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Patterns of Endometrial Histopathology in Patients of Dysfunctional Uterine Bleeding (DUB)

Dr. Manisha Kakkar[1], Dr. Anu Gupta[2], Dr. K. K. Koul[3]

[1]MBBS, MD Pathology, Medical Officer, Postgraduate Department of Pathology, Government Medical College, Jammu

[2]MBBS, MD Pathology, Demonstrator, Postgraduate Department of Pathology, Government Medical College, Jammu

[3]MBBS, MD Pathology, Professor and Head, Postgraduate Department of Pathology, Government Medical College, Jammu

Abstract: ***Dysfunctional uterine bleeding is defined as pathological bleeding from uterus unexplained on basis of inflammation, neoplasia or pregnancy within the uterus. The present study was undertaken with the aim of studying the different histological patterns of endometrium in patients of DUB. This study includes 84 patients with clinically diagnosed DUB who had undergone either hysterectomy or D&C. Study was conducted in Govt. Medical College, Jammu between October 2016 and April 2017. When histological patterns were analyzed, it was found that proliferative endometrium (50%) was most common pattern followed in frequency by secretory endometrium (27.4%), atrophic endometrium (4.7%), irregular shedding (3.6%). Hyperplasia was present in 9.6% of current study subjects. DUB was more common in the perimenopausal age group and multiparity. The occurrence of abnormal findings increases with age.***

Keywords: endometrium, DUB, secretory, atrophic, irregular shedding, hyperplasia, multiparity, perimenopausal

1. Introduction

The normal menstrual cycle is defined as having a mean interval of 28 +/- 7 days with a mean interval of 4 +/-3 days[1]. Any deviation from this normal pattern is considered abnormal. Dysfunctional uterine bleeding (DUB) is abnormal uterine bleeding in a premenopausal woman resulting from alterations in the normal cyclical changes of the endometrium and without an underlying specific pathological cause such as endometritis, polyps, exogenous hormones, hyperplasia, or carcinoma[2]. Excessive menstrual bleeding has several adverse effects, including Iron deficiency anemia, reduced quality of life and increased healthcare expenditure[3]. Tissue diagnosis is a must in the diagnosis of DUB especially in perimenopausal and postmenopausal female[4]. DUB can occur in both ovulatory and anovulatory cycles, from menarche to menopause. The incidence of dysfunctional uterine bleeding is 10% of women in their reproductive years[5]. In various studies, histopathological examination of DUB has shown a spectrum of findings ranging from an apparently normal endometrium like proliferative and secretory to abnormal findings like disordered proliferative, hyperplasia, irregular ripening, irregular shedding, atrophy[6-8]. The purpose of this study was to find out various histological patterns of endometrium in patients of dysfunctional uterine bleeding.

2. Material and Methods

Study design: This was a single centre, hospital based, prospective study on histopathology of endometrium in Dysfunctional Uterine Bleeding, undertaken in the Post Graduate Department of Pathology in GMC, Jammu carried out between October 2016 and April 2017.

Inclusion criteria: Endometrial tissue from patients of all age groups clinically diagnosed as DUB (in whom there was no organic pathology).

Exclusion criteria: If there was any organic pathology found such as fibroid, adenomyosis, leiomyomas, genital tract infections; systemic causes; and DUB due to pregnancy related complications, they were excluded. Material for the study consisted of endometrial tissue obtained by Dilatation and Curettage and Hysterectomy of patients presenting clinically with Dysfunctional Uterine Bleeding, who were either attending OPD or admitted in Obstetrics and gynecology department of our Hospital, sent for histopathological study to the Postgraduate Department of Pathology.

Tissue processing: The gross morphology of the study specimen was recorded and the total tissue submitted was processed. Paraffin block were prepared and tissue section (4-6μ) were cut. The sections were stained with hematoxylin and eosin stain (H&E) and microscopic examination was done. The age and parity of patients were also recorded and then the statistical analysis was done with data obtained.

