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Correlation of Ultrasonography and Histopathological Findings in Perimenopausal Women with Abnormal Uterine Bleeding

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ABSTRACT:

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

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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.

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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	Hyperechoic: Uniform hyperechoic (White) endometrium

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phase	
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 a. Focal, b. Diffuse	Thickening of the endometrial stripe and often appears homogeneously ecchogenic
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 ± SD and median. Normality of data was tested byKolmogorov-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:

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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 ± SD	46.2 ± 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 menstrual bleeding	49	49.00
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

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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 (1case). There was a strong significant correlation

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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)

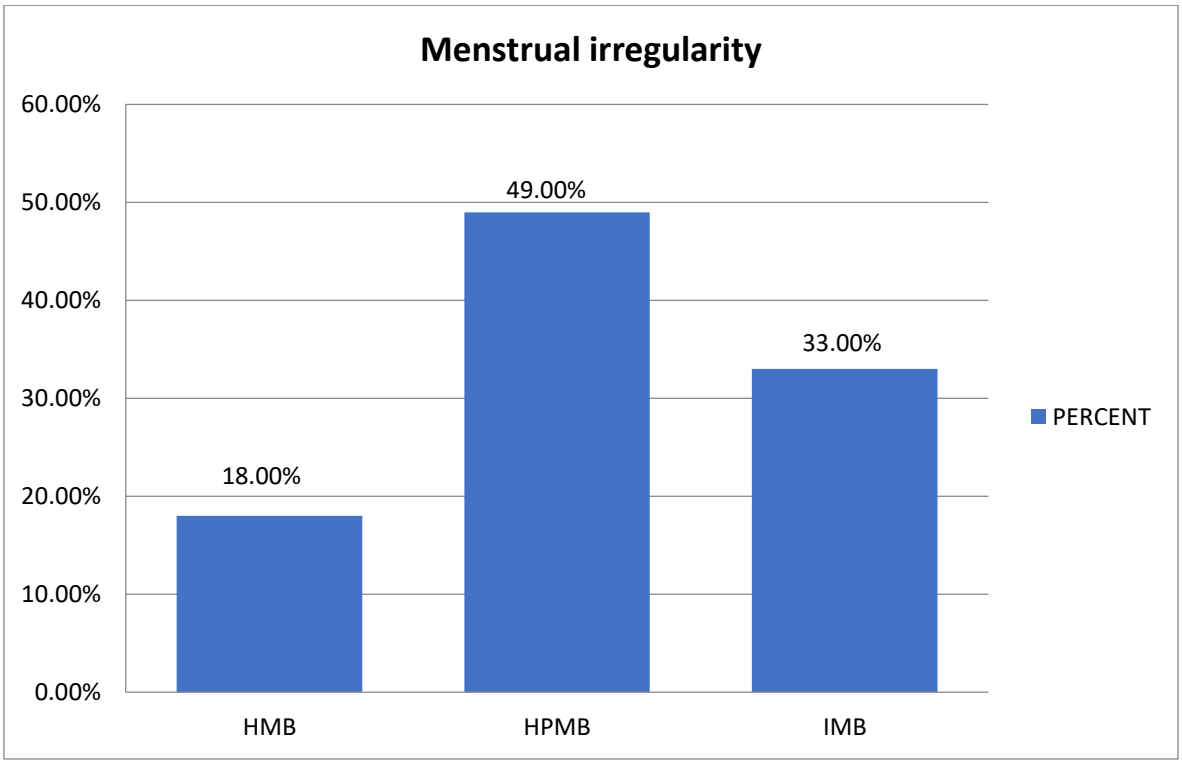

FIGURE 1 DISTRIBUTION OF MENSTRUAL IRREGULARITY

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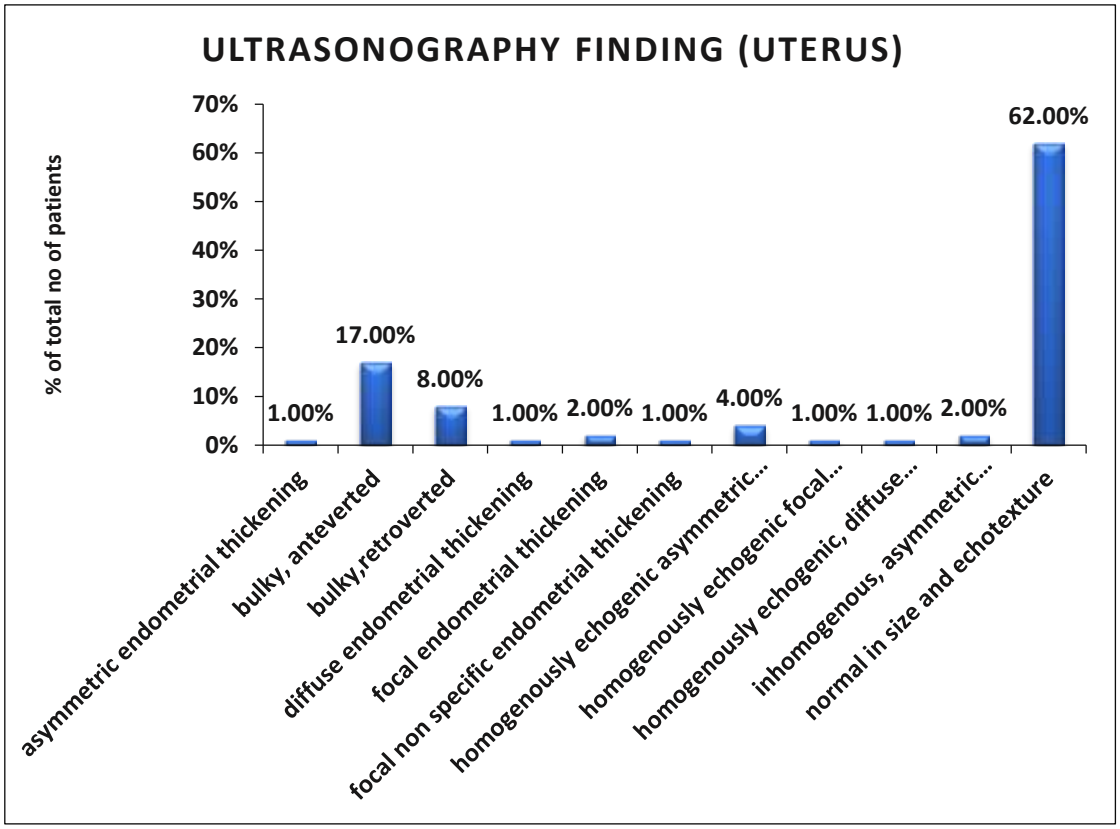

FIGURE 2 ULTRASONOGRAPHY FINDING (UTERUS)

