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Clinco-Pathological Patterns in Women with Dysfunctional Uterine Bleeding

Rehana Khan[1], Rana K Sherwani[2], Safia Rana[3], Seema Hakim[1], Zeeba S Jairajpuri[3]

1. Dept. of Obstetrics and Gynaecology, JN Medical College, AMU, Aligarh, India

2. Dept. of Pathology, JN Medical College, AMU, Aligarh, India

3. Dept. of Pathology,Hamdard Institute of Medical Sciences and Research, Jamia Hamdard, Hamdard Nagar, New Delhi, India

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ABSTRACT

***Background*:** The term dysfunctional uterine bleeding (DUB) refers to any abnormal bleeding from the uterus, unassociated with tumour, inflammation and pregnancy. The histological diagnosis of DUB is very essential for adequate management especially in perimenopausal and postmenopausal females. The present study was undertaken with the aim of evaluating DUB in various age groups, carry out histopathological study of the endometrium and analyze its clinic-pathological patterns.

***Methods*:** The study included 500 cases of atypical uterine bleeding, out of which 120 cases of DUB were included based on clinical features and detailed investigations. Study was conducted in Jawaharlal Nehru Medical College, Aligarh Muslim University, between March 2003 to December 2004 Endometrial tissue was collected by D&C procedure and the samples were sent for histopathological evaluation by pathologist.

***Result*:** Hyperplasia was the commonest endometrial pathology (20.5%) followed by luteal phase insufficiency (15.6%) and secretory endometrium (13.7%). Endometritis including tubercular endometritis (12.7%), post abortal (5.8%), proliferative (6.8%), polyp (3.9%), atrophic (3.9%), exogenous hormone changes (2.9%) and anovulatory cycles(6.8%) made up for the remaining lesions.

***Conclusion*:** DUB occurs secondary to a wide variety of functional and structural abnormalities, warranting a thorough evaluation especially in perimenoupausal females. Menorrhagia is a common symptom and the most likely etiology relates to the patient's age. Significant number of endometrial samples revealed pathology rendering endometrial curetting and biopsy an important procedure. Cervical cytology is a valuable adjunct however histopathology remains the gold standard in diagnosis.

***Corresponding Information*:** Dr Zeeba S Jairajpuri Department of Pathology, Hamdard Institute of Medical Sciences and Research, New Delhi, 110062. India. Email: : zeebasj@rediffmail.com Tel: 011-26059688

Introduction

Excessive uterine bleeding is one of the most common complaints encountered in clinical practice. The social and economic cost of menorrhagia is considerable. Over the years menorrhagia has become a frequent complaint possibly due to easy accessibility to health

services (1). DUB is defined as abnormal bleeding from the uterus, unassociated with tumor, inflammation and pregnancy. The term DUB applied to any abnormal bleeding including disturbances of the menstrual cycle, regular/ irregular uterine bleeding and alteration in the amount or duration of menstrual blood loss, but most commonly implies excessive regular menstrual bleeding or essential menorrhagia. Management of DUB is not complete without tissue diagnosis especially in perimenopause and post menopause (2).

The broad spectrum of causes of abnormal uterine bleeding includes both genital and extra genital lesions. Diagnosis of DUB is given to the group of patients in whom there is no definitive underlying lesion. It can occur at any time between menarche and menopause, in ovulatory and anovulatory cycles. It has been known to be associated with almost any type of endometrium and ranging from normal endometrium to hyperplasia, irregular repining, chronic menstrual irregular shedding and atrophy (3, 4).The incidence of abnormal endometrium findings does not necessarily indicates the true incidence of abnormal endometrial bleeding because it greatly depends upon the time when the endometrial biopsy as performed in relation to cycle & bleeding.

The aim of study was to evaluate DUB in various age groups and carry out histopathological study of the endometrium. Lateral vaginal wall cytology for hormonal assessment was also undertaken wherever possible.

Material and Methods

The present study was conducted in Jawaharlal Nehru Medical College, Aligarh Muslim University, between March 2003 to December 2004 by collaboration of Department of Pathology and Obstetric and Gynecology. Out of the total 500 cases of abnormal uterine bleeding (AUB), 120 cases of DUB were included in the study. All patients were selected based on clinical details along with the relevant investigations. Patients with change in bleeding pattern such as increase in duration or intermenstrual bleeding were included in the study while those with evidence of pelvic pathology, hormonal therapy within 3 mo, intrauterine contraceptive device were excluded.

