

Research Article

Histopathology of endometrium in abnormal uterine bleeding, in correlation with thyroid profile and ultrasonography findings

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ABSTRACT

Background: Abnormal uterine bleeding is the cause for many disturbances in women who are in the reproductive age group. Frequent and prolonged periods will lead to morbidity, social embarrassment, diminished quality of life and compromise of the sexual life.

Methods: It is a hospital based cross sectional study conducted in the department of pathology, Andhra medical college. A total of 270 patients in the age group of 18 to 45 years were included in this study. Endometrial samples were obtained and histopathological examinations were conducted. All the clinical details and investigation reports were collected.

Results: The age group of patients in this study ranged from 18 to 45 years. Maximum numbers of cases (169) were in the age group of 36 to 45 years (62.6%). Most of the patients were multipara (244 cases, 90.37%) and most common presenting complaint was heavy menstrual bleeding (198 cases, 73.3%). Majority of the patients were euthyroid (247 cases, 91.5%). Normal cyclical endometrium was found to be the commonest histopathological pattern with proliferative endometrium in 45.56% and secretory endometrium in 32.59% cases. Leiomyomas were found to be the commonest cause of abnormal uterine bleeding (15.56%). Bulky / enlarged uterus (77%) and type-IV (hyperechoic) endometrium, depicting the secretory endometrial pattern (36.66%) was the most common finding on transvaginal sonography (TVS).

Conclusions: Histopathological examination is the gold standard for studying the pattern of endometrium in various causes of abnormal uterine bleeding.

Keywords: Endometrium, Uterine bleeding, Thyroid, Ultrasonography

INTRODUCTION

Hippocrates hypothesized that the menstrual function is to purge women of their bad humors, which means that menstruation is a process by which a women's body cleans itself of unhealthy elements on a cyclical basis.¹ Many women suffer from various gynecological problems. Abnormal uterine bleeding (AUB) is the commonest presenting symptom, which has a significant morbidity and interferes with the personal, family, social and sexual life. Women of the present generation

experience more number of menstrual cycles, which could be due to decreased parity and reduced length of lactational amenorrhea.²

Endometrial sampling is the gold standard for the evaluation of endometrial neoplasias, hyperplasias, metaplasias, pill induced and functional endometrial abnormalities.³ Transvaginalsonography is useful for the measurement of endometrial thickness and pattern, hyperplasias, organic causes like leiomyomas and endometrial malignancies.⁴ Though newer surgical

diagnostic and therapeutic techniques are available to aid in the management of patients with abnormal uterine bleeding, endometrial curettage was found to be the best investigation. But it was found to be less effective in diagnosing focal lesions like polyps, atypical hyperplasias and malignant lesions. Hence the supportive evidence should be utilized with judicious use of ultrasound examination, magnetic resonance imaging and other imaging modalities available.

The present study was carried out to study the histopathology of endometrium in chronic abnormal uterine bleeding and intermenstrual bleeding in correlation with thyroid profile (T₃, T₄ and TSH) and Transvaginal sonographic findings (endometrial thickness and pattern) in non-gravid women of reproductive age group of 18 to 45 years.

The aim and objectives was to study the histopathology of endometrium in various causes of chronic abnormal uterine bleeding and intermenstrual bleeding in non-gravid women in the reproductive age group of 18 to 45 years and to correlate the histopathology of endometrium in patients with chronic abnormal uterine bleeding, with the pattern and thickness of endometrium by Transvaginal ultrasonography and thyroid profile.

METHODS

It is a hospital based cross sectional study conducted in the department of pathology, Andhra medical college, Visakhapatnam, India from January 2012 to June 2013. A total of 270 patients in the age group of 18 to 45 years were included in this study. All these patients presented with menstrual irregularities like heavy menstrual bleeding, intermenstrual bleeding and breakthrough bleeding for a period of more than 3 months. Endometrial samples obtained by biopsy, dilatation & curettage, fractional curettage and from the endometrium of hysterectomy specimens received in the department of pathology, Andhra medical college, Visakhapatnam were utilized for this study. Histopathological examinations were conducted on 147 dilatation & curettage specimens and 123 hysterectomy specimens. All the clinical details and investigation reports were collected from the patients

Inclusion criteria

- Female patients aged between 18 to 45 yrs.
- Patients with complaints of abnormal uterine bleeding for more than 3 months
- Non-gravid women in the reproductive age group.

