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Evaluation of Endometrial Biopsies and its Clinico-Radiological Corrrelation in Patients with Dysfunctional Uterine Bleeding.

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ABSTRACT

Background: Dysfunctional uterine bleeding is one amongst the commonest conditions for which females consults the gynaecological outpatient department with an estimated 9-30% of women of reproductive age suffering from the complaint of menorrhagia. Its prevalence increases with age, peaking just prior to menopause. Because most cases are associated with anovulatory menstrual cycles, adolescent and perimenopausal women are more vulnerable.[5]. **Objectives:** To study the histopathological spectrum of endometrial biopsies and to correlate it clinico- radiologicaly in reproductive age patients presenting with DUB. **Methods:** It was an 18 months study done over 50 endometrial biopsies which were well established cases of DUB clinically with exclusion of structural lesions radiologically. **Results:** Largest numbers of patients were in the age group of 31-40 years (66%). The most common clinical presentation was menorrhagia (58%) followed by polymenorrhea (20%). In present series Disordered proliferative phase (30%) followed by proliferative phase were the commonest histomorphological patterns observed. **Conclusion:** The cause of Dysfunctional Uterine Bleeding is strongly related to patients age, types of menstrual cycles, ovulatory or anovulatory and menopausal status Thus, histopathological examination in correlation to radiological findings remain the standard procedures for diagnosis.

Keywords: Dysfunctional uterine bleeding, Endometrium, Histomorphological spectrum.

INTRODUCTION

Dysfunctional uterine bleeding (DUB) is well known as one of the common problem in women of late reproductive and the perimenopausal age group. Its incidence increases with the advancing age till menopause.[1] As with the endometrial sampling ,it can be used effectively as the first diagnostic step in DUB, although at times, the interpretation of endometrial biopsy can present as a challenge to the working pathologists. Therefore, the present study was done to evaluate histopathology of endometrium and to observe the incidence of various pathological spectrum in different age groups presenting with DUB along with its radiological correlation.

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Dysfunctional uterine bleeding is well defined as any abnormal bleeding from the uterus in absence of organic disease of the genital tract, pregnancy or general bleeding disorder.[2] DUB has great variation in the endometrial patterns and its management entirely depends upon the type of endometrium. Thus, histopathological study of endometrium plays an important role in its treatment. [3]

Endometrium is known to be a hormonally sensitive and responsive tissue undergoing constant changes during the active reproductive life. The normal menstrual cycle shows an interval ranging from 28 ± 7 days with a mean duration of 4 ± 3 days with total amount of blood loss averaging approximately 30 ml/cycle, but can be as high as 80 ml.[4]

Menorrhagia defines the bleeding that occurs at normal intervals (21 to 35 days) but with heavy flow (>80 ml) or duration (>7 days), metrorrhagia is bleeding that occurs irregularly, acyclic or continuously in between normal cycles irrespective of the amount of blood lost. Bleeding that occurs irregularly and at noncyclic intervals and with heavy flow (>80 ml) or duration (>7 days) is called Menometrorrhagia. Polymenorrhoea is cyclical bleeding which is normal in amount but which occurs at too frequent intervals of less than 21 days. Oligomenorrhea is bleeding that comes at intervals greater than 35 days.[5]

DUB shows its association with anovulatory & the ovulatory cycles of menstrual cycle. Anovulatory cycles are considered as the most common cause of DUB of the women of reproductive age group.[6] While, DUB associated with ovulatory bleeding is poorly understood. However, disordered prostaglandin metabolism and increased lysosomal activity in the endometrial cells explain most cases of ovulatory DUB. In a large proportion of women, the basic disorder may be pituitary overproduction of prolactin, which in excess suppresses progesterone production. Rarely, endometrium lacks progesterone receptors.[7] DUB may also be due to local factors like abnormal platelet aggregation caused by a shift in prostaglandin synthesis.

