropriate management. Therefore, ultrasonography, being noninvasive, easily acceptable by the women and without any complications, is a good diagnostic tool for the evaluation of AUB as an initial procedure. If needed, the patients should be subjected to endometrial biopsy which is the gold standard in ruling out endometrial cancer.

REFERENCES

1. Najeeb R, Awan AS, Bakhtiar U, Akhter S. Role of transvaginal sonography in assessment of abnormal uterine bleeding in perimenopausal age group. *J Ayub Med Coll Abbottabad*. 2010;22(1):87-90.
2. Nazim F, Hayat Z, Hannan A, Ikram U, Nazim K. Role of transvaginal ultrasound in identifying endometrial hyperplasia. *J Ayub Med Coll Abbottabad*. 2013;25(1-2):100- 102.
3. Korhonen MO, Symons JP, Hyde BM, Rowan JP, Wilborn WH. Histologic classification and pathologic findings for endometrial biopsy specimens obtained from 2964 perimenopausal and postmenopausal women undergoing screening for continuous hormones as replacement therapy (CHART 2 Study). *American journal of obstetrics and gynecology*. 1997 Feb 1;176(2):377-80.
4. Lax SF. Molecular genetic pathways in various types of endometrial carcinoma: from a phenotypical to a molecular-based classification. *Virchows Archiv*. 2004 Mar 1;444(3):213-23.
5. Singh S, Best C, Dunn S, Leyland N, Wolfman WL. No. 292-Abnormal Uterine Bleeding in Pre-Menopausal Women. *Journal of Obstetrics and Gynaecology Canada*. 2018 May 31;40(5):e391-413.
6. Vercellini P, Cortesi I, Oldandi S, Moschetta M, DeGiorgi O, Crosignani PG. The role of transvaginal ultrasonography and outpatient diagnostic hysteroscopy in the evaluation of patients with menorrhagia. *Hum Reprod* 1997;12:1768–71
7. Kaur N, Khaira Hk. Comparative Study Of Transvaginal Ultrasonography And Endometrial Biopsy In Evaluation Of Abnormal Uterine Bleeding. *Indian Journal Of Applied Research*. 2018 Apr 9;8(2).
8. Yarandi F, Izadi Mood N, Eftekhari Z, Shojaei H, Sarmadi S. Diagnostic accuracy of dilatation and curettage for abnormal uterine bleeding. *Journal of Obstetrics and Gynaecology Research*. 2010 Oct 1;36(5):1049-52.
9. Grimes DA. Diagnostic dilatation and curettage: a reappraisal. *Am j obstet gynecol* 1982;142(1):1-6