Exclusion criteria

- Abnormal uterine bleeding due to gestational causes like abortions, tubal pregnancies, molar pregnancies and rupture uterus.
- Acute abnormal uterine bleeding.

The material obtained was fixed in 10% formalin, followed by standard grossing techniques. The samples obtained by dilatation and curettage were all embedded and in hysterectomy specimens, the representative areas are taken and processed. Multiple bits were given wherever necessary.

RESULTS

The age group of patients in this study ranged from 18 to 45 years. Maximum numbers of cases (169) were in the age group of 36 to 45 years (62.6%). This was followed by 93 cases in the 26 to 35 years age group (34.4%), and 8 cases in the age group of 18 to 25 years (3 %) (Table 1). Most of the patients were multipara (90.37%), followed by primipara (7.04%), nullipara (1.48%) and grand multipara (1.11%).

Table 1: Age wise distribution of cases.

Age group (years)	Number	Percentage
18 - 25	8	3.0
26 - 35	93	34.4
36 - 45	169	62.6
Total	270	100

The most common presenting complaint observed was heavy menstrual bleeding (73.3%); this was followed by intermenstrual bleeding (11.5%), heavy menstrual bleeding with dysmenorrhoea (9.3%) and intermenstrual bleeding with dysmenorrhoea (5.9%).

Majority of the patients were in the euthyroid group (91.5%) and 23 patients were found to be suffering from hypothyroidism (8.5%). Hyperthyroidism was not observed (Table 2). The maximum numbers of patients with hypothyroidism were in the 36 to 45 years age group (69.6%). This was followed by patients in the age group of 26 to 35 years (30.4%). There were no cases in the age group of 18 to 25 years with hypothyroidism.

Table 2: Distribution of cases based on thyroid profile.

Thyroid profile	Number	Percentage
Euthyroid	247	91.5
Hypothyroid	23	8.5
Total	270	100

Normal cyclical endometrium was found to be the commonest pattern in the histopathological examination of the presenting cases with proliferative endometrium in 45.56% and secretory endometrium in 32.59%. This was followed in frequency by disordered proliferative endometrium (9.63%), simple hyperplasias (9.63%), atrophic endometrium (0.74%), endometrial adenocarcinomas (0.74%), simple endometrial hyperplasia with atypia (0.37%), complex endometrial hyperplasia (0.37%) and low grade endometrial stromal

sarcoma (0.37%). Histopathological examination was found to be very helpful in delineating the different types of the endometrial patterns (Table 3).

In this study leiomyomas were found to be the commonest cause of abnormal uterine bleeding (15.56%) (Figure 1 and 2). Simple hyperplasias without atypia were the next commonest type observed (9.62%) (Figure

4). This was followed by adenomyosis (8.89%) (Figure 3), polyps (6.66%), leiomyoma and adenomyosis combined (4.44%), polyps with adenomyosis (1.85%), polyps with leiomyomas (1.11%), endometritis(1.11%), hyperplasia with polyps (0.37%), simple hyperplasia with atypia (0.37%), complex hyperplasia with atypia (0.37%), adenocarcinoma (0.74%) (Figure 5 and 6) and stromal carcinoma (0.37%) (Figure 7 and 8) (Table 4).

Table 3: Distribution of patients based on the histopathological findings of the endometrium.

Endometrial pattern	Number of patients	Percentage
Proliferative endometrium	123	45.56
Secretory endometrium	88	32.59
Disordered proliferative endometrium	26	9.63
Simple endometrial hyperplasia without atypia	26	9.63
Simple endometrial hyperplasia with atypia	1	0.37
Complex endometrial hyperplasia with atypia	1	0.37
Atrophic endometrium	2	0.74
Endometrial adenocarcinoma	2	0.74
Low grade endometrial stromal sarcoma	1	0.37
Total	270	100

Table 4: Distribution of cases based on the organic causes of abnormal uterine bleeding.