Sample for cytology were collected in the premenstrual phase. Ayer's spatula was used to take the sample from ectocervix and T-zone; smears made were fixed in 95 % alcohol with ether. Lateral Vaginal wall cytology sample was collected and sent for Papanicolaou staining. Endometrial tissue collected by sampling procedures such as endometrial biopsy, dilatation and curettage (D&C) and fractional curettage were sent to the pathology lab for evaluation. The gross morphology 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 sent for microscopic examination by the pathologist.

Results

Out of a total of 500 cases of abnormal uterine bleeding, 120 cases qualified to be of DUB with isolated endometrial pathology as a cause of abnormal uterine bleeding. The rest of the patients were excluded. The age of 120 patients ranged from 13-55 years, the patient were categorized into 5 groups with maximum of 39 cases (32.5 %) in the age between 30-39 years, whilst only 8

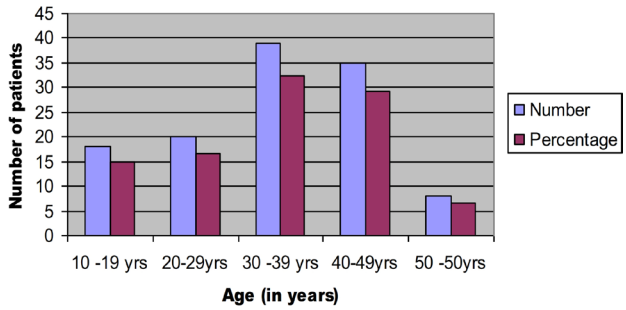

Fig. 1
Distribution of patients according to age groups

cases (6.6%) were in the age group of 50-59yrs (Fig. 1).

Chronically the patients presented with varied complaints ranging from hypomenorrhea to menorrhagia. The most common presenting complaint was of menorrhagia (55.8%) followed by oligomenorrhoea (11.6%), polymenorrhagia (6.6%) and menometrorrhagia (6.6%). Polymenorrhoea and metrorrhagia accounted for 5% each while continuous bleeding per vaginum was seen in 5.8% cases, the least number of patients (1.6% each) presented with post-menopausal bleeding and hypomenorrhoea. An age wise distribution of the bleeding pattern (Table 1) revealed menorrhagia as the most common presentation across all age groups.

We also categorized the patients of DUB on the basis of parity, of these nulliparous which included unmarried females were 21.6%, low parity comprising of para1 and 2 were 19.1% whilst the maximum representation of 38.3% was seen in multiparous para3and para 4 women. Grandmultiparous women i.e. para 5 and more were 20.8% of the cases.

Out of 120, 102 patients were taken up for D & C and the endometrial tissue was sent for histopathological examination. The maximum numbers of cases were of endometrial hyperplasia (20.5%) followed by luteal phase insufficiency (15.6%) and secretory endometrium (13.7%). The least number of cases were accounted for hormonal therapy changes. (Table 2)

Lateral vaginal wall cytology was done in 75patients (62.5%), maximum number of cases showed oestrogen effect found in 37 patients (49.3%) progesterone was found in 20 cases (26.6%), 1 patient (1.3%) had a post ovulatory smear and 15 cases (20%) made up for inflammatory smear. The distribution of cases is seen in Fig. 2.

Table 1
Clinical Presentation of DUB In different Age Groups

Bleeding pattern	10-19 yr	20-29 yr	30-39 yr	40-49 yr	50-59 yr	Total
Menorrhagia	12	9	24	18	4	67
Polymenorrhagia	-	3	2	2	1	8
Polymenorrhoea	2	-	2	2	-	6
Metrorrhagia	1	1	2	2	-	6
Menometrorrhagia	-	2	2	4	-	8
Oligomenorrhea	1	5	4	4	-	14
Continuous bleeding	1	-	3	2	1	7
Post menopausal	-	-	-	-	2	2
Hypomenorrhoea	1			1	-	2
Total	18	20	39	35	8	120

Table 2
Histopathological Diagnoses of Endometrial Samples in different age groups

Histopathological findings	10-19 yr	20-29 yr	30-39 yr	40-49 yr	50-59 yr	Total
Endometrial hyperplasia	-	2	7	9	3	21
Endometrial polyp	-	-	-	3	1	4
Secretory phase	-	4	5	5	-	14
Proliferative phase	-	2	2	3	-	7
Luteal phase insufficiency	-	2	11	3	-	16
Irregular ripening	-	-	2	2	-	4
Irregular shedding	-	-	2	-	-	3
Post abortal curettage	-	4	1	1	-	6
Chronic endometritis	-	1	1	7		9
Atrophic endometrium	-	-	-	1	3	4
Progesterone therapy changes	-	-	-	3	-	3
TB endometritis	-	1	1	2	-	4
Anovulatory cycles	-	2	3	2	-	7
Not done	18	-	-	-	-	18
						120