DUB abnormalities can be easily segregated into: -

- Estrogen related
- Progesterone related

With estrogen related DUB being more common.[6]

Aims & Objectives:

1. To study the histopathological spectrum of endometrial biopsies in clinically diagnosed patients of DUB.
2. To correlate the histopathological pattern with the age, bleeding pattern and radiological findings in patients with DUB.
3. To observe the result and evaluate the obtained data by comparing with the other studies conducted on DUB.

MATERIALS AND METHODS

This was a prospective study done on 50 patients exclusively of DUB over a period of 18 months in the department of pathology of Teerthanker Mahaveer Medical College, Teerthanker Mahaveer University, Moradabad, U.P .Endometrium biopsies were obtained from the department of gynaecology & obstetrics.

Inclusion criteria:

- ❖ Endometrial tissue from patients clinically diagnosed as cases of DUB.

Exclusion criteria:

- ❖ Females presenting with DUB due to pregnancy related complications.
- ❖ Organic lesions involving the genital tract infections, systemic causes, iatrogenic causes, polyp and other lesions.
- ❖ Hysterectomy specimens are also excluded.

Method

For the histopathological examination, endometrial biopsy was received in the pathology department in 10% formalin, grossed and the tissue was processed in the Automated tissue processor. The Paraffin embedded tissue block was sectioned using semi-automated microtome machine, and fine ribbon sections measuring approximately 4 micrometre were taken on a clean glass slide. It was then stained with the routine Harris Haematoxylin and Eosin stain and studied under light microscope.

RESULTS

Table 1: Incidence of DUB in various age groups.

Age (in years)	No. of patients	Percentage(%)
15-20	0	00
21-30	1	02
31-40	33	66
41-50	14	28
>50	2	04
Total	50	100

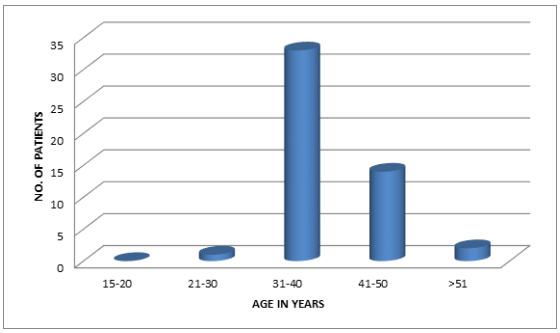

Figure 1: Incidence of DUB in various age groups.

Table 2: Incidence of various bleeding patterns in DUB.

Bleeding pattern	No. of patients	Percentage(%)
Menorrhagia	29	58
Metrorrhagia	2	4
Menometrorrhagia	1	2
Polymenorrhea	10	20
Continuous Bleeding per vaginum(cBPV)	8	16
Total	50	100

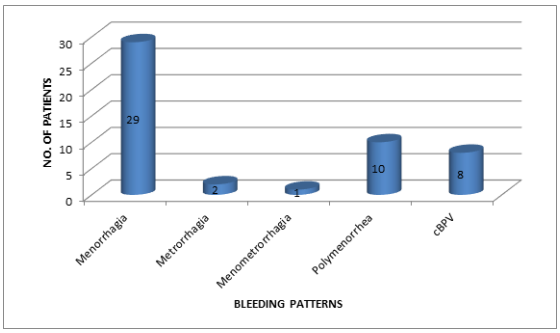

Figure 2: Incidence of various bleeding patterns in DUB.

Table 3: Endometrial patterns in DUB.

Histopathological pattern observed	No. of patients	Percentage(%)
Proliferative phase(PPE)	10	20
Secretory phase(SPE)	09	18
Disordered proliferative phase(DPP)	15	30
Proliferative with SGB*	12	24
Secretory with SGB*	03	6
SGB*	01	2
Total	50	100

*SGB= stromal and glandular breakdown

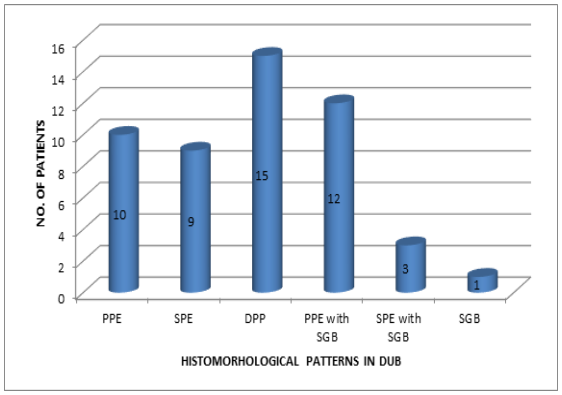

Figure 3: Endometrial patterns in DUB.

