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Original Research Article

An analysis of endometrial bleeding patterns in perimenopausal women

Mukhopadhyay Indrani¹, Rao P. S.^{1*}, Nataraj S.¹, Manash Biswas²

¹Department of Obstetrics and Gynecology, Command Hospital AF, Bangalore, Karnataka, India

²Department of Obstetrics and Gynecology, Military Hospital, Roorkee, Uttarakhand, India

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*Correspondence:

Dr. Rao P. S.,

E-mail: doctorpsrao@gmail.com

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ABSTRACT

Background: Perimenopause is the period surrounding menopause characterized by ovulatory dysfunction and menstrual irregularities. Taking into consideration the importance of perimenopause and its consequences, we decided to study this topic in order to know the different menstrual irregularities in relation to age, the spectrum of endometrial histopathology, in relation to various gynaecological conditions as per the PALMCOEIN classification of AUB.

Methods: The study population comprised of 100 women in the age group of 40- 59 years who reported to our tertiary care centre of Armed Forces for evaluation of abnormal uterine bleeding. The study was a community based cross - sectional descriptive study. Patients were examined, using one of the three techniques – Dilatation and curettage, suction aspiration and hysteroscopy and endometrial biopsy.

Results: Out of the 100 women evaluated for perimenopausal bleeding, heavy menstrual bleeding was the commonest in 53% cases. The maximum no. of cases was in 40-44-year age group (57.44 %). The clinical diagnosis of fibroid uterus was found in 45% cases, AUB (O) in 36% cases, AUB (Polyp) in 8% cases, AUB (Adenomyosis) in 9% cases and AUB (Malignancy) in 2% cases. On endometrial curettage, proliferative type of endometrium was found in 43% cases, secretory type in 18% cases and hyperplasia was found in 37% cases. Out of 2 cases of atypical hyperplasia 1 case each (50%) was found in the age group of 50-54 years and 55-59 years, respectively.

Conclusions: In the present study, there was good correlation between abnormal uterine bleeding, clinical diagnosis and histopathological findings.

Keywords: Abnormal uterine bleeding, Carcinoma endometrium, Endometrial hyperplasia, Perimenopause

INTRODUCTION

Perimenopause is the period surrounding menopause, which is characterized by decreasing ovarian function, inconsistent ovulation with ultimately loss of ovulatory function, resulting in menstrual irregularities which includes various forms of abnormal uterine bleeding. This ill- defined period of life was defined by the World Health Organization (WHO) as the period 2-8 years preceding menopause and 1 year after the final menses. Estrogen levels are overall higher in this age group in response to the increase in FSH secretion. But it is

characterized by insufficient progesterone secretion. These endocrine changes correlate with menstrual irregularities.

In terms of symptomatology, the perimenopause may be even more important than either early or late menopause. Major gynaecological problems seen during the perimenopause include menstrual bleeding disorders and vasomotor symptoms.

Most women have cycles that last from 24 to 35 days, but at least 20 % of women experience irregular cycles.¹

Figure 1 given below is commonly used to explain the various organic causes of abnormal uterine bleeding.²

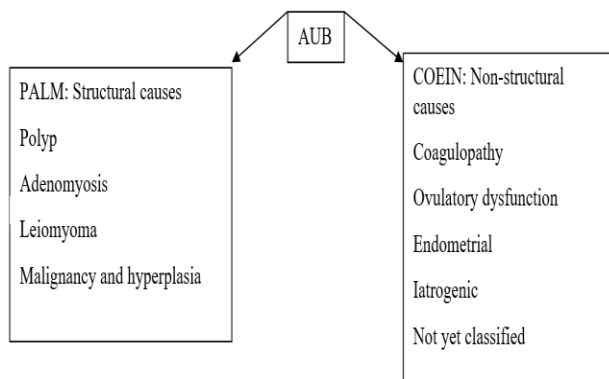


Figure 1: FIGO classification system (PALM-COEIN) for causes of abnormal uterine bleeding.

Abnormal uterine bleeding accounts for repeated visits of a lady to the gynaecologist and this requires intensive evaluation to rule out the various organic and non-organic causes of AUB to finally arrive at the proper management.

