

Study of Dysfunctional Uterine Bleeding with Special Reference To Histopathology of Endometrium

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Abstract:

Background: Dysfunctional Uterine Bleeding is a common gynaecological complaint which has considerable morbidity and constitutes no less than 15-20% of all gynaecological admissions in an institute. A lot of confusion arises in the diagnosis, investigation procedures and management of DUB as so many factors have been put forward to the cause of DUB.

Materials and Methods: This study was carried out in the department of obstetrics and gynaecology, Regional Institute of Medical Science, Imphal, Manipur. A total of 130 patients with dysfunctional uterine bleeding attending the outpatient department and from those who were admitted were selected for this study. A detail history along with a thorough clinical examination including per vaginal examination was done. Dilatation and curettage along with examination under anaesthesia was performed to obtain material for Histopathology.

Results: Majority of the cases were between 31-40 years and menorrhagia was the commonest type of bleeding. Regarding histology, proliferative endometrium was the commonest, followed by secretory and hyperplastic endometrium.

Conclusion: Dysfunctional uterine bleeding occurs more commonly among the adolescents and women around the age of 40 years although it may occur at any time in a woman's life. There may be an inherent hormonal disturbance, as those patients who had abnormal bleeding pattern during menarche are more susceptible to get DUB in later life.

Keywords: Dysfunctional uterine bleeding, Dilatation and curettage, endometrial histology.

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I. Introduction

Menstrual dysfunction is the cause of discomfort, inconvenience and disruption of a healthy life style which affects many millions of women in both developed and developing world. Dysfunctional uterine bleeding occurs commonly at the extremes of reproductive life but nevertheless it may occur from the very first to the last day of life. Menstrual bleeding follows the withdrawals of oestrogen and progesterone and also of progesterone alone. Progesterone has been shown to promote the formulation of lysosomes in the endometrium, Henzlet al¹ and ultrastructural studies have shown that progesterone has stabilizing effect and oestrogens labilizing effect on the lysosomes in the endometrium. It has been shown that oestrogen depresses and progesterone stimulates the activity of the enzyme 15 hydroxy prostaglandins dehydrogenase, a main enzyme catalysing the initial step in the degradation of PGE₂ & PGF₂.² So oestrogen increase & progesterone decreases will increase their concentration & prolong the their action by inhibiting their degradation. Menstrual blood was thought not to clot and to be free of platelets and fibrin. However it is now thought that once clinical bleeding and tissue shedding has started, haemostatic plug formation occurs, but less rapidly and less completely in human skin wounds, Christeaens et al 1982.³ Fibrinosis is initiated in the endometrium by two types plasminogen activator; tissue type and urokinase type; both of which are release by disintegrating endometrium. The hormonal control of plasminogen activator production is such that oestradiol stimulates and progesterone is such that oestradiol stimulates and progesterone inhibits urokinase plasminogen activator, Casslen et al 1986.⁴ The endometrium also generates factors which inhibit platelet aggregation and platelet adhesion. Such factors include prostacyclin (PGI₂); Nitric oxide (NO) and platelet activating factor (PAF) all of which are produced by human endometrium.^{5,6} Another vasoconstrictor which have attracted recent interest is endothelin. It is an extremely powerful vasoconstrictor which is found in various tissues including human endometrium, O Reilly et al 1992.⁷ It has been proposed that as endometrial glandular epithelium breaks down during menstruation, stored endothelin gains excess to the spiral arterioles causing long lasting vasoconstriction. The precise roles for PAF and endothelin in menstruation are not yet clear. Menstruation is finally curtailed by endometrial repair. This process is stimulated physiologically by increasing levels of oestrogen released into the circulation by