A comparison of histopathological findings and hormonal cytology was drawn whereever available, it was possible in 73 cases. Hyperestrogenic states on histopathological examination had estrogenic smear on vaginal cytology. This was seen in 85.5% of endometrial hyperplasia cases and all cases of endometrial polyp, proliferative phase and anovulatory cycles however only 1 case (12.5%) of endometritis had estrogenic smear. Progesterone effect on smear was seen predominantly in cases of secretory endometrium followed by luteal phase defects and irregular ripening while equal numbers were seen in endometritis and atrophic cases, 1 case was of exogenous hormone therapy.

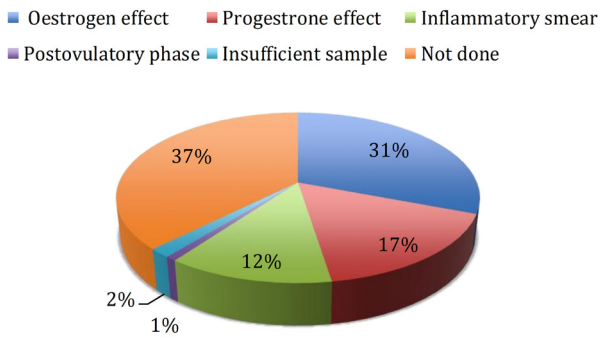

Fig. 2
Distribution of DUB cases according to cytology

Discussion

The problem of DUB in the absence of overt uterine pathology, endocrine or hematological disorder is a common reason for consultation in gynecology OPD (5). DUB can occur any time between puberty to menopause and may be ovulatory or anovulatory. A history of excessive bleeding with regular menstrual cycles is usually associated with ovulation. An anovulatory pattern of bleeding is associated with intermenstural erratic bleeding, seen typically at puberty or in women in mid 30s onwards.

In women of childbearing age, detailed history thorough physical examination and appropriate investigation are main tools to rule out cause of bleeding. DUB is a diagnosis of exclusion (6,7). The usage of D & C to obtain endometrial curettings can be a diagnostic as well as therapeutic procedure (8).

The most likely etiology relates to the patient's age as to whether the patient is premenstrual, premenstrual or postmenopausal (9). Authors suggest DUB occurs most often at extremes of reproductive years, a time when anovulation is common (10). Our patients ranged from 13 – 55 years of age. Maximum representation was of the age group of 30-39 yr (32.5%) closely followed by patients between 40-49 yr (29.1%). Females < 20 years accounted for 15% of the total study group. These findings are in concurrence with other studies. Gleeson 1949 reported an age range of 28-49 yr as the most common group (11). Sutherland in his series on DUB reported 57% patients between the age group 20-40 yr (3), whilst in the present study 49.1% patients comprised this age group. Number of patients more than 20 years varied in different studies, 4% were seen in one of the studies, only 1.5% accounted in another study while it was 15% in our study (3,7).

The presenting complaints ranged from hypomenorrhea to menorrhagia. On analyzing, the distribution of patients according to bleeding pattern, the most common presenting complaint was of menorrhagia (55.8%). This compared favorably with other studies where menorrhagia featured as the dominant complaint (12-14). However metrorrhagia was present in lesser cases as compared to 48% in another study (15). A steady occurrence of most disorders increasing with advancing age was seen. Commonest age group presenting with excess bleeding was 30-39 years as compared to 41-50 yr in other series (7,15).

We also categorized the patients of DUB on the basis of parity. Mutiparous women have a slightly more average blood loss as compared to nulliparous. 38.3% women of parity three and parity four presented with DUB in the present study. A similar trend of 35.6% has been reported in multiparous women (6). However, in cases of grand multiparous women DUB was observed in 40.6% cases, which was in discordance with the present series where it was seen in 20.8% women (6). Reports in literature favor a higher number of DUB patients seen in parity two followed by parity three (16,17). Parity per se has limited role in DUB and its importance lies in relation to patient management.

Histopathological evaluation was done in 102 (85%) out of 120 patients. Hyperplasia was the commonest endometrial pathology (20.5%) followed by luteal phase insufficiency (15.6%) and secretory endometrial (13.7%). Endometritis including tubercular endometritis (12.7%), post abortal (5.8%), proliferative (6.8%), polyp (3.9%), atrophic (3.9%), exogenous hormone changes (2.9%) and anovulatory cycles (6.8%) made up for the remaining lesions.