Cause of AUB	Number of cases	Percentage
Benign endometrial polyps	18	6.66
Adenomyosis	24	8.89
Leiomyomas	42	15.56
Polyp+leiomyoma	3	1.11
Polyp+adenomyosis	5	1.85
Leiomyoma+adenomyosis	12	4.44
Endometritis	3	1.11
Simple hyperplasias without atypia	26	9.62
Simple hyperplasia with atypia	1	0.37
Complex hyperplasia with atypia	1	0.37
Hyperplasia+polyp	1	0.37
Adenocarcinoma	2	0.74
Low grade stromal sarcoma	1	0.37

From the present study it was found that cyclical endometrium, hyperplasias, disordered proliferative endometrium and benign endometrial polyps were most commonly seen in the age group of 36 to 45 years. Less common presentations were seen in the age group of 26 to 35 years and least common presentations in the age group of 18 to 25 years. It was observed that malignancies were the least common in all the age groups. Atrophic endometrium was seen only in 0.74% of cases in the 36 to 45 years age group.



Figure 1: Leiomyoma

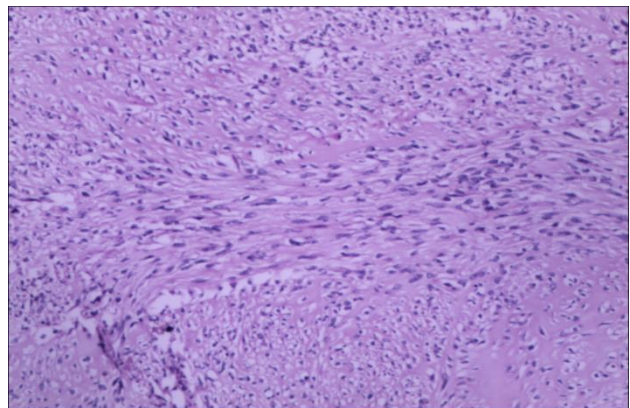


Figure 2: Micrphotograph of leiomyoma (100x).

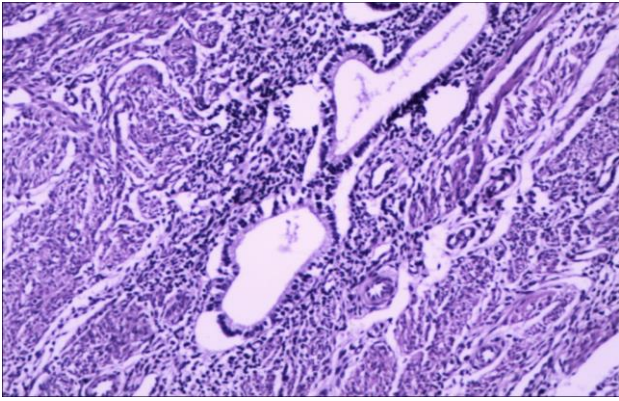


Figure 3: Adenomyosis showing glands and stroma in myometrium (400x).

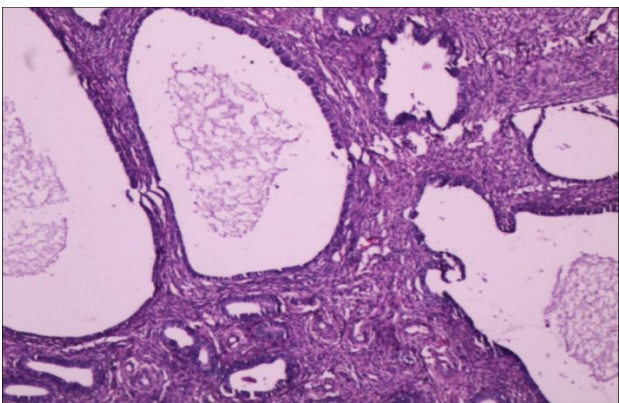


Figure 4: Simple hyperplasia with cystic dilatation of endometrial glands (100 x).