Table 4: Relationship of DUB with Parity.Parity of the patients	No. of patients	Percentage(%)
Nullipara	00	Nil
Primipara (<2)	01	2
Multipara(2-4)	30	60
Grand multipara(5 or more)	19	38
Total	50	100

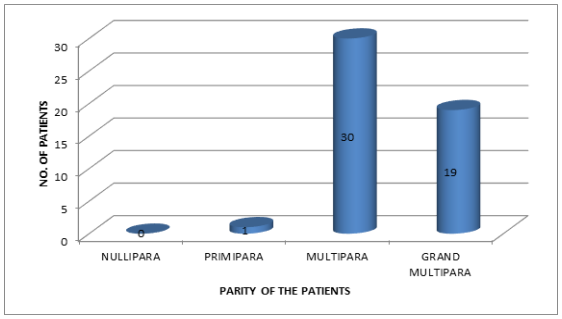

Figure 4: Relationship of DUB with Parity.

Table 5: Comparative chart between the bleeding patterns and various age groups.

Bleeding pattern	Age (in years)					Total no. of cases
	15-20	21-30	31-40	41-50	>50	
Menorrhagia	0	0	22	7	0	29
Metrorrhagia	0	0	2	0	1	3
Menometrorrhagia	0	0	1	0	0	1
Polymenorrhea	0	1	4	5	0	10
Continuous Bleeding per vaginum(BPV)	0	0	4	2	1	7
						50

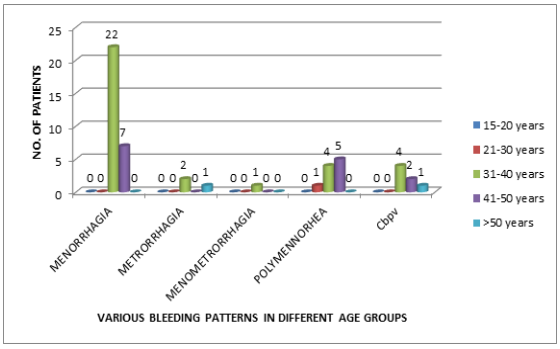

Figure 5: Comparative chart between the bleeding patterns and various age groups.

Table 6: Endometrial patterns in relation with Parity.

Endometrial pattern	Parity			
	<2	2-4	>5	Total no. of cases
Proliferative	0	5	5	10
Secretory	1	6	2	9
DPP	0	11	4	15
Proliferative with SGB	0	7	5	12
Secretory with SGB	0	1	2	3
SGB	0	0	1	1
Total				50

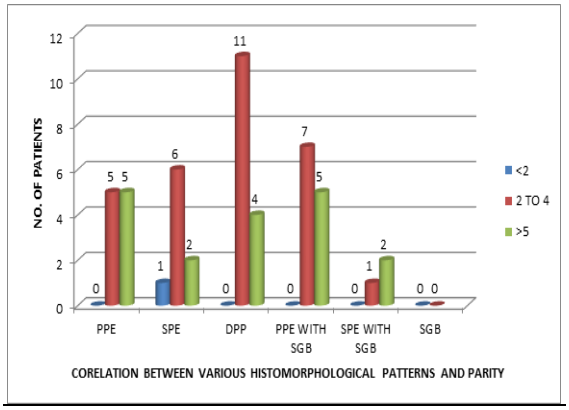

Figure 6: Endometrial patterns in relation with Parity.