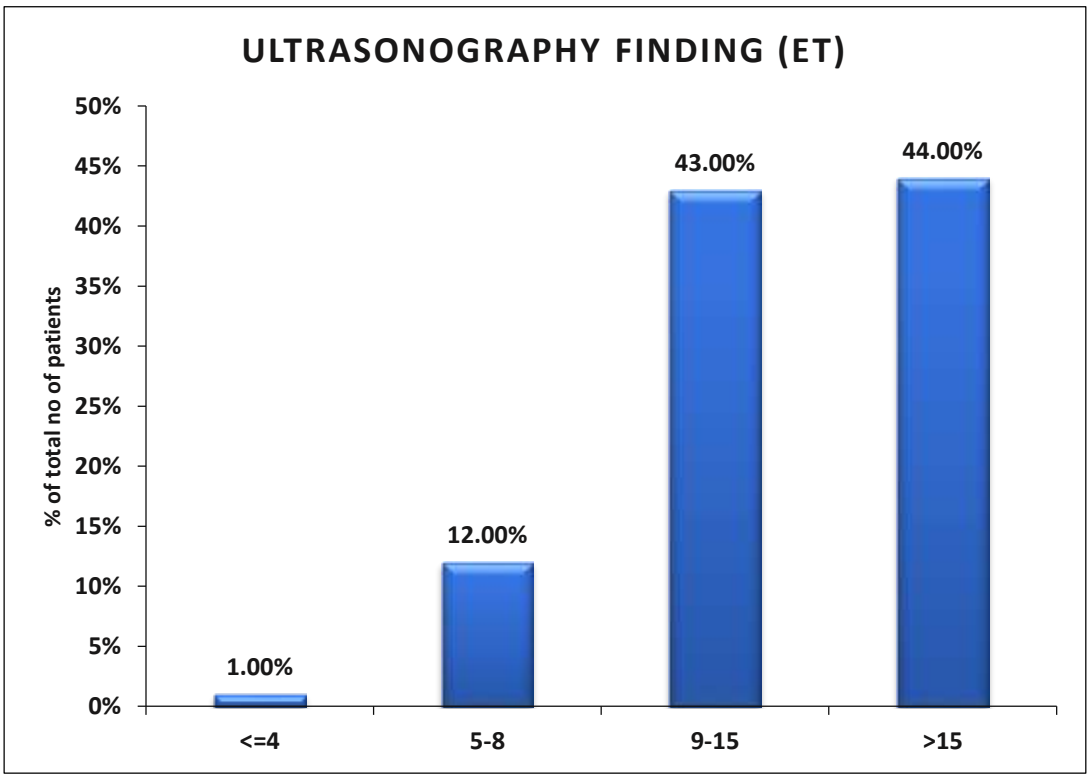

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FIGURE 3 ENDOMETRIAL THICKNESS ON ULTRASONOGRAPHY

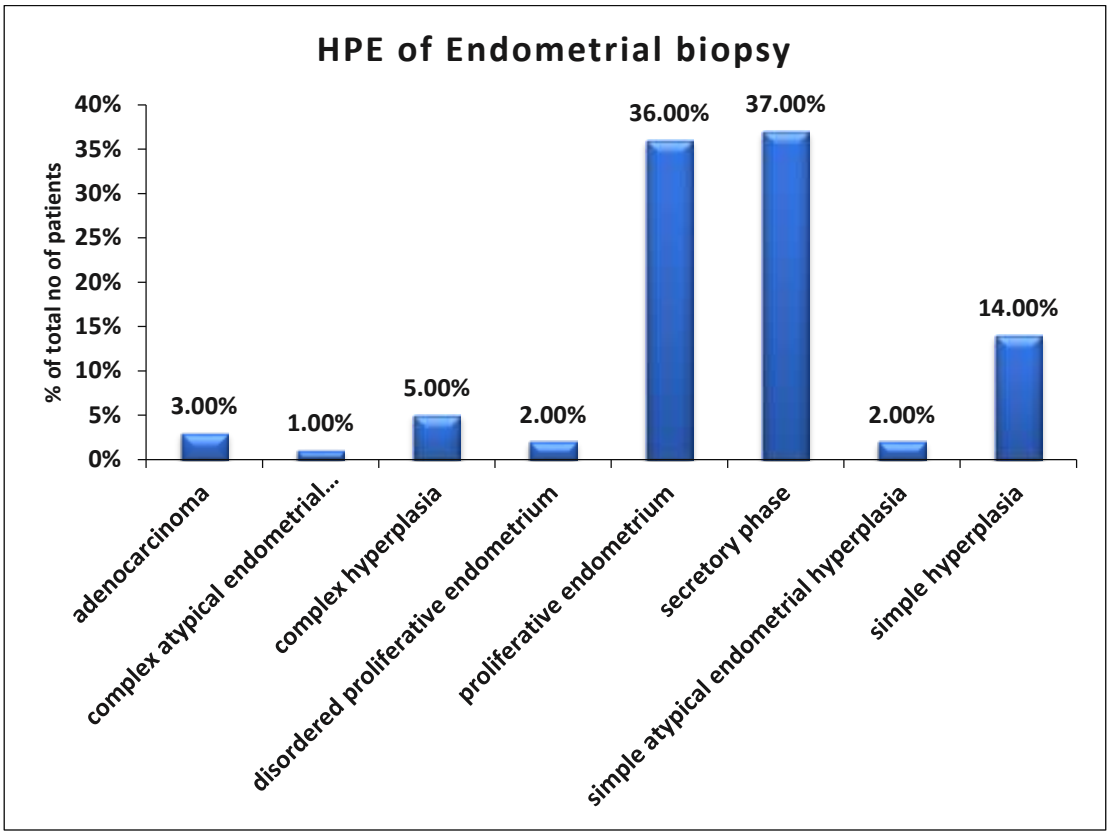

FIGURE 4 HPE OF ENDOMETRIAL BIOPSY

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

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Uterus on USG	HPE of Endometrial biopsy								Total	'p' value
	Secretory Endometrium	Proliferative Endometrium	Simple Hyperplasia	Simple Atypical Endometrial Hyperplasia	Complex Hyperplasia	Complex Atypical Endometrial Hyperplasia	Disordered Proliferative Endometrium	Adenocarcinoma		
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 thickening	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)	
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

