Original article

A clinicopathological study on dysfunctional uterine bleeding at perimenopausal age group

Kazi Morjina Begum[1], Mahbuba Siddiqua[2], Ferdousi Chowdhury[3], Prof. AKM Anwarul Azim[4]

Abstract

Objective : Dysfunctional uterine bleeding is a form of abnormal uterine bleeding when there is absence of organic disease of the genital tract. The objective of this study was to find out the clinical and pathological aspect of women presenting with dysfunctional uterine bleeding at perimenopausal age group.

Methodology : It was a hospital based prospective observational study carried out in the Department of Obstetrics and Gynaecology, Ad-Din Women's Medical College Hospital, Dhaka. Total 62 consecutive patients of DUB who were admitted selected for the study population from July 2011 to March 2012. The clinical presentation and histopathological reports (following dilatation and curettage or hysterectomy) of 62 DUB patients were observed. Twelve of these patients subsequently found to have organic pathological conditions were excluded from the study. Data was analyzed statistically.

Results : Of the studied 62 patients 44 (70.96%) were found to have DUB, 12(19.35%) had organic pathology, and rest 6(9.67%) were found to be normal. Histopathological findings revealed 28(63.63%) cases had proliferative endometrium, 6 (13.6%) had secretory endometrium, while 4 (9.09%) had cystic hyperplasia, only one (2.27%) had atypical hyperplasia and 3(6.8%) cases had atrophic endometrium.

Conclusion : Despite the low incidence of endometrial atypical hyperplasia and carcinoma in perimanopausal women, but they do occur.

Key words : Dysfunctional uterine bleeding, perimenopausal age group, endometrial thickness, LNG-IUS, thermal ballon ablation.

Introduction

Dysfunctional uterine bleeding is a common problem. It affects women's health both mentally, physically and socially. Among women aged 30 to 49 years, one in 20 consults her general practitioner each year with menorrhagia, making DUB one of the most often encountered gynaecological problems. About 30% of all women report having had menorrhagia, and it accounts for two thirds of all hysterectomies and most of the endoscopic endometrial destructive surgery[1].

The generally accepted definition of dysfunctional uterine bleeding is abnormal uterine bleeding which occurs without any clinically detectable organic, systemic and iatrogenic causes[2]. In half of women with menorrhagia there is no organic cause. So, DUB is a diagnosis of exclusion. As DUB can occur during the life span of a woman any time from menarche to menopause but commonly occurs in two extremes of life. About 10% of outdoor patients in gynae department present with DUB[3].

In the first 18 months after menarche, the immature hypothalamo-pituitary-ovarian axis may fail to respond to estrogen and progesterone, resulting in anovulation[4,5] In obese women, the non-ovarian endogenous estrogen may upset the normal menstrual cycle[6].

As menopause approaches, decreases in hormone levels or irresponsiveness to hormones also may lead to anovulatory DUB.

The term includes a variety of separate entities such as mid-month staining, premenstrual staining, normal uterine bleeding occurring at larger than normal interval, profuse or prolonged uterine bleeding of normal duration. The pathology of dysfunctional uterine bleeding is largely unknown, but it occurs in both ovulatory and anovulatory menstrual cycles[4].

Ovulatory dysfunctional uterine bleeding occurs secondary to defects in local endometrial haemostasis, such as (i) Local disorder of prostaglandin receptors in the endometrium (ii) increase of fibrinolytic activity in the endometrium (iii) increase in capillary fragility.

1. Assistant Professor, Department of Obstetrics & Gynaecology, Ad-din Women's Medical College Hospital (AWMCH)
2. Assistant Professor, Department of Obstetrics & Gynaecology, AWMCH
3. Associate Professor, Department of Obstetrics & Gynaecology, AWMCH
4. Professor, Department of Obstetrics & Gynaecology, AWMCH

Correspondence : Dr. Kazi Morjina Begum
e-mail: drmorjina.awmch@gmail.com

Anovular type of bleeding present in 10% of reproductive age group probably represents dysfunction of hypothalamic-pituitary-ovarian axis resulting in continued estrogenic stimulation of endometrium. Anovolar type of bleeding occurs due to systemic disorder, secondary to endocrine, neurochemical or pharmacological mechanisms[5].

In most patients dysfunctional uterine bleeding associated with anovulation, and anovulatory bleeding is common in the pubertal and perimenopausal periods. During these transitional states, the abnormal bleeding has a physiological basis and is secondary to an oestrogen withdrawal. Anovulatory bleeding can also be associated with chronic anovulation. The chronic unopposed oestrogen that characterizes this disorder causes a continuous proliferation of the endometrium. This can result in abnormal bleeding and increases the risk of developing endometrial cancer. Only 2% of endometrial cancer occurs before age 40. The goals of treatment for anovulatory bleeding are to stop the acute bleeding, avert future episodes, and prevent long term complications.

