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Morphological Spectrum of Endometrium in Dysfunctional Uterine Bleeding

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Abstract

Introduction: Dysfunctional uterine bleeding (DUB) is defined as increased abnormal endometrial bleeding unrelated to any anatomic lesions/ organic pathology of the genital tract [1]. It is a common problem in woman of reproductive age and about 20% of women affected will seek consultation [2]. *Objectives:* 1.To study morphological features of endometrium in DUB. 2.To correlate with age, parity and bleeding pattern in women clinically diagnosed as DUB. *Methodology:* Study was conducted for a period of two years (January 2014 to December 2015) in department of Pathology, Shri Nijalingappa Medical College, Bagalkot. Endometrial samples were obtained from endometrial biopsy or from dilatation and curettage (D & C) and studied with routine haematoxylin & eosin slides. *Results:* A total of 284 samples were received. Maximum incidence of DUB was found in age group 41-50 years (37.32%), followed by 31-40 years (35.56%) in multiparous (71.83%) women presenting with menorrhagia (71.83%). Endometrial hyperplasia was the predominant lesion seen in 46.47%, of which simple hyperplasia without atypia were 32.74%, complex hyperplasia without atypia in 7.40%, simple hyperplasia with atypia in 2.11% and complex hyperplasia with atypia in 4.22%. Proliferative endometrium was seen in 19.71%, secretory endometrium in 10.21%, disordered proliferative phase in 4.93%, irregular ripening in 8.80%, irregular shedding in 1.75%, atrophic endometrium in 2.46%, while 5.62% samples were considered inadequate. *Conclusion:* No age was exempted from DUB and highest incidence was noted in 3rd and 4th decades with menorrhagia as the commonest bleeding pattern occurring in multiparous women and microscopically endometrial hyperplasia was most commonly found.

Keywords: Dysfunctional Uterine Bleeding; Menorrhagia; Endometrial Hyperplasia.

Introduction

DUB is one of the commonest problem in females occurring at any time during reproductive life and 20% of affected patients seek consultation[2] because it causes significant morbidity and interferes with daily life activities [3]. More than 80 ml of blood loss during a single menstrual period is considered excessive and it is one of the commonest gynaecological complaint [4]. Bleeding that is excessive in duration, amount and frequency is considered abnormal [5]. The magnitude of menstrual disorders has increased, likely because of shortened breast-feeding intervals, fewer pregnancies per woman, higher frequency of permanent sterilization and later age of conception. Abnormal uterine development, endometrial hyperplasia, endometriosis , uterine neoplasms like polyps, leiomyoma, malignant tumours, psychological upset, endocrine disorders, bleeding disorders, early pregnancy states etc are some of the causes of abnormal uterine bleeding [6].

DUB is defined as increased abnormal endometrial bleeding unrelated to any anatomic lesions/ organic pathology of the genital tract, systemic diseases or due to any complications of pregnancy [1]. It is essential to perform thorough clinical examination of abdomen and pelvis, hysteroscopy if required to rule out any organic diseases of uterus [7]. Dilatation & curettage / endometrial biopsy is performed when systemic or

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local pelvic causes are ruled out since it is a simple, safe and reliable investigation and it gives a direct access to the target organ [8].

Histopathological examination of endometrium in patients with DUB shows a wide spectrum of changes ranging from normal endometrium to hyperplasia with atypia which is a premalignant condition. Its management entirely depends upon the type of endometrium found histopathologically. Thus morphological study of endometrium is essential for adequate treatment. Hence this study was conducted.

Materials and Methods

Prospective study of two years.

Inclusion Criteria

Endometrial samples(biopsy or dilatation & curettage) obtained from patients clinically diagnosed as DUB.

Exclusion Criteria

Patients presenting with DUB due to pregnancy related complications, organic lesions involving the genital tract infections, systemic causes, endometrial polyps, iatrogenic causes like intrauterine contraceptive device, exogenous hormones like oral contraceptive pills, progesterone pills etc and other lesions. Also hysterectomy specimens were excluded from this study.

The endometrial samples were fixed in 10% formalin for 12-24 hours and the entire tissue was taken for routine processing. 5µ thickness sections taken from paraffin blocks were stained with Haematoxylin and Eosin (H&E) and studied under light microscopy.

Results

The total number of endometrial samples received were 284. Minimum age at presentation of DUB was 20 years and maximum was 65 years. Most common age group affected was between 4th and 5th decade (Table 1) in multiparous women (71.83%) followed by grand multipara (15.50%) and least commonly seen in nullipara (3.87%).

