Original Article

HISTOPATHOLOGICAL SPECTRUM OF ENDOMETRIAL LESIONS IN PATIENTS WITH ABNORMAL UTERINE BLEEDING

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ABSTRACT

Objective: To determine pattern of different endometrial lesions in patients presenting with abnormal uterine bleeding.

Study design: Descriptive, cross sectional study.

Place & duration of study: Department of Pathology Combined Military Hospital, Multan, from 4th May 2016 to 4th November 2016.

Materials and Methods: A total of 150 cases of endometrial curettings and endometrial biopsies were included in the study. Sample size was calculated using WHO sample size calculator. The patients were selected by non-probability, consecutive sampling technique, who presented with abnormal uterine bleeding, for a duration of more than 3 months, between 30 to 60 years of age. Patients with pregnancy and pregnancy related conditions, history of chronic heart disease or any malignancy and bleeding disorders like coagulopathy or hemophilia were not included in the study. The specimens was fixed in 10 % buffered formalin, grossed and stained with Hematoxylin and Eosin to examine morphology. The morphology was reviewed by a histopathologist who has more than 5 years of experience after post-graduation to establish diagnosis.

Results: Our study included a total of 150 study cases having abnormal uterine bleeding meeting inclusion criteria of our study. Mean age of our study cases was 46.44 ± 6.49 years. Our study results have indicated that majority of our patients i.e. 102 (68%) were aged 46 – 60 years. Majority of our study cases i.e. 92 % were married and only 8 % patients were un – married. Mean disease duration was 4.33 ± 1.07 months and majority of our patients i.e. 108 (72%) presented with disease duration of 3 – 5 months. Proliferative phase endometrium was observed in 16.7%, secretory phase in 22 (14.7%), disordered proliferative endometrium in 16%, atrophic endometrium in 3.3%, chronic endometritis in 16 %, endometrial polyps in 8.7%, endometrial hyperplasia in 12%, endometrial carcinoma in 2%, hormone induced changes in 9.3% and squamous metaplasia in 1.3% of our study cases.

Conclusion: Proliferative endometrium was predominantly more common followed by chronic endometritis and secretory phase in our study. Disordered proliferative endometrium and endometrial polyp showed significant association with marital status. Prolonged disease duration was associated with disordered proliferative endometrium, endometrial polyps and endometrial hyperplasia. Atrophic endometrium was seen in reproductive age group. Finally, endometrial hyperplasia and endometrial carcinoma were significantly associated with increasing age.

Key words: Abnormal uterine bleeding, endometrium, histopathological pattern.

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INTRODUCTION

Endometrium is a dynamic tissue which undergoes cyclic changes including a proliferative phase, ovulation, secretory phase, predecidual changes, breakdown of stroma and ultimately casting off of superficial layer of endometrium during menstruation. Clinically, abnormal uterine bleeding may be defined as variations in frequency, amount and duration from normal pattern of menstrual cycles. It also includes postmenopausal bleeding [1,2].

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History, physical examination and laboratory investigations may not be sufficient to reach a definitive diagnosis of abnormal uterine bleeding and it is often necessary to sample endometrium for histopathological analysis. There are a variety of ways to sample endometrium, but endometrial curettage is the method of choice. Very few, if any lesions can escape detection by endometrial curettage. It has sensitivity greater than endometrial biopsy [3].

There is a long list of causes of abnormal uterine bleeding which can be broadly categorized into organic causes and dysfunctional uterine

bleeding. The organic causes include endometrial polyps, chronic endometritis, endometrial hyperplasias and endometrial carcinomas. If no organic cause is found, abnormal uterine bleeding is labeled as dysfunctional uterine bleeding. Anovulation is the most common cause of dysfunctional uterine bleeding which results from hormonal imbalances [4,5].

Histological spectrum of endometrial lesions is greatly influenced by the age of the patient. In older age group, particularly after menopause, endometrial hyperplasias and endometrial carcinomas are more prevalent, whereas dysfunctional uterine bleeding is more common in younger age group [6].

A study carried out in Pakistan in 2011 for evaluating the spectrum of endometrial lesions in abnormal uterine bleeding found endometrial lesions in order of following frequencies: hormonal imbalances (41%), endometrial polyp (21%), and chronic endometritis (18%) [7]. Another study in Nepal reported secretory phase to be 22.58% and disordered proliferative to be 13.40% [2]. A similar study in India which included 119 patients found that proliferative endometrium accounted for 35.22% and endometrial hyperplasia for 23.86% in perimenopausal age group whereas atrophic endometrium accounted for 25.80% and endometrial hyperplasia for 19.35% in postmenopausal age group [8].