developing ovarian follicle. There is increasing evidence that oestrogen induced endometrial proliferation is mediated by epidermal growth factor (EGF) is produced by the endometrium with maximal production in the late proliferative phase of the cycle.⁸ It seems likely that endometrial EGF contributes to repair of both glandular and stromal tissues, although the glandular effects are predominant, Haining et al 1991.⁹ Developing tissue need a blood supply and thus angiogenesis is an important part of endometrial repair. Vascular endothelial growth factor (VEGF) is a highly potent endothelial mitogen produced by the endometrium, Charnock-Jones et al.¹⁰ Production of VEGF is stimulated both by oestrogen and hypoxia.¹¹ These data suggest a role for VEGF in endometrial repair at the start of the menstrual cycle. Abnormalities in menstruation could thus result either from a purely local disturbance or dysfunction in prostaglandin metabolism in the endometrium or could be secondary to some dysfunction in the oestrogen or progesterone secreted by the ovary. Treatment is easy and clear cut in those cases, where an organic cause can be found out but it is that group in which no organic cause can be found out, poses problem for us. This group is normally referred to as DUB, a term which is a diagnosis of exclusion. DUB is a common gynaecological complaint with considerable morbidity and constitutes no less than 15-20% of all gynaecological admission in an institute. Considering the incidence of DUB, plenty of unexplored area remains in the field of diagnosis, histopathology, investigations and overall management of DUB.

II. Aims And Objectives

2.1 To study the changes in the endometrium and various effects of hormone therapy on endometrium in cases of DUB

2.2 Incidence of hysterectomy as a surgical treatment in cases of DUB

III. Materials And Methods

This study was carried out in the department of obstetrics and Gynaecology of Regional Institute of Medical Science, Imphal, Manipur. The materials for this study were collected from patients attending the outpatients department or through the emergency of Obstetrics and Gynaecology department during the period between October 2014 and February 2016. The present investigation was based on the study of 130 cases. A detail history was followed by a thorough clinical examination was performed including per vaginal examination for all the cases. This was followed by examination of blood for Hb%, CBC, coagulation screen and a bleeding time. Routine examination of urine and stool were also done. Some special investigations were undertaken in the form of dilatation of the cervix and uterine curettage, thyroid function test and also histology of removed organs in cases of hysterectomy. Management comprised of reassurance and general measure, antiprostaglandins, hormone, uterine curettage and hysterectomy in some cases.

IV. Results And Analysis

TABLE – 1 Analysis of 130 cases of provisionally diagnosed DUB.

Dysfunctional uterine bleeding	100	76.97%
Organic causes	30	23.03%

Of the total number of 130 cases provisionally diagnosed as DUB, in 30 cases organic cause could be found out and no organic cause could be found out in remaining 100 cases and they were stamp as Dysfunctional uterine bleeding.

Table – 2 Dub In Relation To Age And Parity

Parity	Age below 20 years	Age between 20-40 years	Age above 40 years	Total no. of cases	Percentage
Nullipara	15	9	2	26	26%
Para-1	4	7	4	15	15%
Para-2	2	17	2	21	21%
Para-3	1	14	11	26	26%
Para-4	0	2	4	6	6%
Para-5 or more	0	2	4	6	6%
Total	22	51	27	100	100%

From the above table it was found that of all the patients, 26% were nulliparous, 15% were para-1, 21% were para-2, 26% were para-3, 6% were para-5 or more.

Table – 3 Age Distribution In Dub Cases

SL	Age in years	No. of real DUB cases	Percentage	No. of Organic cases	Percentage
1.	Below 20	22	22%	4	13.33%
2.	21-30 years	20	20%	6	20%
3.	31-40 years	31	31%	8	26.66%
4.	Above 40	27	27%	12	40%
	Total	100	100%	30	100%

It was found that, 22% cases were below 20 years, 20% cases were between 21-30 years, 31% cases were between 31-40 years and the rest were above the age of 40 years. Majority of the organic cases were found above 40 years while majority of DUB were from age group 20-40 years especially in between 31-40 years.

Table – 4 Parity Distribution In Dub

SL. NO	PARITY	No. of real DUB cases	Percentage	No. Of organic cases	Percentage
1.	Nulliparous	26	26%	4	13.33%
2.	Para 1-4	68	68%	19	63.34%
3.	Para 5 or more	6	6%	7	23%
	Total	100	100%	30	100%

Majority of the cases of both real DUB and organic cases were in parous patients, 68% for real DUB and 63.33% were of organic cause.