In contrast to normal menstrual cycles which are characterized by a regular balance between gonadotrophin & ovarian hormone resulting in ovulation and cyclical uterine bleeding is chacraterized by an imbalance between adenohypophysis and ovary. Since the endometrium is the target of this endocrine imbalance, abnormal bleeding is merely a symptom of endocrine dysfunction[7].

Diagnosis should be suspected by history along with meticulous examination and confirmed by endometrial biopsy.

Methodology

It was a hospital based prospective observational study. Total 62 patients were selected in this study according to inclusion criteria.

Inclusion criteria

All the patients with abnormal uterine bleeding without any organic or systematic causes were included in this study.

Exclusion criteria

Patients with abnormal uterine bleeding but having organic or systematic causes were excluded.

Results

The study revealed that of the 62 cases 70% were in the age group of 45-52 years and only 12% of cases fall in age group of 53-55 years (table-1). Forty two percent patients had menorrhagia and only 4% had sudden 2/3 bouts of bleeding in postmenopausal women. Other clinical presentations were polymenorrhagia 32%, polymenorrhoea in 14% and continuous bleeding in 8% of the cases (table-2).

Through trans-vaginal ultrasonography (TVS), endrometrial hyperplasia was detected 66%. Endometrial atrophy was found 4% and 30% patients had normal endometrium (table-3). According to Histopathology only 12(19.35%) had organic pathology (table-4). Of the 12 patients with organic pathology, 41.66% were suffering from fibroid uterus, 25% had adenomyosis, 16.66% had endometrial polyp. Equal number of patients had (8.33%) carcinoma cervix and pelvic inflammatory disease (table-5).

All of 44 DUB cases' samples sent to histopathology laboratory for tissue diagnosis. Findings include 28(63.63%) cases had proliferative endometrium, 6 (13.6%) had secretory endometrium, while 4 (9.09%) had cystic hyperplasia, only one (2.27%) had atypical hyperplasia and 3(6.8%) cases had atrophic endometrium (table-6).

Among 50 patients, medical treatment was received by 35 where synthetic progesterone was used in 24 (68.57%), combined pill in 6 (17.14%) and tranexamic acid in 5 (14.28%). In case of surgical intervention among 44 patient only curettage was done in 10 (22.72%), curettage with hysterectomy in 8 (18.18%), medical therapy with hysterectomy in 8 (18.18%), medical therapy with curettage and hysterectomy in 14 (31.81%) and lastly direct hysterectomy in 4 (9.09%).

Table-1: Distribution of patients according to age group (n-60).

Age group	Number	Percentage (%)
40-44	9	18
45-48	23	46
49-52	12	24
53-55	6	12
Total	62	100

Table-2 : Distribution of patients by to various clinical presentation of (DUB) (n=50)

Category	No. of patients	Percentage %
Menorrhagia	21	42
Polymenorrhoea	7	14
Polymenorrhagia Sudden 2/3 of bleeding in postmenopausal	16	32
women	2	4
Countinuous	4	8

Table-3 : Distribution of patients by to Ultrasonographic (TVS) findings of endometrial thickness (n=50)

Category	No. of patients	Percentage %
Hyperplasia	33	66
Atrophic	2	4
Normal endometrium	15	30

Table-4 : Distribution of patients by histopathology findings.

Category	No. of patients	Percentage %
DUB	44	70.96
Organic pathology	12	19.35
Normal endometrium	6	9.67

Table-5 : Distribution of the patient according to organic pathology n-12

Category	No. of patients	Percentage %
fibroid uterus	5	41.66
adenomyosis	3	25
endometrial polyp	2	16.66
pelvic inflammatory disease	1	8.33
carcinoma cervix	1	8.33
Total	12	100

Table-6 : Distribution of patients by Histopathological findings of endometrium (n=44)

Category	No. of patients	Percentage %
Profilerative phase	28	63.60
Secretary phase	6	13.60
Atrophic endometrium	3	6.80
Cystic hyperplasia	4	9.09
Atypical hyperplasia	1	2.27

Table-7 : Distribution of patients by Mode of treatment of DUB patients in present series (n = 50)

Mode of treatment		No.	Percentage %
Medical (n = 35)	Synthetic progesterone	24	68.57
	Oestrogen & Progesterone (Combined pill)	6	17.14
	Tranexamic Acid +NSAID Naproxen)	5	14.28
Surgical (n = 44)	Curettage only	10	22.72
	Curettage followed by hysterectomy	8	18.18
	Medical therapy followed by hysterectomy	8	18.18
	Medical therapy+curettage followed by hysterectomy	14	31.81
	Direct Hysterectomy	4	9.09

Discussion

Regarding age group these findings were somehow comparable to study done by Muzaffar et al[8].