The rationale of this study is to evaluate the histological patterns of endometrium in patients with abnormal uterine bleeding in Southern Punjab. This data will enable us to know health literacy and design various screening programmes. In addition, this data will guide gynaecologist to modify their treatment strategies.

MATERIALS AND METHODS

This descriptive cross-sectional study was carried out at Department of Pathology, Combined Military Hospital, Multan from 4th May 2016 to 4th November 2016, after the approval of ethical committee. A total of 150 cases of endometrial curettings and endometrial biopsies were included in the study. Sample size was calculated using WHO sample size calculator. The patients were selected by non-probability, consecutive sampling technique, who presented with abnormal uterine bleeding, for a duration of more than 3 months, between 30 to 60 years of age. Patients with pregnancy and pregnancy related conditions, history of chronic heart disease or any malignancy and bleeding disorders like coagulopathy or hemophilia were not included in the study. The cases were selected from CMH laboratory after taking informed consent from patients. The specimens was fixed in 10 % buffered formalin, grossed and stained with Hematoxylin and Eosin to examine morphology. The morphology was reviewed by a histopathologist who has more than 5 years of experience after postgraduation to establish diagnosis.

The collected information was analyzed by using SPSS version 18. The quantitative variables e.g. age and duration of disease was presented as mean ± standard deviation. The qualitative variables e.g. endometrial pathologies, marital status, age groups and disease duration were presented as frequencies and percentages. Effect modifiers like age, duration of disease and marital status were controlled through stratification. Post stratification, Chi square test was applied. *P* value less than or equal to 0.05 was taken as significance.

RESULTS

Our study included a total of 150 study cases having abnormal uterine bleeding meeting inclusion criteria of our study. Mean age of our study cases was 46.44 ± 6.49 years (with minimum age of the patients was 30 years while maximum age was 58 years). Our study results have indicated that majority

of our patients i.e. 102 (68%) were aged 46 – 60 years. (Table-1)

Majority of our study cases i.e. 92 % were married and only 8 % patients were un – married. Mean disease duration was 4.33 ± 1.07 months and majority of our patients i.e. 108 (72%) presented with disease duration of 3 – 5 months (Table-1).

Proliferative phase endometrium was observed in 16.7% secretory phase in 22 (14.7%), disordered proliferative endometrium in 16%, atrophic endometrium in 3.3%, chronic endometritis in 16 %, endometrial polyps in 8.7%, endometrial hyperplasia in 12% (Table-2) and miscellaneous histopathological diagnosis (including endometrial carcinoma) was made in 12.7% of our study cases (Table-3). Histopathological diagnosis have been stratified with regards to age, disease duration and marital status. Photomicrographs of some of endometrial lesions from our study were taken (Figure-1a,b,c,d,e,f). A significant statistical association was not seen among age, marital status, disease duration and histopathological diagnosis with *p*- value > 0.05

Table-1: Distribution of Cases according to effect modifiers (Mean Age 46.44 ± 6.49 years, n=150)

Effect modifiers		No. of patients (n=150)	Percentage
Age groups	30-45 years	48	32
	45-60 years	102	68
Marital Status	Married	138	92
	Unmarried	12	8
Disease duration	3-5 months	108	72
	>5 months	42	28

Table-2: Distribution of endometrial lesions among study cases (excluding miscellaneous endometrial pathologies).

Endometrial lesions	No. of patients	Percentage
Proliferative phase	25	16.7
Secretory phase	22	14.7
Disordered proliferative	24	16
Chronic endometritis	24	16
Atrophic endometrium	5	3.3
Endometrial polyp	13	8.7
Endometrial hyperplasia	18	12

Table-3: Distribution of miscellaneous endometrial pathologies among study cases

Miscellaneous Pathologies	No. of patients	Percentage
Endometrial Carcinoma	03	2.0
Squamous Metaplasia	02	1.3
Hormone induced changes	14	9.3