Diagnostic procedures to evaluate perimenopausal bleeding include dilatation and curettage, endometrial biopsy, transvaginal sonography and/or hysteroscopy. Taking into consideration the importance of perimenopause and its consequences, we decided to study this topic in order to know the different menstrual irregularities especially heavy menstrual bleeding, frequent and heavy menstrual bleeding, frequent menstrual bleeding, intermenstrual bleeding, prolonged bleeding etc. with which the patients present; common gynaecological conditions with stress on fibroids, AUB(O), adenomyosis, polyps and carcinoma in relation to age; the spectrum of endometrial histopathology to include atrophic, proliferative and secretory endometrium, various types of hyperplasia (simple, complex and atypical) by using diagnostic techniques of dilatation and curettage, endometrial biopsy and hysteroscopy.³

METHODS

This study was a community based cross - sectional descriptive study done to study the correlation between clinical and histopathological patterns of the endometrium in perimenopausal women with uterine bleeding, to find out the incidence of benign and/malignant lesions as the cause of perimenopausal bleeding and also was used in screening of symptomatic perimenopausal women to rule out premalignant lesions or endometrial cancer.

The study was conducted in Command Hospital Air Force Bengaluru from 01 Sep 2013 to 30 Aug 2015. The study population comprised of 100 women in the age

group of 40- 59 years who had come to tertiary care centre for evaluation of abnormal uterine bleeding and were selected from a duly constituted sampling frame using a random number table.

All women presenting with symptoms of heavy menstrual bleeding, frequent and heavy menstrual bleeding, frequent menstrual bleeding, intermenstrual bleeding and continuous bleeding were included. They were evaluated for benign reproductive tract lesions to include leiomyoma uteri, endometrial polyp and adenomyosis. Thereafter categorized to include histopathological patterns of endometrial neoplasia like Simple, complex and atypical endometrial hyperplasia and endometrial carcinoma.

Proliferative and Secretory types of endometrium presenting with different clinical features and uterine lesions were also included. All women with coagulation disorders (thrombocytopenia, von willebrand's disease, and leukaemia), Hypothyroidism, Liver diseases and those on Hormone therapy and Contraceptive devices or injections, were excluded. Also, women with symptoms of infrequent menstrual bleeding and shortened menstrual bleeding were excluded.

Consent was taken from each patient before commencing the study. After a detailed history taking and examination, using a random number table all women were randomly assigned to one of the three techniques – Dilatation and curettage, endometrial suction aspiration and hysteroscopy for assessing the uterine cavity to determine various endometrial bleeding patterns.

RESULTS

Observations were made after assessment of the 100 women

Table 1: Distribution of menstrual disorders in patients with perimenopausal bleeding.

Menstrual disorder	No. of cases	%
Heavy menstrual bleeding	53	53
Intermenstrual bleeding	21	21
Frequent menstrual bleeding	9	9
Frequent and heavy menstrual bleeding	15	15
Prolonged menstrual bleeding	2	2
Total	100	100

Heavy menses was the commonest symptom as seen in 53% cases, intermenstrual bleeding was seen in 21% cases, frequent menses in 9% cases, frequent and heavy menses in 15% cases and prolonged bleeding in 2% cases. This has been depicted in Table 1.

Figure 2 shows that the commonest presentation in all the age groups is heavy menstrual bleeding followed by intermenstrual bleeding.

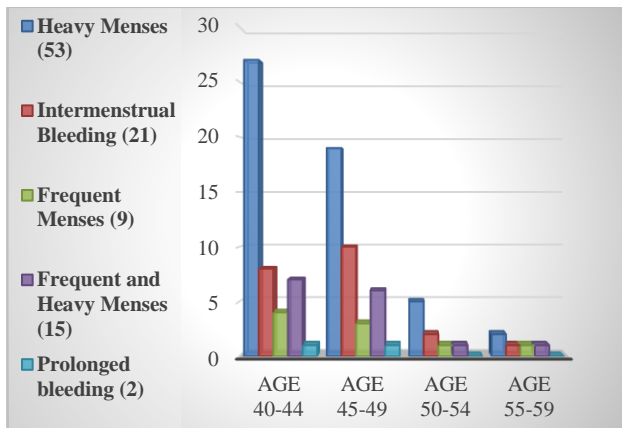


Figure 2: Clinical presentation of abnormal uterine bleeding according to various age groups.

The maximum no. of cases (56) of a particular pathology in 40-44-year age group followed by 45-49-year age group (35 cases). In 40-44-year age group there were 30 cases (66.66%) of fibroid uterus followed by 11 cases (24.44%) in 45-49-year age group.

In 40-44-year age group there were 20 cases (55.55%) of AUB followed by 15 cases (41.66%) in 45-49-year age group. In 40-44-year age group there were 2 cases (22.22%) of adenomyosis. In 40-44-year age group and 45-49-year age group there were an equal no of cases of polyp -4 each (50%).

In 55-59-year age group there were 2 (100%) cases of Ca endometrium. The above values have been depicted in Table 2.

Table 2: Correlation between clinical diagnosis and age.