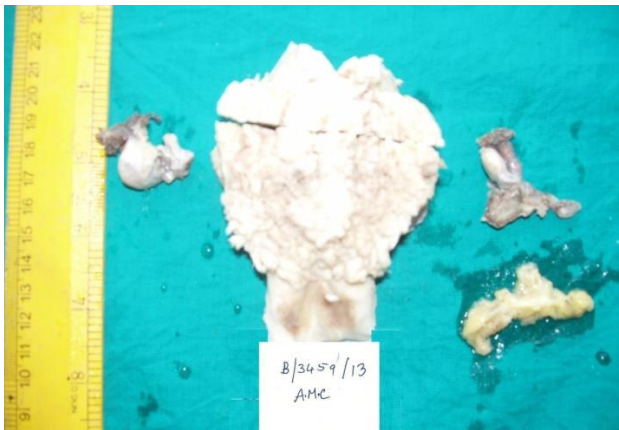


Figure 5: Well differentiated endometrial

Endometrial hyperplasias are most commonly seen in nulliparous women (25%) followed by multiparous women (11%).

Bulky / enlarged uterus was the most common finding (77%) on transvaginal sonography (TVS). Normal sized uterus was seen in only 23% cases. On TVS whole thickness of the endometrium was in the 4 to 10 mm range in 69.25% of cases. In 18.51% of cases it was in

the 10.1 to 12 mm range, followed by 11.48% of cases in the 12.1 to 24 mm thickness. Only 0.74% cases were found in the thickness range of <4 mm (Table 5). The most common was type-IV (hyperechoic) endometrium, depicting the secretory endometrial pattern (36.66%) (Figure 12). Type – II (three line) endometrial pattern depicting the proliferative endometrium was seen in 34.07% of cases (Figure 10). Type - III (atypical) endometrial pattern was seen in 15.55% of the cases (Figure 11) and type – V (hyperechoic & thickened) endometrial pattern was seen in 12.96% of the cases in the present study. Only 0.74% of the cases could be included in the type –I (single line/atrophic) group (Figure 9) (Table 6). Dilatation and curettage need not be considered when the transvaginal sonography findings are in favour of atrophic endometrium.

Table 5: Endometrial thickness on transvaginalsonography.

Whole thickness of endometrium (mm)	Number	Percentage
<4	2	0.74
4 – 10	187	69.25
10.1 – 12	50	18.51
12.1 – 24	31	11.48
Total	270	100

Table 6: Pattern of endometrium on transvaginalsonography.

Endometrial pattern	Number	Percentage
TYPE - I (single line)	2	0.74
TYPE - II (three line)	92	34.07
TYPE - III (atypical)	42	15.55
TYPE-IV (hyperechoic)	99	36.66
TYPE-V (hyperechoic & thickened)	35	12.96
Total	270	100

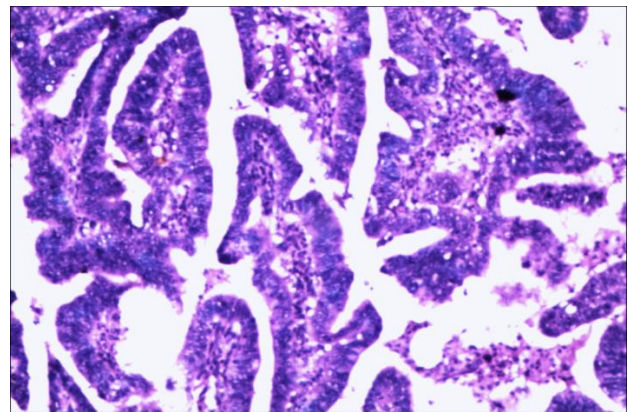


Figure 6: Well differrentiated adenocarcinoma with back to back arrngement of glands and enlarged hyperchromatic nuclei (100 x)



Figure 7: Endometrial stromal sarcoma.