3. Definitions

Proliferative Phase: Early Proliferative phase of endometrium showed round and short narrow glands, lined by cuboidal to columnar epithelium in a compact stroma. Mid Proliferative phase showed longer curved glands. Stromal edema of variable amount was noted. Stromal cells had mitotic activity. Late Proliferative phase was characterized by tortuous glands with pseudo stratification with dense stroma showing numerous mitotic figures.

Secretory Phase: Early secretory phase showed sub nuclear vacuolation of glandular epithelium. Moderate oedema of the stroma. Mid secretory glands showed distended lumen filled with secretions. Tall columnar cells with an oval basal nucleus lined the glands with the stroma showing marked oedema. Late secretory glands were closely packed, with no

stromal oedema. Pre-decidual stromal cells and spiral arteries were also seen.

Disordered proliferative endometrium: It denotes an endometrial appearance that is hyperplastic but without an increase in endometrial volume. Disordered proliferative endometrium resembles simple hyperplasia but the process is focal rather than diffuse.

Atrophic endometrium: Characterized microscopy by sparse small glands which were lined by cuboidal epithelium. Small spindle cells were present in stroma.

Irregular shedding: Irregular shedding is due to a lag in the shedding of the secretory endometrium. Both proliferative and secretory glands were seen. Necrotic fragments were seen.

Endometrial hyperplasia: It is defined as a proliferation of glands of irregular size and shape with an increase in the glands/stroma ratio. In general, there are 4 types of hyperplasia: simple, complex, simple with atypia, and complex with atypia. Classification of endometrial hyperplasia:

Type	*Description*
Simple	Dilated glands that may contain some outpouching and abundant endometrial stroma
Complex	Glands are crowded with very little endometrial stroma, and a very complex gland pattern and outpouching formations
Simple with atypia	Is the same as above, but also contains cytologic atypia. This refers to hyperchromatic, enlarged epithelial cells with an increased nuclear to cytoplasmic ratio.
Complex with atypia	

4. Results

Total 84 patients with clinically diagnosed DUB who had undergone either hysterectomy or D & C were included in the study. Of theses 62 had undergone hysterectomy and 22 had undergone D & C.

Age: In the current study, mean age of the study subjects was 45.38 ± 6.68 years with minimum and maximum age of 28 and 70 years respectively. As shown in figure 1, the maximum patient burden (n=40) (47.6%) was present in the age group of 41-45 years showing that DUB was most common in the perimenopausal age group.

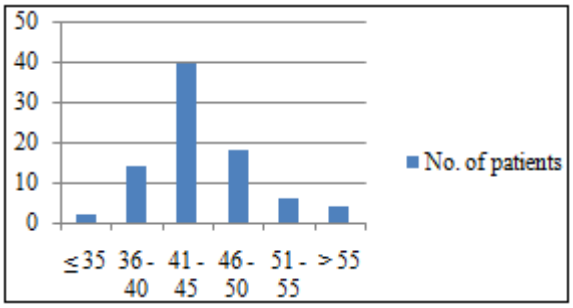

Figure 1: Distribution of patients according to different age groups

Parity: In the current study, the prevalence of DUB increases with increasing parity. Maximum number of patients were of para 3 (n=40) (47.6%) as shown in figure 2.

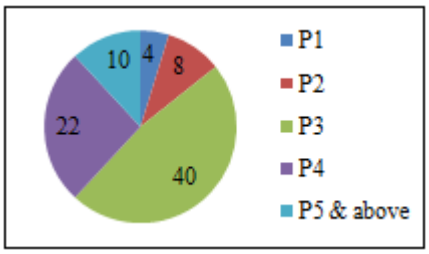

Figure 2: Distribution of patients according to parity.