Table 2 shows that menorrhagia was the commonest bleeding pattern seen in 204 patients (71.83%) followed by metrorrhagia seen in 27 patients (9.50%). Polymenorrhagia was the least common bleeding pattern seen in 3 patients (1.05%) only.

Histopathological examination of endometrium revealed wide morphological spectrum in DUB as shown in Table 3.

Table 1: Distribution according to various age groups and parity.

Age group (years)	Number of patients (%)	Nullipara	Primipara	Multipara	Grand multipara
<20	1 (0.35%)	O	1	0	0
21-30	45 (15.84%)	5	13	26	1
31-40	101 (35.56%)	4	7	79	11
41-50	106 (37.32%)	1	2	79	24
≥51	31 (10.91%)	1	2	20	8
Total	284 (100%)	11 (3.87%)	25 (8.80%)	204 (71.83%)	44 (15.50%)

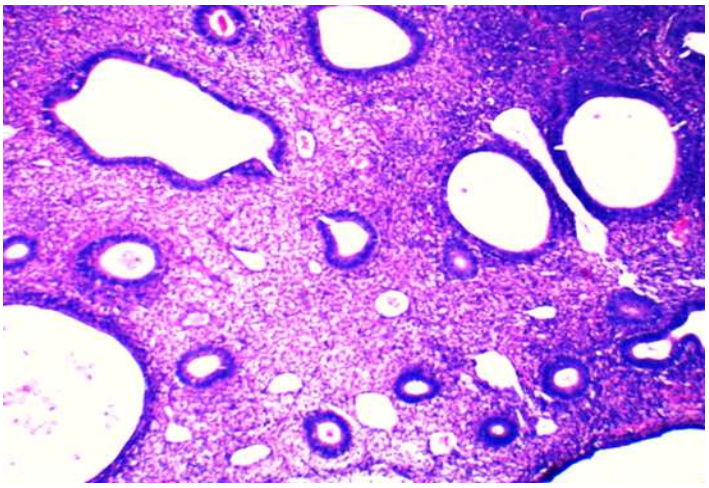

Fig. 1: Microphotograph showing simple hyperplasia without atypia(variable sized glands: few small circular to large cystically dilated lined by stratified columnar epithelium with frequent mitotic activity, surrounded by compact cellular stroma) (H&E, X100)

Table 2: Relationship of DUB with bleeding pattern

Bleeding pattern	No. of patients (%)
Menorrhagia	204 (71.83%)
Metrorrhagia	27 (9.50%)
Menometrorrhagia	15 (5.28%)
Polymenorrhagia	3 (1.05%)
Polymenorrhoea	5 (1.76%)
Intermenstrual bleeding	14 (4.93%)
Post menopausal bleeding	16 (5.63%)
Total	284 (100%)

Table 3: Endometrial patterns in DUB

Endometrial pattern	Number of patients (%)
Proliferative endometrium	56(19.71%)
Secretory endometrium	29(10.21%)
Disordered Proliferative endometrium	14(4.93%)
Irregular Ripening	25(8.80%)
Irregular Shedding	5(1.75%)
Atrophic endometrium	7(2.46%)
Simple Hyperplasia without Atypia	93(32.74%)
Simple Hyperplasia with Atypia	6(2.11%)
Complex Hyperplasia without Atypia	21(7.40%)
Complex Hyperplasia with Atypia	12(4.22%)
Inadequate	16(5.62%)
Total	**284(100%)**

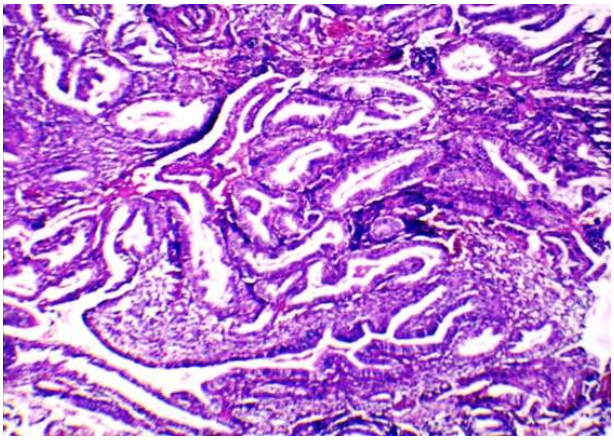

Fig. 2: Microphotograph showing complex hyperplasia without atypia (Increased gland to stroma ratio, complex branching and back to back arrangement of endometrial glands. (H&E, X100)