Age group	40-44	45-49	50-54	55-59	Total
AUB (Leiomyoma)	30 (66.66%)	11 (24.44%)	3 (6.66%)	1 (2.22%)	45
AUB (Ovulatory)	20 (55.55%)	15 (41.66%)	1 (2.77%)		36
AUB (Adenomyosis)	2 (22.22%)	5 (55.55%)	2 (22.22%)	-	9
AUB (Polyp)	4 (50%)	4 (50%)	-	-	8
AUB (Malignancy)	-	-	-	2 (100%)	2
Total	56	35	6	3	100

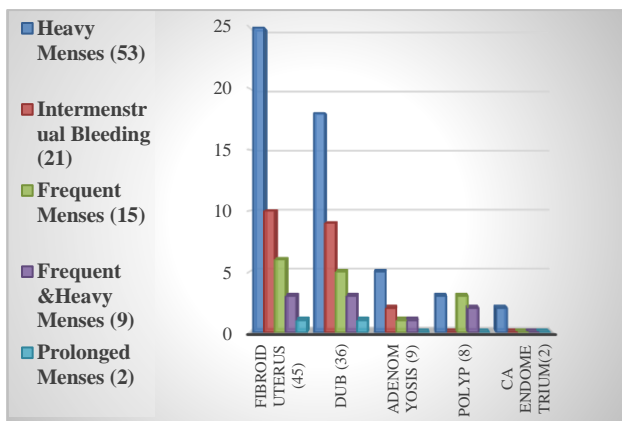


Figure 3: Correlation between clinical diagnosis and menstrual disorder.

Figure 3 shows the correlation of endometrial pathology with the various symptoms. Out of 45 cases of fibroid uterus, 25 (55.55%) presented with heavy menstrual bleeding. Out of 36 cases of AUB(O) 18 (50%) presented with heavy menstrual bleeding, 9 (25%) presented with intermenstrual bleeding. Out of 9 cases of adenomyosis 5 (55.55%) presented with heavy menstrual bleeding, 2 (22.22%) presented with intermenstrual bleeding. Out of 8 cases of polyp 3 (37.50%) presented with heavy menstrual bleeding, 3 (37.5%) presented with frequent

and heavy menstrual bleeding. Out of 2 cases of Ca endometrium both presented with heavy menstrual bleeding.

On endometrial curettage, proliferative type of endometrium was found in 43% cases, secretory type in 18% cases and hyperplasia was found in 37% cases. Out of 37 cases of hyperplasia 27 cases (72.9%) constituted simple hyperplasia, 8 cases (21.6) constituted complex hyperplasia and 2 cases (5.4%) constituted atypical hyperplasia. Carcinoma endometrium constituted 2% of cases. This has been depicted in Table 3.

Table 3: Different types of endometrium in perimenopausal women on endometrial curettage

Type of endometrium	No. of cases	%
Proliferative endometrium	43	43
Secretory endometrium	18	18
Hyperplastic endometrium	37	37
Simple hyperplasia	27	72.9
Complex hyperplasia	8	21.6
Atypical hyperplasia	2	5.4
Carcinoma endometrium	2	2

Table 4 describes the histological diagnosis with relation to the various age groups. Out of 43 cases of proliferative endometrium the maximum no. 21 (48.83%) were present

in the age group Of 40-44 years, 18 (41.86%) were present in 45-49-year age group. Out of 18 cases of secretory endometrium 7 (38.88%) were found in the age group of 40-44 years, 10 (55.55%) were present in 45-49-year age group. Out of 27 cases of simple hyperplasia 12 (44.44%) were found in the age group Of 40-44 years, 9 (33.33%) were found in 45-49-year age group, 4 (14.81%) were found in 50-54-year age group and 2 (7.40%) in 55-59-year age group.

Out of 8 cases of complex hyperplasia 1 (12.5%) case was found in the age group of 45-49-year age group, 2 (25%) were present in 50-54-year age group and 5 (62.5%) cases were present in 55-59-year age group. Out of 2 cases of atypical hyperplasia 1 case each (50%) was found in the age group of 50-54 years and 55-59 years, respectively. Only 2 (100%) cases of Carcinoma endometrium were present in the age group of 55-59 years.

Table 4: Histological diagnosis in relation to age.

Endometrial histology	40-44	45-49	50-54	55-59	Total
Proliferative endometrium	21 (48.83%)	18 (41.86%)	3 (6.97%)	1 (2.32%)	43
Secretory endometrium	7 (38.88%)	10 (55.55%)	1 (5.55%)	-	18
Simple hyperplasia	12 (44.44%)	9 (33.33%)	4 (14.81%)	2 (7.40%)	27
Complex hyperplasia	-	1 (12.5%)	2 (25%)	5 (62.5%)	8
Atypical hyperplasia	-	-	1 (50)	1 (50%)	2
Carcinoma endometrium	-	-	-	2 (100%)	2

Table 5: Histological findings in relation to abnormal uterine bleeding.