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Endometrial thickness (mm)	HPE of Endometrial biopsy								Total	'p' value
	Secretory Endometrium	Proliferative Endometrium	Simple Hyperplasia	Simple Atypical Endometrial Hyperplasia	Complex Hyperplasia	Complex Atypical Endometrial Hyperplasia	Disordered 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)**	**100 (100.00)**	

DISCUSSION:

In present study group of women with AUB, when considering the parity, it was observed that para 3 and above were (60%). Maximum incidence of AUB was seen in para 3 and above which is in concordance with studies conducted by Bhattacharji et al[10](46%), Devi P.K et al[11](48.6%), Pillai et al[12] (87%), Joshi and Deshpande et al [13](61.5%) , Mehrotra V.G et al[14](46%) and Sadia K et al[15](54%).

In the present study, heavy and prolonged menstrual bleeding was the commonest type of bleeding (49%) followed by intermentrual bleeding in (33%) cases. In study conducted by Gupta A et al[16], Sreelakshmi et al[17], commonest symptoms were heavy and prolonged menstrual bleeding i.e (72%) and (83.7%) respectively.

In this study, (62 %) of the patients had normal size and echotexture of the uterus on ultrasonography. Uterus was bulky in 25% of cases. 13 % had endometrial thickening on USG. In present study, adenocarcinoma was seen only in cases with bulky uterus (2 cases) or uterus with asymmetric endometrial thickening (single case) and complex atypical hyperplasia was seen only in bulky anteverted uterus (single case). Simple atypical hyperplasia was seen only in patients with inhomogenous asymmetric endometrial thickening (2 cases). Proliferative and Secretory endometrium were seen with normal uterus or bulky uterus without any endometrial thickening. There was a strong significant correlation between uterine findings on USG and Endometrial biopsy findings.

Endometrial carcinoma (Adenocarcinoma) was seen only in cases with endometrial thickness >15 mm i.e. 3 cases. Complex typical and complex atypical hyperplasia was also seen only in cases with endometrial thickness >15 mm i.e. 5 and 1 cases respectively. There was a strong significant correlation between endometrial thickness as detected by USG and Endometrial biopsy findings on histopathology.

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In study by Shobhitha et al[18] endometrial hyperplasia was detected in (45.45%) off which endometrial carcinoma was seen in (1.8%) cases.

The histopathology received from the endometrial biopsy showed various findings of normal cycles of menstruation i.e secretory phase (37%) and proliferative phase endometrium(36%). Endometrial hyperplasia(22%), disordered proliferative endometrium (2%) and endometrial carcinoma (3%) cases were detected in this study. According to Bhosle et al[19], (66.1%) of their cases had proliferative endometrium, (16.1%) had secretory endometrium and (17.8 %) patients showed simple hyperplasia without atypia. These statistics were similar to current study. In the study done by Sadia K et al[15], Damle RP et al[20], proliferative phase was the most common histological pattern followed by secretory phase, simple hyperplasia without atypia, complex hyperplasia without atypia, atrophic endometrium, and endometrial adenocarcinoma in that order , similar to this study results.

Disordered proliferative endometrium on EB was seen in 2 cases i.e 2% and in study conducted by Sreelakshmi et al[17] incidence was (6.6 %) off 135 cases similar incidence was seen in Gopalan U et al[21] study.

Sreelakshmi et al[17] reported that endometrial hyperplasia is a common histopathological finding in perimenopausal women often causing symptoms of irregular or prolonged bleeding , comprising of 18.5% of cases. Doroiswami S et al[22] (68%), Khare et al[23] (36.2%) observed high incidence of endometrial hyperplasia. We observed endometrial carcinoma (adenocarcinoma) in 3 patients (3 %). Sreelakshmi et al[17] encountered 1 case (0.7%) of endometrial carcinoma above the age of 45 years similar results were also reported by Khare et al[23] 3 cases of malignancy(6 %) and Dangal G. et al[24] (3%) .

Since endometrial hyperplasia is one of the greatest risk factors for the development of endometrial carcinoma, early diagnosis and initiation of treatment of the same is of utmost importance in the evaluation of perimenopausal women with AUB. So, perimenopausal women with heavy or irregular menstrual bleeding are often advised to have an endometrial sample taken to exclude endometrial cancer.

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.

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