Table 7: Type of bleeding in relation to endometrial change.

Endometrial change	Bleeding pattern					Total
	Menorrhagia	Metrorrhagia	Meno-metrorrhagia	Polymenorrhea	cBPV	
Proliferative	7	0	0	3	0	10
Secretory	8	0	0	1	0	9
PPE with SGB	4	1	0	5	2	12
SPE with SGB	0	1	1	0	1	3
DPP	9	0	0	1	5	15
SGB	1	0	0	0	0	1
Total						50

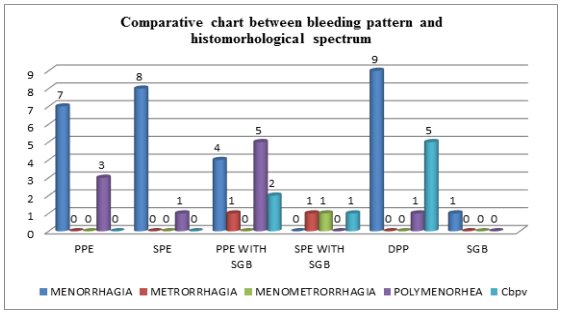

Figure 7: Type of bleeding in relation to endometrial change.

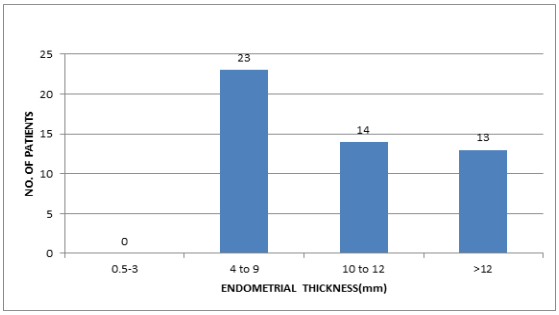

Figure 8: Relationship between endometrial thickness and the menstrual phase.

Table 8. Relationship between endometrial thickness and the menstrual phase.

Endometrial thickness	No. of patients	Percentage
0.5-3	00	00
4-9	23	46%
10-12	14	28%
>12	13	26%
Total cases	50	100%

Table 9. Correlation between endometrial thickness on ultrasonography and histomorphological patterns.

Histomorphological pattern	No. of patients with Endometrial Thickness(in mm)				Total no. of cases
	0.5-3mm	4-9mm	10-12mm	>12mm	
DPP	00	05	05	05	15
PPE	00	06	01	03	10
SPE	00	06	02	01	9
PPE With SGB	00	05	05	02	12
SPE with SGB	00	00	01	02	3
SGB	00	01	00	00	1
					50

DISCUSSION

Table10: Comparative chart for age distribution in different studies of DUB

Studies conducted	Total no. of cases	Age distribution pattern in DUB	
		Most common age of presentation(in years)	Least common age of presentation(in years)
Mohammad et al[8]	260	41-50	21-30
Khare et al[9]	187	<40	40-50
Riaz et al[10]	100	45-49	40-44
Malukani et al[11]	400	31-40	41-50
Dadhani et al [12]	150	41-50	>50
Patil R et al[3]	190	31-40	<20
Kayastha et al[13]	100	41-45	<35
Nanavati et al[14]	410	31-40	<30
Annigeri et al[15]	190	31-40	<20
Kariappa et al[16]	205	31-40	<20
Nagarjuna et al[17]	100	21-30	11-20
Present study	50	31-40	>50

Our study significantly revealed that the occurrence of DUB was more in the mid reproductive age group, i.e. in the 4th decade and least in the 6th decade. The result of our study was in concordance with the other studies done by Malukani et al, Patil R et al, Nanavati et al, Annigeri et al, Kariappa et al showing maximum cases of DUB in the 4th decade of life with least number of cases seen in the 3rd decade of life. Whereas, the studies by Mohammad et al, Riaz et al, Dadhani et al, Kayastha et al showed presentation of DUB in a slightly later age groups of 41-50 years' age in maximum no. of patients, thus eliciting different age distribution from our study.