Histology	Heavy menstrual bleeding (53)	Inter menstrual bleeding (21)	Frequent and heavy menstrual bleeding (15)	Frequent menstrual bleeding (9)	Prolonged menstrual bleeding (2)
Proliferative endometrium (43)	23 (53.48%)	14 (32.55%)	6 (13.95%)	-	-
Secretory endometrium (18)	10 (55.55%)	5 (27.77%)	2 (11.11%)	1 (5.55%)	-
Simple hyperplasia (27)	15 (55.55%)	1 (3.70%)	5 (18.51%)	4 (14.81%)	2 (7.40%)
Complex hyperplasia (8)	3 (37.5%)	1 (12.5%)	2 (25%)	2 (25%)	-
Atypical hyperplasia (2)	1 (50%)	-	-	1 (50%)	-
Carcinoma endometrium (2)	1 (50%)	-	-	1 (50%)	-

Out of 43 cases of proliferative endometrium 23 (53.48%) cases were associated with heavy menstrual bleeding. Out of 18 cases of secretory endometrium 10 (55.55%) cases were associated with heavy menstrual bleeding, 5 (27.77%) cases with inter menstrual bleeding. Out of 27 cases of simple hyperplasia 15 (55.55%) cases were associated with heavy menstrual bleeding, 1 (3.77%) case with inter menstrual bleeding. Out of 8 cases of complex hyperplasia 3 (37.5%) cases were associated with heavy menstrual bleeding, 1 (12.5%) case with inter menstrual bleeding. Out of 2 cases of atypical hyperplasia 1 each (50%) was associated with heavy menstrual bleeding and frequent menstrual bleeding. Out of 2 cases of carcinoma endometrium 1 case each (50%) was associated with heavy menstrual bleeding and frequent menstrual bleeding. This has been depicted in Table no.5.

DISCUSSION

In today's world we all can appreciate that the perimenopause is a separate entity from menopause, and this is a highly individualistic process when there are a

whole lot of menstrual, emotional and physiologic changes. The years before menopause that encompasses the change from normal ovulatory cycles to cessation of menses are known as the Perimenopausal transitional years, when there are marked irregularities of menstrual cycles and increasing months of amenorrhoea when anovulatory cycles become more prevalent and hence cycle length increases. Perimenopause may serve as an ideal time to reinforce the importance of good health practices, periodic medical screening, recognition of otherwise silent disease and motivation for a healthier life style for the rest of patient's life. Considering the importance of this gynaecological entity, 100 women in the age group of 40- 59 years who had come to our institution with symptoms of abnormal uterine bleeding were selected using a random number table and evaluated clinically and histologically by taking endometrial curettings.

In our study on 100 perimenopausal women the commonest presentation was heavy menses (53% cases) followed by intermenstrual bleeding (21% cases), frequent and heavy menses (15% cases), frequent menses (9% cases) and prolonged bleeding in 2% cases. In

almost all the age groups the predominant symptomatology was of heavy menstrual bleeding followed by intermenstrual bleeding. Muzaffar et al found menorrhagia in 51.9% cases and polymenorrhoea in 9.2% cases.⁴ Jaiswar et al evaluated women with abnormal uterine bleeding and found metrorrhagia in 18% cases and polymenorrhoea in 8 % cases.⁵ In a study by Babbar K et al it was seen that the most common presentation during perimenopause was menorrhagia (62.1%).⁶ It is thus noticed that the findings of our study with regards to various menstrual abnormalities are in conformity to various studies mentioned in the review of literature.

Leiomyoma

Similar to the findings of our study where most of the cases (66.6%) of fibroid uterus were in 40-44 years age group, the Black Women's health study wherein an incidence rate per 1000 woman- year was 34.4% showed a peak at ages 40-44 years; being 45.6%.⁷ A study carried out by Jutras and Cowan also found that leiomyomas occurred most frequently in fourth and fifth decades of life.⁸ Cornîtescu et al in their study revealed that 49.6% of AUB patients had leiomyomata.⁹ Thus, it is seen that our results are in conformity to findings of other studies.