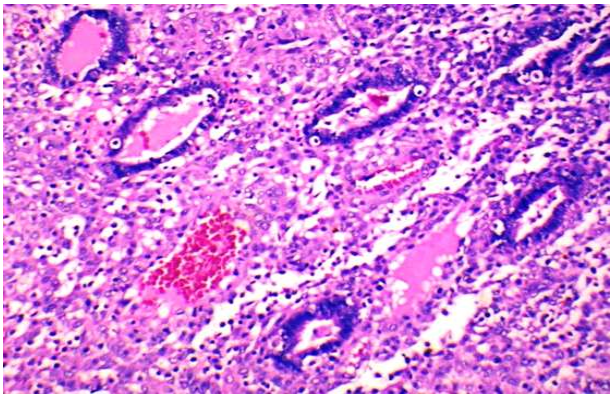

Fig. 3: Microphotograph showing irregular ripening of endometrium with glands in proliferative phase and decidualisedstroma (glandular and stromal discordance-incomplete secretory changes) (H&E, X100)

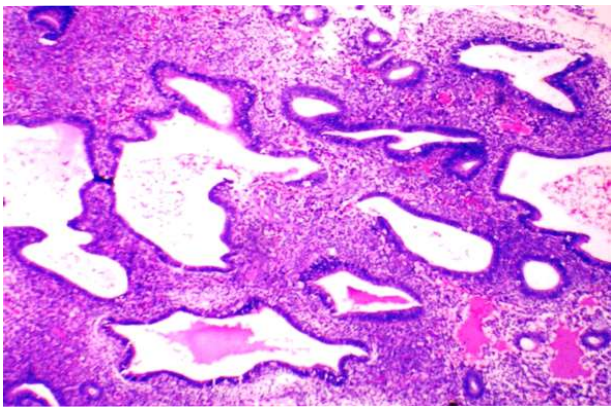

Fig. 4: Microphotograph showing Disordered proliferative phase (Disorganised proliferative glands with focal branching and glandular dilatation) (H&E, X40)

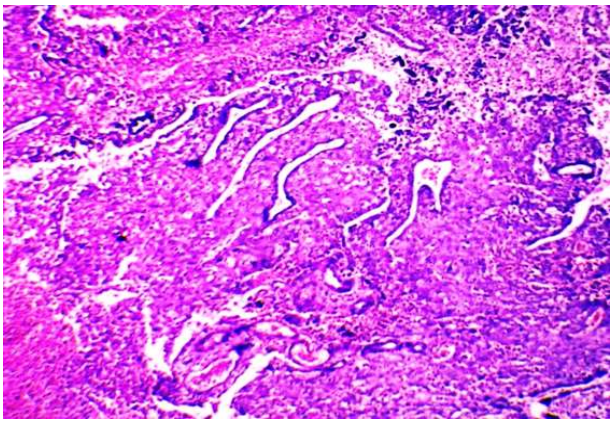

Fig. 5: Microphotograph showing irregular shedding of endometrium-persistence of secretory changes: decidualisedstroma with proliferative glands on 5^{th} /6^{th} day of menstrual cycle. (H&E, X40)

Endometrial hyperplasia was the commonest pattern seen in 132 (46.47%) patients. Among endometrial hyperplasia, simple hyperplasia without atypia (Figure 1) was the commonest type seen in 93 (32.74%) patients, followed by complex hyperplasia without atypia(Figure 2) seen in 21 (7.40%) patients. Proliferative endometrium was the next commonest type seen in 56 (19.71%) patients following endometrial hyperplasia. Secretory endometrium was seen in 29 (10.21%) patients, irregular ripening (Figure 3) in 25 (8.80%) patients, disordered proliferative (Figure 4) endometrium in 14 (4.93%) patients, atrophic endometrium in 7 (2.46%) patients and irregular shedding (Figure 5) in 5 (1.75%) patients while 16 (5.62%) of samples were inadequate for evaluation (Scant endometrial tissue with predominantly blood clot, autolysed samples/ suboptimal fixation that hindered the microscopic evaluation were considered inadequate).

Table 5: Comparison of various histopathological patterns of endometrium in DUB by various authors.