Endometrial hyperplasia, the commonest histopathological diagnosis was observed in 20.5% cases, all were simple glandular hyperplasia. In a similar study, 18.3% cases were diagnosed as having hyperplasia of different types and two thirds of it fell in the perimenopausal age group (18). A similar trend of 24.7% endometrial hyperplasia cases has been observed by some authors. (14) A favourable comparison can be drawn with the present study. Reports in literature show a variable incidence of endometrial hyperplasia, which varies from 6.66% through 10.5% to 15% (19-21). The variation could be attributed to socioeconomic status and occurrence of risk factors like obesity, diabetes, sedentary life style and early diagnosis. Identification of endometrial hyperplasia is important as it is thought to be a precursor of endometrial carcinoma. The incidence of endometrial hyperplasia peaks around perimenopausal and postmenopausal women (22). The maximum number of patients in our study were in the perimenopausal group [(35)29.1%] and lesser number in the postmenopausal age group [(8) 6.66%] Abnormal uterine bleeding in these age groups requires further evaluation to exclude malignancies.

Luteal phase insufficiency is a term used to describe a state characterized by relative or absolute abnormality in progesterone secretion following

ovulation. This was the second most common diagnosis, making up for 16 cases (15.6%). The condition is most accurately expressed in terms of hormonal abnormality but may be associated with a number of morphological features. Amongst the functional disorders of endometrium, which featured in the histopathological diagnosis, irregular ripening (3.9%) and irregular shedding (2.9%) both of which are morphological features of luteal phase insufficiency along with anovulatory cycles (6.8%) were the other pathologies observed.

Secretory phase endometrium was found in 13.7% cases comparing favorably with 14% and 22% in other studies (23, 24). However substantially higher number of cases have been reported in other studies 30.8% and 35.4% (6,14) Proliferative endometrium on the other hand was seen in only 6.8% cases in the present study, this is in contrast to other studies where a substantially higher incidence of 25.8% , 46.6%, 54% has been reported (6,14,24).

Amongst women undergoing endometrial biopsy the prevalence of endometrial polyps is 10-24%, the incidence rises with increasing age, peaks in the fifth decade and gradually decreases after menopause. The present study showed an incidence of 3.33% with majority of the patients in the age group 40-49 years. This was in concordance with 1.3% cases with polyps in the perimenopausal age group (18). However other studies have shown a progressively increased detection pattern of polyps in the older age group (20).

Chronic nonspecific endometritis along with tubercular endometritis comprised the inflammatory lesions. A total of 9 cases (8.8%) of chronic endometritis were seen in our study with a higher detection rate in the age group 40-49 yr, (6.8%) similar to 7.2% in another study (20). Chronic endometritis usually follows pregnancy, intrauterine contraceptive devices insertion and abortion. It may be due to viral, chlamydial or gonococcal infections. Tubercular endometritis on the other hand is known to be associated with infertility and menorrhagia, 4 cases (3.9%) of tubercular endometritis were seen in the present study.

The exact cause of bleeding in atrophic endometrium is not known, it is postulated to be due to anatomic vascular variation or local abnormality in hemostatic mechanism (7). In the present study 4 cases (3.9%) of atrophic endometrium were seen predominantly in the age group 50-59 years in concordance with other studies but lower than some (7,24). Exogenous hormone effect was seen in three patients (2.9%) with pattern of progesterone therapy changes, similar to 2.3% and 2.8% in other studies (14, 25). Uterine bleeding due to pregnancy related complication was observed in younger women (5.9%) most of who were in the 20-29 years age group. This was in agreement with 5% pregnancy related complication in Nepal (18). It is suggested that in patients in the reproductive age group who present with abnormal uterine bleeding, complication of pregnancy should be ruled out.

Lateral vaginal wall cytology was done wherever possible and it was available in 73 patients. A comparative analysis of histopathological and cytological features was done in these patients, estrogenic cytology was seen in lesions of hyperestrogenic status on histopathology. No relevant study was available to the best of our knowledge to this effect. Routine cytological examination may be helpful in establishing a confident diagnosis.

Conclusion

Excessive menstrual blood loss is a common reason for women to seek medical help and leads to large demands in health resources. Dysfunctional uterine bleeding occurs secondary to a wide variety of functional and structural abnormalities, thorough evaluation is warranted especially in women of perimenoupausal age group. Menorrhagia is a common symptom and

the most likely etiology relates to the patient's age. Significant number of endometrial samples revealed pathology rendering endometrial curetting and biopsy an important procedure. Cervical cytology is a valuable adjunct however histopathology remains the gold standard in diagnosis.

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