In a study of 1000 cases of DUB, Sutherland found that 14% patients had organic pathology. In another study, 20 patients (20%) out of 100 cases showed organic pathology9, in the study done by Banerjee, 20 patients (28.5%) out of 70 showed organic pathology[10] which were more or less similar to the present study.

DUB patients may come with different types of menstrual disorders e.g menorrhagia, polymenorrhagia, polymenorrhoea, metrorrhag ia even intermenstrual bleeding. But most common form is functional polymenorrhoea and polymenorrhagia. Jeffcoate stated that 50% patients present with DUB with polymenorrhoea and polymenorrhagia[11].

Begum showed 78% had menorrhagia, 12.5% polymenorrhoea and polymenorrhagia, 8.75% continuous bleeding and 1-2% had intermenstrual bleeding[9]. In the study reported by Banerjee, 54% had menorrhagia, 30% polymenorrhoea and 14% continuous bleeding[10]. In the present study, 42% suffered from cyclical bleeding, 32% had polymenorrhagia, 14% had polymenorrhoea and 4% had post menopausal bleeding which is more or less similar to Jeffcoate study[12].

USG is a valuable tool in evaluating women presenting with a complaint of abnormal vaginal bleeding by demonstrating anatomic finding frequently not discernible on pelvic examination, such as small cyst leiomyoma and even endometrial carcinoma and in

evaluating the endometrium in terms of its thickness. USG can also be of value in confirming some diagnoses that are generally made clinically by exclusion such as break through bleeding from oral contraceptive[1].

Goldstein et al. studied of 111 cases, by TVS, found that 31(27.9%) women had an abnormal endometrium hyperplasia in 13.5%, polyps in 5.4%, sub-mucous myoma in 5.4% and adenocarcinoma in 3.6%[13].

In this study USG was done mainly by TVS route and 66% revealed hyperplasia, 30% normal and 4% atrophic endometrium.

In another study the two most common findings were proliferative and secretory endometrium. This finding is similar to the other studies[14]. Endometrial hyperplasia is a precursor of endometrial cancer. The incidence of endometrial hyperplasia without and with atypia peaks in early 50's and early 60's respectively[15,16].

In the study by Vercillini et.al histopathological report of endometrium showed atypical hyperplasia in (0.7%) and endometrial carcinoma in (0.5%) in her group-3 (45-50 years)[17]. Histopathological findings of the present study, was about similar to the above studies.

In choosing the most appropriate and effective medical treatment, some help may be gained from endometrial histology in the second half of the cycle.

Progesterone may be used to arrest severe uterine bleeding by large dose in case of endometrial hyperplasia or administered cyclically either in second half (from 15th to 25thday), particularly with premenstrual spotting or throughout the cycle (15thto 25th day) in cases of endometrial hyperplasia. Fraser treated 10 women with ovulatory menorrhagia with progesterone at a dose of norethisterone 5 mg three times daily or MPA 10 mg three times from day 5 to 215. Similarly high dose of NE in 22 women decreased MBL significantly[11].

In the study by Begum, 26 patients were treated by synthetic progesterone. In the present study, 24 out of 35 patients were advised synthetic progesterone. Twenty two patients had good cycle control after 3-6 months of regimen. In 4 patients bleeding had controled during taking drug but started to bleed again when drug was discontinued. One patient responded poorly and 2 did not come for follow up. Progesterone acts better in anovular bleeding.

Combined OCP has great advantage of correcting any abnormality of menstrual cycle and producing regular bleeding as well as reducing the amount MBL. In the study by Begum, 11 patients were treated by low- dose oral contraceptive cyclically for 3-6 months. Of these patients, 8 resumed normal cyclical bleeding later on, failure occurred in 3 in the form of break through bleeding or irregular bleeding. In the study by Banerjee, 8 patients treated by OCP for 3-6 months in a cyclical bleeding and success rate were 100%[10].

In present study, 11 patients were advised to continue, OCP as they were taking pills and their bleeding was under control. 8 patients were symptom free for 3-6 months and in 3 patients, response was not satisfactory. Response was more or less similar to first reference.

Antifibrinolytic agents are potent inhibitor of fibrinolysis and have shown to normalize or reduce MBL in 50% case. It is effective in most types of menorrhagia, Milsum, Bonner and Sheppard18 treated 75 cases with tranexamic acid, of which 75% showed reduction in bleeding. In present study, 5 patients were treated by tranexamic acids. Among them 3 patients were symptom free for 3-6 months and 2 patients developed spotting. Response rate was quite satisfactory.

