ISSN 2515-8260 Volume 09, Issue 02, 2022

Clinicopathological study of abnormal uterine bleeding in perimenopausal women attending a tertiary care district hospital

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Abstract

Background: Abnormal Uterine Bleeding (AUB) is defined as any bleeding that does not correspond with the frequency, duration or amount of blood flow of a normal menstrual cycle. Endometrial biopsy is important in perimenopausal age group women (40-55 years) to rule out endometrial pathology and malignancy. This study was done to assess Clinicopathological aspects and different histopathological patterns related to Abnormal Uterine Bleeding as no studies have been done in this region of Karnataka, India.
Methods: This is a cross sectional study done from 2019 to 2020. All female patients in the perimenopausal age group presenting with symptoms of AUB were included. Patients less than 40 years of age and endometrial tissues inadequate for opinion on microscopy were excluded. Relevant history and clinical data regarding pattern and duration of abnormal uterine bleeding was retrieved. Endometrial biopsy tissues was processed and stained by H&E. The diagnosis was done and results analysed.
Results: Present study included 94 biopsies of which 6 biopsies were inadequate for opinion. The most common age group presenting with AUB was 40-45 years (53.40%). The most common symptom was menorrhagia. The commonest histopathological pattern among all the perimenopausal age was disordered proliferative endometrium followed by simple hyperplasia without atypia. Other patterns were proliferative endometrium, secretory endometrium, simple hyperplasia, carcinomas etc. The commonest etiology of AUB was Dysfunctional Uterine Bleeding (46.59%) followed by Endometrial hyperplasias. (23.86%)
Conclusions: Correlation with clinical history, radiological investigations along with endometrial biopsy establishes etiology and diagnosis for patients with AUB.

Keywords: Endometrium, biopsy, endometrial hyperplasia, carcinoma

Introduction

Menstruation is a cyclical bleeding from the uterine endometrium in response to ovarian

ISSN 2515-8260 Volume 09, Issue 02, 2022

hormones which is under the control of hypothalamo pituitary-ovarian-axis. Abnormal uterine bleeding (AUB) is defined as bleeding pattern that differs in frequency, duration and amount from a pattern observed during a normal menstrual cycle or after menopause abnormal uterine bleeding is a very common gynecological condition that affects all age groups. One third of patients attending gynecology OPD present with complaints of abnormal uterine bleeding Under the category of AUB, further definitions may be subdivided based on volume of menstruation, regularity, frequency, duration, chronicity and timing related to reproductive status The abnormal bleeding can be caused by a wide variety of disorders and may be the common presenting complaint in patients with malignant or premalignant endometrial lesion [1]. It has been estimated that around 6% of women aged 25-44 years consult their general physician due to excessive menstrual loss every year. One of the major causes of excessive or erratic menstruation is inadvertent use of contraceptive modalities. In the past, repeated childbirth and lactation caused prolonged amenorrhea, thus alleviating proliferative activity of endometrium. AUB is of concern because it may have serious medical and social consequences, as bleeding may cause anemia, undue disruption of women's daily activities and sexual life. Endometrial assessment is performed to diagnose malignancy or pre-malignant conditions and to evaluate the hormonal influences of the endometrium. It is important to evaluate the endometrial histopathology in a woman who has no improvement in her bleeding pattern following a course of medical therapy of three months [12]. It is well established that AUB is significant cause of morbidity, but the underlying causes of AUB may vary from one region to another [2].

Perimenopause (often referred to as the menopausal transition) is the time period during which women go from premenopause (the reproductive years) into menopause. The median length of perimenopause has been estimated to be any time between 4 and 11 years, which includes the year following the last cycle. Women are most likely to exhibit signs of perimenopause sometime in their 40s, although some women exhibit signs as early as their 30s or as late as their 50s. There are epidemiological surveys which suggest that approximately as many as 10% of women in their early 30s could be approaching their perimenopause transition [3]. Peri-menopausal is the most common age group for Abnormal Uterine Bleeding and most of the cases were para <2 [1]. A recent study reported higher incidence of AUB with increasing parity and the incidence of AUB among peri menopausal women ranged from 60% to 90%. These variations may be due to different demographic characteristics [1].

Histopathololgical study of the endometrium is the most common investigation employed by gynaecologists to evaluate abnormal uterine bleeding and is particularly important in postmenopausal women to rule out malignancy and thereby plan for treatment modalities. This study is therefore conducted with the objectives to determine the spectrum of lesions of the endometrium with respect to age and clinical features. The other objective was to determine different histological patterns of endometrium in perimenopausal age group women with abnormal uterine bleeding.