Table – 5 Different Types Of Bleeding In Relation To Different Age Groups In Dub

Type of bleeding	<20 years	20-40 years	>40 years	Total no. of cases	Percentage
Menorrhagia	10	20	11	41	41%
Metrorrhagia	4	9	4	17	17%
Polymenorrhoea	3	5	3	11	11%
Polymenorrhagia	2	3	4	9	9%
Hypomenorrhoea	1	3	1	5	5%
Menometrorrhagia	0	4	1	5	5%
Premenstrual spotting	2	5	1	8	8%
Oligomenorrhoea	0	2	2	4	4%
Total	22	51	27	100	100%

It is evident that the commonest type of DUB is menorrhagia (41%) followed by metrorrhagia (17%). The least common type of bleeding in this series was oligomenorrhoea.

Table.6 Endometrial Pictures In Different Age Groups In Dub

Types of endometrium	< 20 years	20-40 years	>40 years	Total no. of cases	Percentage
Proliferative	2	7	14	23	32.85%
Secretory	1	15	3	19	27.14%
Hyperplastic	0	8	6	14	20%
Proliferative with irregular	1	4	1	6	8.75%
Irregular ripening	0	3	1	4	5.72%
Atrophic	0	0	2	2	2.85%
Irregular shedding	0	2	0	2	2.85%
Total	4	39	27	70	100%

In the above table, of the total 100 cases of real DUB, 70 cases underwent dilatation and curettage which shows that the commonest type of endometrium was proliferative endometrium (32.85%), followed by secretory endometrium (27.14%).

Table No.7 Endometrial Picture In Organic Cases In Different Age Groups

Types of endometrium	Age below 20 years	Age 20-40 years	Age above 40 years	Total No. Of cases	Percentage
Proliferative	0	5	3	8	29.62%
Secretory	0	3	2	5	18.52%
Hyperplastic	0	1	1	2	7.40%
Adenomatous polyp	0	3	2	5	18.52%
Irregular ripening	0	0	1	1	3.70%
Dysplasia & atypical hyperplasia	0	0	2	2	7.40%
Atrophic	0	0	1	1	3.70%
Misc. Chorionic villi	1	2	0	3	11.12%
Total	1	14	12	27	100%

Above table shows the endometrial picture of organic cases where proliferative endometrium was found in 29.62% cases, secretory endometrium in 18.52% cases, and hyperplastic endometrium in 7.40% and 5 cases of adenomatous polyp of endometrium.

Table no. 8 treatment of patients aged below 20 years

Treatment given	No. Of cases	Recovered	Improved	Continuation of Abnormality
General measures & haematinics	23	8	2	13
General measures, progesterones & antiprostaglandins	13	4	1	8
Blood transfusion, i.v oestrogen / progesterone	8	3	0	5
Curettage with or without follow-up progesterone	5	0	5	0
Specific measures	1(ITP),1(PID) 1(Hypothyroid)	0	3	0

Above table shows that in age group below 20 years, most of the patients responded to treatment with general measures with haematinics, progesterone, antiprostaglandins and progesterone.

Table No.9 Treatment Of Patients Age Between 20-40 Years

Treatment given	NO. of cases	Recovered	Improved	Continuation of Abnormality
General measures,haematinics & progesterone	51	10	2	39
Anti prostaglandins& curettage	39	7	1	31
Curettage, progesterone with anti prostaglandins	31	9	3	19
Repeat curettage	6	5	0	0
Hysterectomy	14	0	0	0

Of the total 51 cases in which general measures and haematinics along with progesterone or combined oestrogen progesterone compounds were given, only 10 cases were recovered. Anti prostaglandin followed by curettage was performed on 39 cases out of which 7 cases recovered. 14 cases (19.60%) underwent hysterectomy.