Table 11: Comparative chart for bleeding pattern distribution in different studies of DUB.

Studies conducted	Total no. of cases	Bleeding pattern in DUB	
		Most common	Least common
Mohammad et al[8]	260	Menorrhagia	Polymenorrhea
Malukani et al[11]	400	Menorrhagia	Metrorrhagia
Dadhaniet al[12]	150	Menorrhagia	--
Patil et al[3]	190	Menorrhagia	Metrorrhagia
Kayastha et al[13]	100	Irregular bleeding	Prolonged bleeding
Nanavati et al[14]	410	Menorrhagia	Metrorrhagia

Katuwal et al	120	Menorrhagia	Polymenorrhea
Annigeri et al[15]	190	Menorrhagia	-
Sushila L et al	50	Metrorrhagia	Polymennorhea
Kariappa et al[16]	205	Menorrhagia	Oligomennorhea
Nagarjuna et al[17]	100	Menorrhagia	Polymenorrhea
Present study	50	Menorrhagia	Menometrorrhagia

Maximum number of patients coming to the OPD of gynaecology diagnosed as DUB presented with Menorrhagia as the commonest bleeding problem preceding the other less commonly seen bleeding presentations like polymenorrhea, continuous BPV, metrorrhagia and menometrorrhagia in descending series with total cases of each being 29,10,8,2and 1 respectively, accounting to 58%,20%,16%,4%,2% each.

The bleeding pattern observed in the present study was comparable to the bleeding pattern seen in the other studies done by Mohammad et al, Malukani et al, Patil R et al, Nanavati et al, Katuwal et al ,Aannigeri et al, Nagarjuna et al showing menorrhagia as the commonest bleeding pattern in all DUB cases. Whereas L Sushila devi et al and Kayastha et al showed metrorrhagia as the commonest clinical presentation.

Table 12: Comparative chart for various Histopathological pattern distribution in different studies of DUB

Studies done	Total no. of cases	Histopathological pattern in DUB	
		Most common	Least common
Khare et al[9]	187	Proliferative phase	Endometritis
Annigeri et al[15]	190	Proliferative phase	Secretory hyperplasia
Dadhani et al[12]	150	Proliferative phase	Irregular Proliferative phase
Nagarjuna et al[17]	100	Proliferative endometrium	Irregular ripening & pill endometrium
Nanavati et al[14]	410	Proliferative endometrium	Atrophic endometrium
Kariappa et al[16]	205	Proliferative endometrium	Atrophic endometrium
L sushila devi et al[21]	50	Proliferative endometrium	Irregular shedding
Malukani et al[11]	400	Proliferative endometrium	Atrophic endometrium
Patil R et al[3]	190	Endometrial hyperplasia	Secretory hyperplasia
Present study	50	DPP	Stromal and glandular breakdown

The present study conducted showed Disordered Proliferative endometrium as the commonest histopathological pattern which was also seen as the 2nd commonest histopathological pattern observed after the proliferative phase in the study done by Katuwal et al. But when combining Proliferative pattern with its stromal and glandular breakdown components, Proliferative phase endometrium became the most commonest histopathological pattern which can easily be compared with the commonest pattern seen in the other studies done by Khare et al, Annigeri et al, Dadhani et al, Nagarjuna et al, Nanvati et al, Kariappa et al, L Sushila Devi et al, Malukani et al. Whereas, other studies showed Irregular Rripening and shedding as the least commonly seen finding on histopathology, our study found stromal and glandular breakdown as the least occurring endometrial finding on histopathology in cases reported as DUB.

Anovulatory pattern of bleeding also came out as the commonest cause of DUB in our study with histopathology showing DPP 15 cases (30%}as the commonest finding, Proliferative endometrium with stromal and glandular breakdown with 12 cases (24%)and Proliferative phase alone 10 cases (20%} as the most usual findings. Ovulatory cycle was seen in less number of cases presenting mainly as only Secretory phase endometrium 9 cases (18%), Secretory endometrium with SGB 3 cases (6%) and only Stromal and Glandular breakdown 1 case (2%) on histopathology.