Materials and Methods

The present cross-sectional study was done in Department of Pathology, Kodagu Institute of Medical Sciences and Madikeri. All female patients in the perimenopausal age group (40-55 years) [4] presenting with symptoms of abnormal uterine bleeding to OPD and wards of Department of Obstetrics and Gynaecology, Kodagu Institute of Medical Sciences, Madikeri were included in this study. Relevant clinical data regarding age, pattern and duration of abnormal bleeding, menstrual history and obstetric history, use of exogenous hormones, physical and gynecological examination findings, lab investigation results and sonological findings were obtained from case records. The following were the exclusion criteria: Patients

ISSN 2515-8260 Volume 09, Issue 02, 2022

less than 40 years of age, patients who presented with abnormal uterine bleeding due to non-endometrial causes like lesions of the myometrium and adnexa and patients with uterine bleeding due to intra-uterine Devices. Dilatation and Curettage & Endometrial Biopsy were necessary to obtain endometrial tissue.
All the endometrial sample specimens were fixed in 10% formalin, processed and embedded in paraffin and 3-4 μ thick sections were made. Sections were stained with hematoxylin and eosin stain. The data was recorded using Microsoft Excel (2007 version) and analysed using SPSS software. The results are explained in frequency and percentage.

Results

Present study included 94 biopsies of which 6 biopsies were inadequate for opinion. The most common age group presenting with AUB was 40-45 years (53.40%) followed by 46-50 years as shown in Table 1. The most common symptom was menorrhagia. The commonest histopathological pattern was disordered proliferative endometrium followed by simple hyperplasia without atypia. Other patterns were atrophic endometrium, polyp, endometritis, deficient secretory phase, carcinomas etc as shown in Table 2. The commonest etiology of AUB was Dysfunctional Uterine Bleeding (46.59%) followed by Endometrial hyperplasias. (23.86%).

Table 1: Age distribution of various Endometrium lesions

Diagnosis	**Age Range**		
	40-45 years	**46-50 years**	**51-55 years**
Disordered Proliferative Endometrium	17	4	0
Simple endometrial hyperplasia without atypia	11	7	1
Proliferative endometrium	12	6	0
Secretory endometrium	3	4	1
Irregular	2	3	1
Endometrial Polyp	1	3	2
Carcinoma	1	2	1
Cystic glandular hyperplasia	0	2	0
Atophic endometrium	0	0	1
Endometritis	1	0	0
Deficient Secretory	0	1	0
Inactive	0	0	1
Total	48	32	8

Table 2: Spectrum of Endometrial lesions

Endometrial patterns obtained on histopathology Endometrial patterns	**No. of cases**	**Percentage of cases**
Disordered Proliferative Endometrium	21	23.9%
Simple endometrial hyperplasia without atypia	19	21.6%
Proliferative endometrium	18	20.5%
Secretory endometrium	8	9.1%
Irregular	6	6.9%
Endometrial Polyp	6	6.9%
Carcinoma	4	4.6%
Cystic glandular hyperplasia	2	2.2%
Atrophic endometrium	1	1.1%
Endometritis	1	1.1 %
Deficient Secretory	1	1.1%
Inactive	1	1%
Total	88	100%

ISSN 2515-8260 Volume 09, Issue 02, 2022

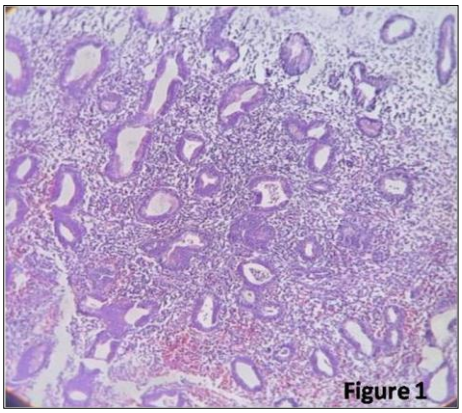

Fig 1: Sections studied show few dilated and irregular glands randomly interspersed among proliferative endometrial glands with normal gland to stoma ratio. (H & E stain, 10 X)

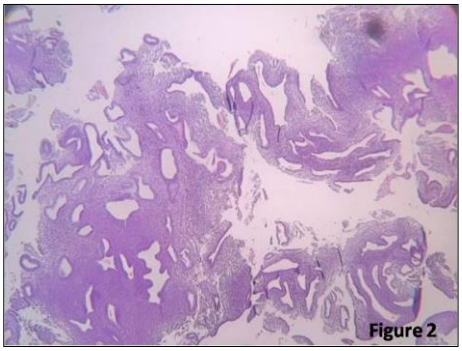

Fig 2: Sections studied shows back to back endometrial glands lacking intervening stroma hyperplastic changes suggestive of Simple Hyperplasia without Atypia. (H & E Stain, 10 X)