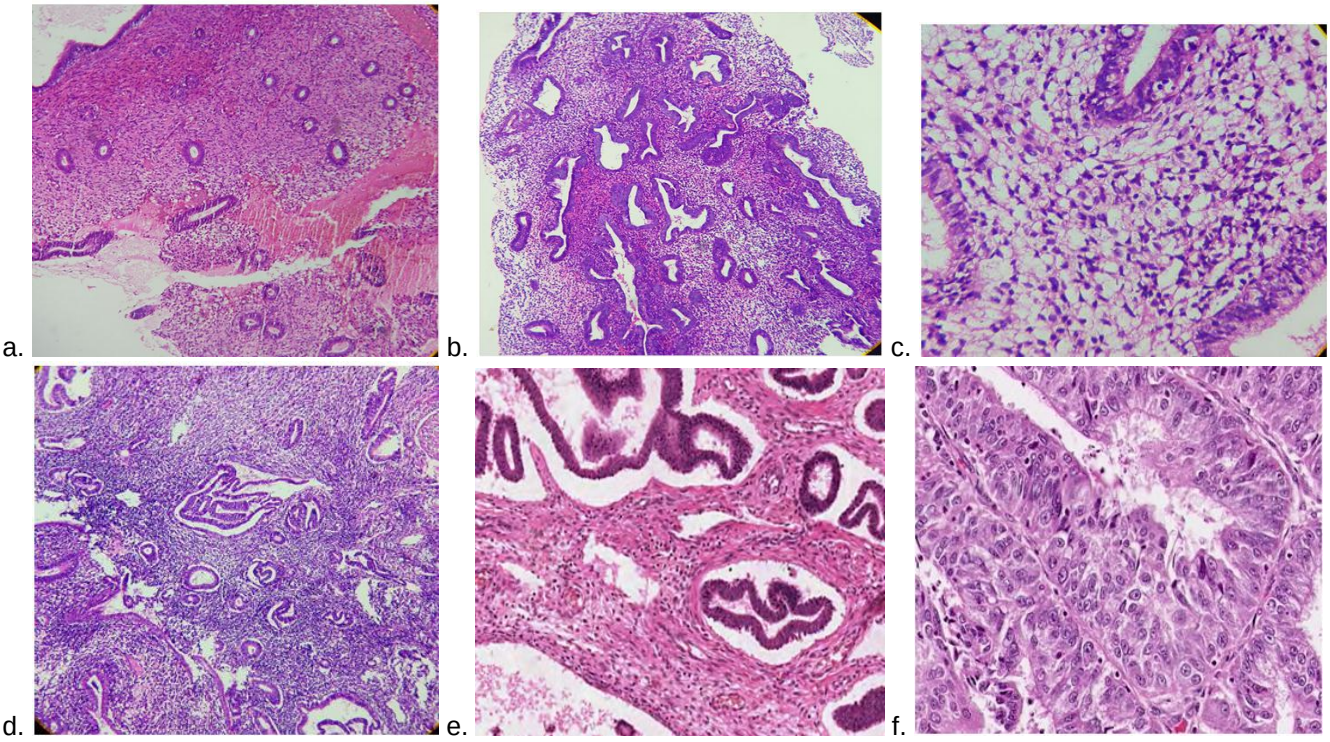

Figure-1: Photomicrographs of endometrial pathologies
a. Proliferative phase endometrium, b. Disordered proliferative endometrium, c. Chronic endometritis,
d. Endometrial hyperplasia, e. Endometrial polyp, f. Endometrial carcinoma

DISCUSSION

Menstrual problems account for much of the morbidity, affecting one in every five women during their life span. Specifically, abnormal uterine bleeding (AUB) is one of the most common debilitating menstrual problems. A study based on epidemiology of menstrual disorders in developing countries revealed that the prevalence of AUB in developing countries including Pakistan was about 5-15%9. Within the study period there were 400 AUB cases out of 1600 gynaecological cases which gave an AUB prevalence of 25% per 100 gynaecological cases. Out of 400 AUB cases, 241 (60%) participants were recruited into the study. Risk factors of AUB include female genital tract pathologies, pregnancy related disorders, and systemic illnesses [10].

Spectrum of common pathologies that can be detected histologically in AUB include hormonal imbalance pattern (disorderly proliferative endometrium, non-secretory endometrium with stromal and glandular breakdown, luteal phase defect and pill effect), atrophic endometrium, endometritis, endometrial polyp, endometrial hyperplasia and endometrial carcinoma. However endometrial pathologies were noted in only about half of the cases of AUB and hormonal imbalance pattern dominated the clinical picture. AUB has remained one of the most frequent indications for hysterectomy in developing countries but 40% of cases were not associated with any definitive organic pathology. Hysterectomy is often correlated with complications such as bleeding, bladder or bowel damage, infection, thrombosis, ovary failure and early onset of menopause [11].