The current study done also compared the role of parity with the different histopathological patterns of DUB seen in our studied cases and it was observed that DPP presenting as the commonest pattern under microscopy was maximally seen in the Multipara females with 11 out of 15 cases of DPP. Proliferative phase endometrium with stromal and glandular breakdown, Secretory endometrium also showed up with more cases i.e.7 out of 12 and 6 out of 9 respectively in the Multiparas. While, Proliferative phase endometrial pattern showed up with equal cases in Multiparas and Grand Multipara females ,i.e. 5 out of 10 cases each.

Table 13: Comparative chart for parity distribution in different studies of DUB.

Studies	NO. of cases	DUB with Parity	
		Maximum cases	Minimum cases
Patil R etal[3]	190	Multipara (1-3)	Primipara(1-2)
Khan R etal[20]	120	Multipara	Primipara(1-2)
Kayastha etal[13]	100	Grand Multipara	Nullipara
Malukani etal[11]	400	Primipara	Grand Multipara
Nanavati etal[14]	410	Primipara	Grand multipara
Present Study	50	Multipara	Primipara

When comparing the DUB cases in relation with the parity of the patient , the result of present study showing maximum no. of DUB cases in Multipara(2-4) nearly matched with the other studies

done by Patil R etal , R Khan etal which also showed maximum cases in multipara females and minimum cases in Primipara females . Whereas, the studies done by Malukani etal , Nanavati etal showed maximum cases in Primipara and minimum cases of Grand multipara ,while Kayastha etal had Grand multipara making the most of the DUB cases and nullipara being the least in number with complaint of DUB.

On the Radiological front, Maximum no. of patients demonstrated endometrial thickness of 4-9 mm that correlated with the Proliferative pattern observed on histopathology. Similar correlation was observed with overlapping ET of 10-12 mm and 4-9 m correlating with the Secretory phase. While an ET of >12 mm showed Disordered Proliferation showing dys-correlation. The sensitivity of 100% was inferenced in all the cases of Proliferative endometrium, correlating with the radiological diagnosis. Whereas, all cases of Secretory phases on histopathology showed a sensitivity of 75 % on comparing with the endometrial thickness on ultrasonography.

CONCLUSION

From the present study conducted in the tertiary health care centre of Moradabad, on the females who came to the hospital with complaint of irregular menstrual disturbances and diagnosed as cases of DUB, it was inferenced that the incidence of DUB was seen to occur maximally in females of 4th decade, i.e. between age of 31-40 years (66%)with age of presentation of women being in the range of 21-55 years and showing a mean age of presentation of 40 years. The commonest bleeding complaint reported with the gynaecology & obstetrics OPD in these patients was Menorrhagia (58%) followed by polymenorrhea. Multipara females of age 31-40 years (75%) were seen to be affected most with DUB amongst females of other parity. Anovulatory cyclical pattern was most usually seen. The commonest histological pattern was Disordered Proliferative Phase endometrium (30%) followed by Proliferative Phase endometrium with stromal & glandular breakdown (24%) and Proliferative phase endometrium (20%), least case of Stromal and glandular breakdown (2%) were reported.

On historadiological correlation, there was a very well established correlation found between the endometrial thickness and the histopathological pattern. The commonest pattern was Proliferative phase endometrium in to which was matching with 4-9mm endometrial thickness on ultrasonography, also giving a true sensitivity of 100% by defined criteria for radiological finding of endometrial thickness (4-9mm) with histomorphological diagnosis.

The cause of Dysfunctional Uterine Bleeding is strongly related to patients age, types of menstrual cycles, ovulatory or anovulatory and menopausal status.[18,19] Evaluation of women with DUB is necessary especially around the perimenopausal age group to detect any abnormal changes and intervene early. Histopathological examination in correlation to radiological findings remain the standard procedures for diagnosis.

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