Table 1: Types of histological patterns

Histopathological pattern	*Number of patients (n)*	*Percentage (%)*
Proliferative	42	50
Secretory	23	27.4
Irregular shedding	3	3.6
Disordered proliferative pattern	4	4.7
Atrophic	4	4.7
Hyperplasia	8	9.6

Table 2: Types of Hyperplasia

Type of Hyperplasia	Number of patients (n)
Simple without atypia	4
Simple with atypia	2
Complex with atypia	2

Histological findings

In the patients enrolled in the current study, majority of the patients had normal histological pattern. When histological patterns were analyzed it was found that 50% patients (n=42) had proliferative endometrium, 27.4% patients (n=23) had secretory endometrium, 3.6% patients (n=3) had irregular shedding; and 4.7% (n=4) had atrophic endometrium. Hyperplasia was present in 9.6% (n=8) and disordered proliferative pattern in 4.7% (n=4) of the study specimen. Among the patients with histopathological findings of hyperplasia, 4 patients had simple hyperplasia without atypia, 2 patients had simple hyperplasia with atypia and 2 patients had complex hyperplasia with atypia. While assessing the distribution of histological findings of endometrium in the different age groups of patients it was found that the normal histological findings were more common in younger age group and hyperplasias more come in elderly. All patients diagnosed with hyperplasia had parity 3 or above.

5. Discussion

DUB is one of the most common cause in patients undergoing hysterectomy[9]. Dysfunctional uterine bleeding may occur in a state of low estrogen, high estrogen or abnormalities in the relative proportions of estrogen and progesterone[10].DUB is a common cause for the patient seeking medical advice and require repeated hospitalizations, if left untreated. The prevalence increases with the increasing age peaking prior to menopause. The perimenopausal women have anovulatory cycle leading to DUB.

In the current study, mean age of the study subjects was 45.38 ± 6.68 years with minimum and maximum age of 28 and 70 years respectively. The maximum patient burden (n=40) (47.6%) was present in the age group of 41-45 years showing that DUB was most common in the perimenopausal age group. This finding was concordant to study by Muzaffar M[11] et al wherein menstrual disorders were most common in 41-50 years age group accounting for 48% cases. Nepal N[12] et al showed DUB in 40.6% of study subjects in 41-50 years age group. In the current study, the prevalence of DUB increases with increasing parity. Maximum number of patients were of para 3 (n=40) (47.6%). This finding was consistent with the finding seen in Divya KN[13] et al wherein maximum patients were para 3. Also, in a study by Khan R[14] et al showed 38.3% patients having para 3 & 4.

In the patients enrolled in the current study, majority of the patients had normal histological pattern. When histological patterns were analyzed it was found that 50% patients (n=42) had proliferative endometrium, 27.4% patients (n=23) had secretory endometrium, 3.6% patients (n=3) had irregular shedding; and 4.7% (n=4) had atrophic endometrium. This finding was concordant with findings seen in study by Divya KN[13] et al wherein among the cases of DUB, proliferative phase accounted for 66.3% and secretory phase accounted for 21.3%, 9 cases (8.6%) of atrophic endometrium, two cases (1.9%) of irregular shedding.

In the current study, proliferative pattern was found most commonly in 50% of specimen. Nayak AK[15] et al reported proliferative pattern in 41.88% of the study subjects. Gazozai S[16] et al in 31% and Somboonporn W[17] et al in 75% reported proliferative pattern. The next common pattern of DUB in the present study was secretory phase constituting 27.4% of the specimen. This finding was consistent with the finding seen in study by Katuwal N[18] et al (38.3%).

Irregular shedding was seen in 3.6% of the current study subjects. Nayak AK[15] et al reported 3.13% cases of irregular shedding. In the current study, atrophic endometrium constituted 4.7% of the study specimen. Nayak AK[l5] and Katuwal N[18] reported atrophic endometrium in 4.1% and 2.5% of samples respectively.

Hyperplasia was present in 9.6% (n=8) and disordered proliferative pattern in 4.7% (n=4) of the current study specimen. Baral R[19] reported hyperplasia in 18.3% cases. Khan R[14] et al reported hyperplais in 20.5% of study subjects in their study. Though Purandare and Jhallam reported low incidence of 7% of hyperplastic endometrium[20].

Histopathological evaluation of endometrium helps to exclude the local causes of bleeding and establishes the diagnosis of DUB, identifies its types, delineate its clinical correlation and finally helps to determine the mode of management.

6. Conclusion

DUB is more common in the perimenopausal age group and multiparity. The most common histopathological finding is proliferative endometrium followed by secretory endometrium. The occurrence of abnormal findings increases with age. It is very important to evaluate every case of DUB histologically to rule out hyperplasias and malignancy.

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