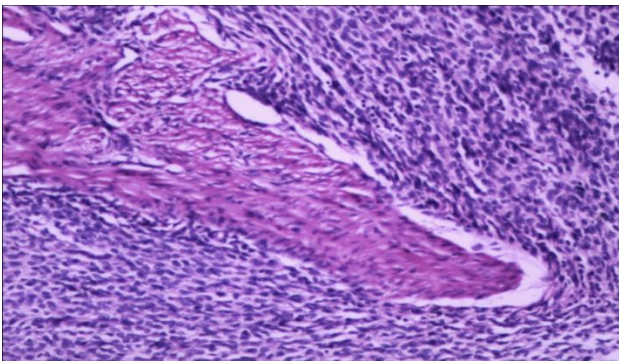


Figure 8: Endometrial stromal sarcoma invading the muscle showing spindle cells (400x).



Figure 9: Atrophic endometrium.



Figure 10: Proliferative endometrium.

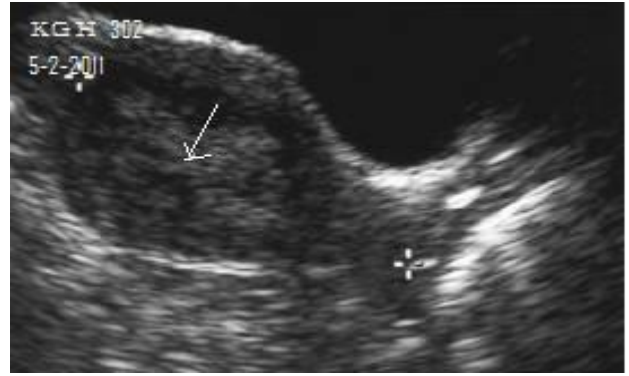


Figure 11: Atypical hyperplasia.

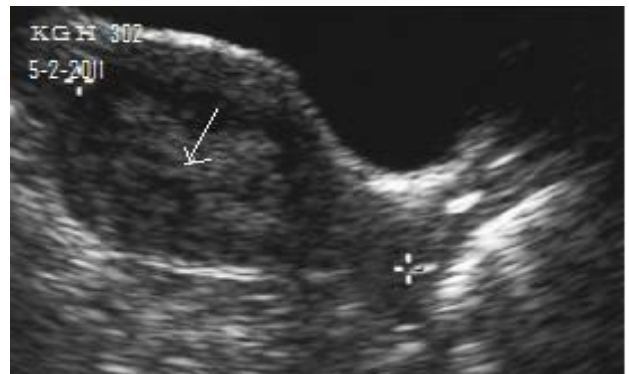


Figure 12: Secretory endometrium.

DISCUSSION

In this study maximum numbers of cases were in the perimenopausal age group. It was closely comparable to the previous studies Anjali Singh et al, Doraiswamy S et al and Dadhania B et al.⁵⁻⁷ The parity distribution of cases in our study is comparable to those observed by Acharyaveena et al, which was showing that abnormal uterine bleeding is more common in multiparae.⁸

The pattern of bleeding in women included in the present study is comparable to the findings observed by Acharyaveena et al in their study.⁸ Heavy menstrual bleeding corresponds to menorrhagia, polymenorrhagia and irregular / acyclical / continuous bleeding.

In the present study it was observed that the normal cyclical endometrium is the commonest type found in 78% of the patients. This observation was correlated to the association of the normal cyclical endometrium with adenomyosis, leiomyomas and benign endometrial polyps. Malignancies were found in 1.1% of the cases only as the patients in the age group of 18 to 45 years rarely present with malignancies. Most of the malignancies are usually seen in patients aged above 55 years. In this study benign endometrial polyps were seen in 9.3% of the cases which is well within the range of the normal presentation pattern of 2 to 23%. Leiomyomas were observed in 20% and adenomyosis in 15% of the cases in the present study. This observation is comparable

to the study conducted by Doraiswamy S et al (34%).⁶ Hyperplasias were observed in 9.6% cases in the present study, which is less when compared to the study conducted by Dadhania B et al (25%).⁷ Disordered proliferative endometrium was found in 9.6% of cases in the present study. In the observations of Jignashaparmar et al it was 33.3% and in the study of Doraiswamy S et al it was found in 20.5% cases.⁹ In the study of Dadhania B et al. 2.6% of cases were found to be having disordered proliferative endometrium.