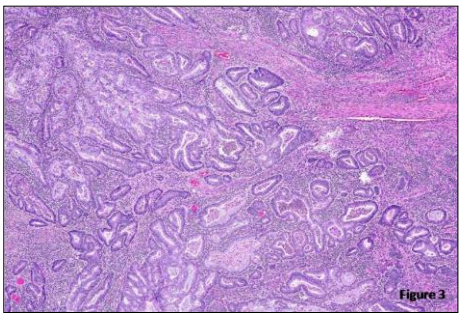

Fig 3: Sections studied shows tumour comprised of cells arranged in papillary and villoglandular structures with increased gland to stroma ratio suggestive of endometrial carcinoma. (H&E Stain, 40 X)

Discussion

AUB is a common condition accounting for 25% of gynecological operations and 20% of outpatient visits [5]. The diagnosis is different among various age groups and histopathological examination helps in diagnosis. Previously, the cause of abnormal uterine bleeding was thought to be chronic inflammation. Now, it has been clear that abnormal uterine bleeding is due to various causes ranging from functional to malignancy [6]. Abnormal uterine bleeding occurring as heavy, prolonged or acyclic flow at menopausal transition or as spotting or minimal bleeding at post-menopausal period may be alarming and needs thorough evaluation, since this may be the only clinical manifestation pointing towards endometrial cancer [7] Endometrial carcinoma is the most common malignancy of the female genital tract, ranking second to carcinoma cervix. Overall, 2% to 3% women develop endometrial

carcinoma during their lifetime. It occurs primarily in postmenopausal women and is increasingly virulent with advancing age. Any factor that increases exposure to unopposed estrogen increases the risk for endometrial cancer. Majority of women with endometrial cancer present with postmenopausal bleeding (90%) but in only about 15% of women is endometrial cancer the cause of postmenopausal bleeding [8].

The commonest age group presenting with excessive bleeding in our study was 40-45 years. A similar incidence was reported by Yusuf *et al*., [9] and Muzaffar *et al*, [10].

In present study, most common menstrual disturbance found was menorrhagia in 47% cases. This may be explained as many patients in perimenopausal age group have anovulatory cycles resulting in menorrhagia. Our findings are consistent with studies by Sajitha K *et al*., [11], Aseel Ghazi Rifat *et al*., [12], Rajshri P. Damle *et al*., [13] Usha G. Doddamani *et al*. [14] in which the most common symptom was menorrhagia.

In majority of the patients AUB was diagnosed due to Disordered Proliferative Endomterium (23.9%) in origin followed by Simple endometrial hyperplasia without atypia (21.6%), uterine fibroids (20.5%) and In a study Soleymani *et al*. [15] included patients of all ages, benign findings included disordered proliferation (93.4%), polyps (3.9%), hyperplasia (2.5%), and malignancy (0.7%) In a study by Simender Mesci-Haftaci *et al*., [16] it was found that the majority of patients had benign findings (44.8%), followed by polyps (30%), endometrial hyperplasia (24%) and adenocarcinoma (1.2%).

The second most common lesion was Simple Endometrial hyperplasia (21.6%) which is in concordance with Rajshri P. Damle *et al*., [13] (23.86%), Dangal G *et al*., [17] (23%) and Slobada L *et al*., [18] (22.6%). Doroiswami S *et al*., [19] (68%) observed high incidence of endometrial hyperplasia in 40-49 years of age group. Identification of endometrial hyperplasia is important because they are thought to be precursors of endometrial carcinoma. Two cases of endometrial carcinoma were found in peri menopausal age group. The risk of development of endometrial cancer is 29% in patients with complex atypical hyperplasia and 2% in patients with hyperplasia but without atypia this is to emphasize the fact that all patients with endometrial hyperplasia diagnosed on ultrasound must have a thorough endometrial evaluation by Dilatation and Curettage [3].

In present study of perimenopausal age group, proliferative endometrium was observed in 20.5% of cases which is very much in alliance with study done by Rajshri P. Damle *et al*., [13] reported 34.09% while Sujata Jetley *et al*., [20] reported 30.6% of proliferative endometrium in peri-menopausal age group study. Bleeding in the proliferative phase may be due to anovulatory cycle, such cases shows progressive rise of estrogen to comparatively high levels, which is then followed by a sudden fall in estrogen due to feedback inhibition of pituitary or of FSH secretion and bleeding results.

Conclusion

Correlation with clinical history, radiological investigations along with endometrial biopsy establishes etiology and diagnosis for patients with AUB. Benign lesions of endometrium and myometrium are the most common causes for abnormal uterine bleeding in perimenopausal women, but the possibility of endometrial hyperplasia and particularly the cancers of uterus must be considered particularly with the advancing age. A comprehensive clinicopathological study will usually help in arriving at the correct diagnosis. However, in view of the wide array of causes, abnormal uterine bleeding continues to be a diagnostic challenge, especially during perimenopause.

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