Hysterectomy is justified when conservative treatment fails and blood loss impaired the health of the patient. Presence of endometrial hyperplasia with atypia is an indication of hysterectomy. In the study, by Begum, 50 patients out of 80 (62.5%) underwent hysterectomy who had previous curettage but showed no improvement, 33 patients had direct hysterectomy and all of their families were complete. Banerjee in his study showed that 33 out of 50 patients (66%) underwent hysterectomy and 21 patients were 41-45 years of age and 12 were above 45 years. In the present study, 34 patients out of 50 had hysterectomy. Among them, 4 had hysterectomy as primary treatment and the remaining 8 patients had medical treatment followed by hysterectomy and 14 patients had medical treatment and curettage followed by hysterectomy and 8 patients had curettage[18].

Conclusion

The present study showed DUB most common in perimenopausal age group (>40 years). Histopathological evaluation of endometrium helps exclude the local causes and establishes the diagnosis of DUB, clinical correlation to histopathological findings and finally helps to determine the mode of management.

Reference

1. Pitkin J.Dysfunctional uterine bleeding. BMJ 2007; 334;1110-1111.
2. Dutta D.C. Dysfunctional Uterine Bleeding. Text book of gynaecology contraception. 5th edition. New Central Book Agency.
3. Whitfield CR. Dysfunctional Uterine Bleeding. Dewhurst's text book of obstetrics and gynaecology for postgraduates, 7th edition. Oxford k, Blackwell scientific publication 2007;145-156.
4. Bayer SR, DeChemey AR Clinical of major gynaecological operations IPGM&R among 100 cases. Dissertation. Bangladesh College of Physicians and surgeon. 1996.
5. Bayer SR, De-Cherney AH. Clinical manifestations and treatment of dysfunctional uterine bleeding. JAMA 1993; 269:1823-8.
6. Fayez JA. Dysfunctional uterine bleeding. Am Fam Physican 1982;25:109-15.
7. De Cherne A. Current obstetrics and gynaecology diagnosis and treatment. 10th edition, Lange medical books /Mc Graw-hill. 2007; 221-229.
8. Muzaffar M, Akhtar K, Yasmin S, Rehman M, Iqbal W, Khan M. Menstrual irregularities with excessive blood loss: a Clinicopathological correlation. J Pak Med Assoc 2005; 55:1-4. PMID: 16304868
9. Dr. Niloufar Begum, Shameem Afza. Clinical presentation, per operative findings and histopathological findings of Dysfunctional Uterine Bleeding of 100 cases" Dissertation. Dhaka, Bangladesh college of physicians and surgeon, 2003.
10. Choudhury Bani, Roy Banarjee. A study of complication and outcome of major gynaecological operations IPGM&R among 100 cases. Dissertation. Bangladesh College of Physician and Surgeons 1996;
11. Rahbar N, Faranoush M, Ghorbani R, Alsadat AB. Screening of Von Willebrand Disease in Iranian Women With Menorrhagia. Iran Red Crescent Med J. 2015; 17(1): e18244.
12. Kumar P, Malhotra N. Dysfunctional Uterine Bleeding. Jeffcoate's principles of gynaecology international edition, revised and updated by, 7th, edition. Jaypee Brothers MedicaL Publishers (P) Ltd 2008; 450-455.
13. Goldstein SR, Seltser I, Horan Ck, Snyder JR, Schwartz¬ LB. Ultrasonography based triage for perimenopausal patients with abnormal uterine bleeding. Am-J-Obsted-Gynecol. 1997; 177(1):102-8.
14. Layla S, Nabeel S; Histopathological Pattern of Endometrial Sampling Performed for Abnormal uterine bleeding. Bahrain Medical Bulletin, 2011;33(4):1-6.
15. Ellenson LH, Ronnett BM, Kurman RJ; Precursor lesions of Endometrial Carcinoma. In Kurman RJ, Ellenson LH, Ronnett BM editors; Blausteins Pathology of the Female Genital Tract. 6th edition, New York: Springer Verlag, 2011: 385 -92.
16. Reed SD, Newton KM, Clinton WL,Epplein M,Garcia R, Allison Ket al.; Incidence of Endometrial Hyperplasia. Am J Obstet Gynecol., 2009; 200(6): 678.el -678.6. 17. Dangal G; A study of endometrium of patient
17. Vercellini P, Cortesi I, Oldani S, Moschetta M, De Giorgi O, Crosignani PG. The role transvaginal ultrasonography and outpatients diagnostic hysteroscopy in the evaluation of patients with menorrhagia. Hum Reprod. 1997;12(8):1768-71.
18. BonnarJ, Sheppard BL. Treatment of menorrhagia during menstruation: randomized controlled trial of ethamsylate, mefenamic acid, and tranexamic acid. BMJ 1996; 313(7073):579-82