Table no. 9 incidence of hysterectomy in dub casesdiagnosed provisionally

Type of patient	Number Of patient	Number of hysterectomy	Percentage
Age < 20 years			
Functional	22	0	0%
Organic cases	4	0	0%
Age 20-40 years			
Functional	51	14	27.45%
Organic	14	14	71.42%
Age > 40 years			
Functional	27	18	66.66%
Organic	12	11	91.66%
TOTAL	130	53	40.76%

Above table shows that out of total 130 cases provisionally diagnosed as DUB, 53 patients (40.76%) ultimately underwent hysterectomy. No patient under the age of 20 years required hysterectomy. In the age group between 20 to 40 years, out of 65 cases, 24 (36.92%) patient required hysterectomy. In the age group above years, 29 (74.35%) out of 39 underwent hysterectomy. Out of 100 real DUB cases, 32 (32%) required hysterectomy.

V. Discussion

Abnormal and excessive uterine bleeding is a distressing problem in any women's life which may extend from menarche to perimenopausal period. In this study, 130 cases were provisionally diagnosed as DUB of which no organic causes can be found in 100 cases (76.9%) and were treated as real DUB. In 30 cases (23.03%), one or more than one cause of bleeding was ultimately detected and were treated as organic DUB. It was found that of the total 100 cases of DUB proper, 22 cases (22%) were from age group less than 20 years, 51 cases (51%) were in the age group between 20 and 40 years. These findings correlates well with those of Banerjee¹² and Sarbajna.¹³

The incidence of DUB in nulliparous patient was 26% while in parous women the incidence was 74%. In organic cases, the incidence in nulliparous and parous patient was 13.33% and 86.67% respectively. These

findings tally well with general agreement that DUB is more common amongst parous patient than in nulliparous. It is evident from this study, that by far the commonest type of bleeding in DUB is menorrhagia (41%), metrorrhagia in (17%), polymenorrhea in 11% of cases, polymenorrhagia in 9% of cases, premenstrual spotting in 8% of cases, menometrorrhagia in 5% of cases, hypomenorrhea in 5% and oligomenorrhea in 4% of cases and these findings correlates with those of Moghal N.¹⁴ It was found that, of the total 70 cases of real DUB cases which underwent curettage, 23(32.75%) showed proliferative endometrium, 19(27.14%) showed secretory endometrium and 14(20.00%) showed hyperplastic endometrium. Rest were proliferative with irregular ripening (8.57%), irregular ripening (5.72%), atrophic (2.85%) and irregular shedding in (2.85%).

Treatment of DUB cases, vary according to the age, parity, desire for children, severity and persistence of symptoms and histopathological study of endometrium. Explanation and reassurance are essential for every patient and for some this may be all that is necessary. Administration of progestational agent to the DUB patients have given a new dimension to the therapeutic approach.¹² According to Kistner 1964,¹⁵ progestogen treatment should be continued for 9 months to 1 years. Antiprostaglandins have also some value in the management of DUB cases. Anderson et al¹⁶ have shown in their studies that the anti prostaglandin mefenamic acid reduces the mean MBL from 119 ml to 60 ml. In this study also anti prostaglandin mainly mefenamic acid was found to improved 5 out of 13 cases treated in the age group below 20 years and 8 out of 39 cases treated along with curettage in the age group between 20-40 years. According to Te Linde (1977), curettage is of great value as a therapeutic procedure also but Nilsson and Rybo¹⁷ had the opinion that prolonged beneficial effect of curettage in DUB cases were unlikely.

From this study, it was evident that no patient below 20 years required hysterectomy. The incidence of hysterectomy amongst provisionally diagnosed DUB (130) was 40.76%. But in real DUB (100) cases the incidence was 32%. The general incidence of hysterectomy (32%) in this series was a little more than quoted by different authors (20%-30%). Combination of hysterectomy with or without bilateral salpingo-oophorectomy as atreatment of DUB cases particularly in the patients at about the end of their reproductive life is invaluable. This is accepted by most of the gynaecologist as one of the best answer to this problem especially patients with age 40 years or above.

VI. Conclusion

DUB occurs more commonly among the adolescents and women around the age of 40 years although it may occur at any time in a women's life. It is more common amongst parous women than nulliparous. Menorrhagia is the commonest presentation. Histopathological study of the endometrium of the patients between 20-40 years reveals more incidence of secretory endometrium wherease those patients below 20 years and above 40 years reveals more incidence of proliferative endometrium. Hysterectomy was the mainstay of treatment in the age group above 40 years and was required in 74.35% of cases.

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