Endometrial pattern	Pilli GS et al[34] (2002)	Rajesh Patil et al[43] (2013)	BhoomikaDadhania et al[5] (2013)	Present Study
Proliferative	34 (34%)	42 (22.10%)	32 (21.33%)	56 (19.71%)
Secretory	13(13%)	37(19.47%)	23(15.33%)	29(10.21%)
Irregular ripening	--	31(6.32%)	4(2.67%)	25(8.80%)
Irregular shedding	2(2%	--	Deficient secretory phase = 1(0.67%)	5(1.75%)
Endometrial hyperplasia	44(44%)	76(40%)	40(26.67%)	132(46.47%)
Atrophic endometrium	--	--	--	7 (2.46%)
Disordered proliferative	--	--	Irregular proliferative =4(2.67%)	14(4.93%)
Others	7(7%)	2(1.06%)	38(25.34%)	
Inadequate	--	--	Proliferative with focal dysplasia = 6-4%	16(5.62%)
Total	100	190	150	284

Discussion

The present study was done to evaluate the histopathology of endometrium in 284 cases who were clinically diagnosed as DUB taking into account the age of women, phase of her menstrual cycle, parity, bleeding pattern and iatrogenic use of hormones.

DUB was observed in all age groups. The youngest age was 20 years and oldest age was 65 years. The maximum incidence of DUB was found in the age group 41-50 years (37.32%) followed by 31-40 years (35.56%) while study conducted by Rajesh Patil et al [9] and Mitra K et al [10] found DUB predominantly in age group of 31-40 years as 45.26% and 62% respectively.

In the present study, DUB was observed in women of various parity. Maximum number of cases were seen in multiparous women 204 (71.83%) compatible with the study by Rajesh Patil et al [9] and Pilli et al [11] who also found DUB in multiparous women as 71.58% and 87% respectively. Minimum number of cases were seen in nulliparous women i.e, 11 cases (3.87%) in the present study and 4.74% by Rajesh Patil et al [9] and 6% by Pilli et al [11] while Sushila Devi et al [12] found DUB more common in nulliparous women.

The most common bleeding pattern encountered in the present study was menorrhagia 71.83% comparable with the study by Rajesh Patilet al [9] (73.16%) while Sharma Juhi et al [8] and Muzaffar et al [4] showed menorrhagia as bleeding pattern in 57.44% and 51.9% cases only.

Comparison of various histopathological patterns of endometrium in DUB by various authors is shown in Table 5.

In the present study endometrial hyperplasia was the most commonest endometrial pattern seen in 132(46.47%) patients which is in concordence with the findings of Pilli GS et al [11], Rajesh Patil et al [9] and BhoomikaDadhania et al [3].

Proliferative endometrium was the next commonest type of endometrial pattern seen in 56 (19.71%) patients following endometrial hyperplasia which is in concordance with the findings of Pilli GS et al [11], Rajesh Patil et al [9] and Bhoomika Dadhania et al [3].

Incidence of secretory endometrium found in various studies is illustrated in table 5 which shows range from 13 to 19.47% while present study shows 29(10.21%) cases only.

Incidence of irregular ripening was seen in 25(8.80%) patients, while other studies showed incidence ranging from 2.67% to 6.32%.

Incidence of irregular shedding was seen in 5(1.75%) patients comparable with the study done by Pilli GS et al [11] which showed 2(2%) cases only.

In the present study disordered proliferative endometrium was seen in 14 (4.93%) patients, atrophic endometrium in 7 (2.46%) patients and 16 (5.62%) samples were inadequate for evaluation. While study done by BhoomikaDadhania et al [3] showed irregular proliferative endometrium in 2.67%, proliferative endometrium with focal dysplasia in 4%, deficient secretory phase in 0.67% and various other lesions were 25.34% i.e, menstrual endometrium 12%, endometrial changes due to exogenous hormones or pill endometrium in 10%, aria-stella reaction in 0.67%, secretory hyperplasia in 0.67% and chronic endometritis in 2% cases.

Conclusion

1. It was observed that no age was exempted from DUB and highest incidence was noted in the age group of 41-50 years (37.32%) followed by 31-40 years (35.56%).
2. Menorrhagia was the commonest bleeding pattern seen in 204 (71.83%).
3. Majority were multiparous women i.e, 204 (71.83%) patients.
4. Endometrial patterns varied in cases of DUB.
5. Endometrial hyperplasia was the most commonest pattern seen in 132 (46.47%) patients followed by proliferative endometrium seen in 56 (19.71%) patients.
6. Both types of patterns: endometrial hyperplasia and proliferative endometrium presenting as DUB are anovulatory type and can be treated medically. Thus, histopathological study of endometrium in DUB is helpful to distinguish anovulatory from ovulatory DUB and also it is important to exclude other organic pathology (such as chronic endometritis) which plays an important role in its management.
7. Atypical hyperplasia (simple and complex) was observed in 18 (6.33%) cases and is considered as a precancerous condition for endometrial carcinoma, hence histopathological study of endometrium is useful for early diagnosis of hyperplasia and further management.

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