Prevalence of abnormal uterine bleeding in developing countries including Pakistan is about 5-15%. One half of women by age 45.5 years, three quarter by age 47.8 years & 95% by age 50.8 years experience menstrual disturbance. It has been estimated that around 6% of women aged 25 - 44

years consult their general physician about excessive menstrual loss every year, around 35% of these referred to hospital and 60% of them underwent hysterectomy in the next 5 years. Over 75000 hysterectomies are now carried out every year & 25-30% of them are for menstrual disturbance [7].

Our study included a total of 150 study cases having abnormal uterine bleeding meeting inclusion criteria of our study. Mean age of our study cases was 46.44 ± 6.49 years (with minimum age of the patients was 30 years while maximum age was 58 years). Our study results have indicated that majority of our patients i.e. 102 (68%) were aged 46 – 60 years. A study conducted by Abid et al7 in Karachi reported 40.3 ± 11.06 years mean age of the patients with abnormal uterine bleeding which is close to our study results. Sajitha et al [12] from India also reported majority of patients abnormal uterine bleeding were from age group of 46 – 60 years. Vaidya et al [2] from Nepal also reported that majority of patients with abnormal uterine bleeding were from reproductive and perimenopausal age groups which is in compliance with our study results. Salvi et al [13] from India reported 45.8 ± 1.53 years mean age of the patients with abnormal uterine bleeding which is similar to our study results. Ghani et al [14] from Iraq and Bolde et al [15] and Singh et al [16] from India have reported similar results.

Majority of our study cases i.e. 92% were married and only 8% patients were un – married. Abid et al [7] reported 73% ladies with abnormal uterine bleeding were married which is quite lower than being reported in our study. The reason for this difference is due to our inclusion criteria as we only included patients with ages more than 30 years while Abid et al [7] included patients with their ages starting from 18 years which are more young and more likely to be unmarried.

Mean disease duration was 4.33 ± 1.07 months and majority of our patients i.e. 108 (72%) presented with disease duration of 3 – 5 months.

Proliferative phase endometrium was observed in 16.7%, secretory phase in 22 (14.7%), disordered proliferative endometrium in 16%, atrophic endometrium in 3.3%, chronic endometritis in 16%, endometrial polyps in 8.7%, endometrial hyperplasia in 12% and miscellaneous histopathological diagnosis was made in 12.7% of our study cases (including 2% endometrial carcinoma). Abid et al [7] reported endometrial polyps in 14%, chronic endometritis in 12%, atrophic endometrium 6%, endometrial hyperplasia in 5% and endometrial carcinoma was 2%. These findings of Abid et al [7] are similar to that of our study results. Another study in Nepal reported secretory phase to be 22.58%, disordered proliferative to be 13.40% and endometrial carcinoma to be 2.48% which is nearly the same as in our study and also attesting to the fact that endometrial carcinoma is rarest endometrial pathology seen in endometrial curettings [2]. Also both Abid et al and study from Nepal showed endometrial carcinomas to be significantly associated with increasing age which is again the same thing which we see in our study [2,7]. A similar study in India which included 119 patients found that proliferative endometrium accounted for 35.22% and endometrial hyperplasia for 23.86% in perimenopausal age group whereas atrophic endometrium accounted for 25.80% and endometrial hyperplasia for 19.35% in postmenopausal age group [8]. These results are in compliance with that of our study results. Salvi et al [13] also reported from India proliferative endometrium being predominant histopathological diagnosis in these patients which is same as that of our study findings. Ghani et al [14] from Iraq and Bolde et al [15] and Singh et al [16] from India have also reported proliferative endometrium being more common histopathtological

finding which is in compliance with that of our study results.

CONCLUSION

Proliferative endometrium was predominantly more common followed by chronic endometritis and secretory phase in our study. Disordered proliferative endometrium and endometrial polyp showed significant association with marital status. Prolonged disease duration was associated with disordered proliferative endometrium, endometrial polyps and endometrial hyperplasia. Atrophic endometrium was seen in reproductive age group. Finally, endometrial hyperplasia and endometrial carcinoma were significantly associated with increasing age.

AUTHORS CONTRIBUTION

Saad Masood: Entire research work, sample collection, analysis, write-up.

Muhammad Tahir Khadim: Concept and overall supervision.

Syed Salman Ali: Literature review, help in sample collection.

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