Thyroid profile and abnormal uterine bleeding

In the present study on 270 patients, it was observed that 247 (91.5%) cases were in the euthyroid category and 23 cases (8.5%) were in the hypothyroid category. None of the studied cases were found to be suffering from hyperthyroidism. Among the 23 patients suffering from hypothyroidism, a total of 16 patients were in the age group of 36 to 45 years and 7 cases were in the 26 to 35 years age group. These patients were included in this study as they were all suffering from heavy menstrual bleeding and majority of them had normal cyclical endometrium.

In a study titled “thyroid dysfunction in dysfunctional uterine bleeding” on 100 cases by Tejenderkaur et al it was found that 85 cases were in euthyroid state and in the remaining cases, 14 cases were in hypothyroid state and one case was having hyperthyroidism.¹⁰ In another study titled “thyroid dysfunction in dysfunctional uterine bleeding” on 100 cases by Sangeethapahwa et al, it was observed that 22 cases were hypothyroid, 2 cases were hyperthyroid with the rest of 76 cases in the euthyroid category.¹¹ In a study titled “thyroid profile in menstrual disorders” on 50 patients in the reproductive age group by Sharma N et al 22% (11 cases) were found to be behaving hypothyroidism and 14% (7 cases) were in the hyperthyroidism category.¹²

Comparison of the histopathological findings with the thickness of the endometrium on transvaginal-sonography

In the present study 100% sensitivity was observed with Transvaginalsonography in the 4 to 10 mm thickness group (proliferative endometrium), >12mm thickness group (hyperplastic endometrium) and in the <4mm (atrophic endometrium) group. False positives were observed in 64 cases. A sensitivity of 56.8% was observed in 10.1 to 12 mm thickness group (secretory endometrium). False negatives were observed in 38 cases.

Comparison of the histopathology of the endometrium with the endometrial patterns on transvaginal-sonography

The sensitivity was found to be 100% in Type-I (single line pattern), Type-III (atypical endometrium), Type-IV

(hyperechoic endometrium) and Type-V (hyperechoic and thickened endometrium). In Type –II (three line pattern) a sensitivity of 74.7% was observed in the present study. False negative cases (31) were observed in Type-II pattern. Hysteroscopy and magnetic resonance imaging in combination with histopathological study will help in detecting the causes of abnormal uterine bleeding which can guide properly in the management of these cases.

Transvaginalsonography was not helpful in detecting most of the benign endometrial polyps and all the adenomyosis lesions. Transvaginalsonography was found to be a useful tool in detecting most of the cases of fibroid uterus. An endometrial thickness of <4 mm is diagnostic of atrophic endometrium. Endometrial curettage need not be considered in such cases.

Transvaginalsonography was found to be helpful in detecting the malignancies, hence will be of help for planning the further investigation and follow up. Endometrial thickness on Transvaginalsonography cannot be considered as the sole criterion for the diagnosis of proliferative and secretory endometrium. An atypical pattern of endometrium on Transvaginalsonography needs histopathological confirmation, as Transvaginalsonography cannot differentiate the various types of the endometrium. Hence it is concluded that histopathological examination is the gold standard for studying the pattern of endometrium in various causes of abnormal uterine bleeding.

CONCLUSION

Endometrial cause of abnormal uterine bleeding is age related pathology. Histopathological examination of endometrial biopsy is a major diagnostic tool in evaluation of abnormal uterine bleeding and a specific diagnosis could help the physician to plan therapy for successful management of abnormal uterine bleeding. Thyroid dysfunction is associated with menstrual disturbances which get relieved with normalization of thyroid status, so thyroid assessment should be performed in all patients with menstrual irregularities as this would avoid unnecessary hormonal treatment and surgery in dysfunctional uterine bleeding patients. Both transvaginal sonography and hysteroscopy can detect endometrial intracavitary abnormalities with varying accuracies that can supplement and enhance the accuracy of tissue diagnosis.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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