Out of 45 cases of fibroid uterus 24 (55.55%) presented with features of heavy menstrual bleeding. The cause of heavy menstrual bleeding in fibroid is due to its interference with myometrial contraction. Mondal reported heavy menstrual bleeding in 44 (56.4%) cases.¹⁰ Buttram and Reiter in their detailed review of studies found association of heavy menstrual bleeding with fibroid to be 30% and the range varied from 17 to 62%.¹¹

AUB(O)

The mechanisms involved in anovulatory bleeding vary, but each reflects an abnormal pattern of steroid hormone stimulation which may include estrogen breakthrough, estrogen withdrawal and progestin breakthrough bleeding. In present study, the total no of cases of AUB were 36. Out of 36 cases of AUB 18 (50%) presented with heavy menstrual bleeding, 9 (25%) presented with inter menstrual bleeding. Pilli et al in their study on 100 cases of DUB found heavy menstrual bleeding in 34% of cases, inter menstrual bleeding in 23% cases and frequent menstrual bleeding in 11% cases.¹²

Polyp

Polyps were taken to include endometrial and endocervical polyps. These are epithelial outgrowths from the surface.

In present study, the total no of cases of polyp were 8 (8%). In 40-44-year age group there were 4 cases (50%) of polyp and a similar figure of 4 cases (50%) was observed in 45-49-year age group. Madan and Al-Jufairi

(2001) found the same in 53 patients (9.5%), Jyotsna et al (2004) in 5 (6.6%) cases and Jaiswar et al in 6 (12%) cases.^{4,13,14} Similar to the results of our study Dr. Malavalli found polyps in 10% of perimenopausal women.¹⁵

Adenomyosis

In present study, the total no of cases of adenomyosis were 9 (9%). In 40-44-year age group there were 2 cases (22.22%) followed by 5 cases (55.55%) in 45-49-year age group. Similar to the results of our study Fl. Cornîtescu et al. found adenomyosis in 9.85 % of cases of AUB.⁸ Most of these cases of adenomyosis presented with heavy menstrual bleeding. Malik et al found 67% cases in 40-50 years age group with heavy menstrual bleeding in 55.85% cases and inter menstrual bleeding in 33.33% cases and Majumdar and Saha also observed a higher incidence (53%) in 4th to 5th decade in late reproductive and early menopausal age group and found heavy menstrual bleeding in 25 (22%) cases, inter menstrual bleeding in 11 (9%) cases and frequent menstrual bleeding in 34(30%) cases.^{16,17}

Histopathology of endometrial samples

On endometrial curettage of 100 perimenopausal women the predominant pattern was proliferative type of endometrium as seen in 43% cases, mainly seen in cases with heavy menstrual bleeding. Out of 37% cases of hyperplasia 27% constituted simple hyperplasia, 8% constituted complex hyperplasia and 2% constituted atypical hyperplasia. Carcinoma endometrium constituted 2% of cases.

Proliferative endometrium

In our study patients with proliferative phase endometrium, were around 43%. Bharadwaj and co-workers found the same in 56 (52.3%) cases and Pilli et al in 34% cases.^{11,18}

In a study done by Bolde SA et al the most common histological pattern of endometrium included proliferative endometrium (22.8%) followed by endometrial hyperplasia (19.40%).¹⁹ Study by Doraiswami et al also showed predominant number of cases of AUB to be normal physiologic phases such as proliferative, secretory and atrophic menstrual pattern. The bleeding in the proliferative phase may be due to anovulatory cycles and bleeding in the secretory phase is due to ovulatory dysfunctional uterine bleeding.²⁰

Secretory endometrium

On endometrial curettage of 100 perimenopausal women secretory type of endometrium was found in 18% cases. With respect to different menstrual abnormalities Rosario (1969) found secretory type of endometrium to be associated with 19.04% cases of heavy menstrual

bleeding and with 25% cases of inter menstrual bleeding.²¹ Fl. Cornițescu et al found it in only 8.6%.⁸ Desai and Patole in 23% of perimenopausal women.²²

Endometrial hyperplasia

Endometrial hyperplasia is an overgrowth of endometrial glands and stroma characterized by a proliferative glandular pattern with varying degrees of architectural and cytologic atypia. Out of 37 cases of hyperplasia 27 (72.9%) constituted simple hyperplasia, 8 (21.6%) constituted complex hyperplasia and 2 (5.4%) constituted atypical hyperplasia. Carcinoma endometrium constituted 2% of cases. On endometrial curettage proliferative type of endometrium was found in 43% cases, secretory type in 18% cases and hyperplasia was found in 37% cases. Carcinoma endometrium constituted 2% of cases.

Out of 2 cases of atypical hyperplasia 1 each (50%) was found in the age group of 50-54 years and 55-59 years respectively

Patil and Dave found endometrial hyperplasia in 15(30%) cases.²³ With respect to menstrual disorder, out of 27 cases of simple hyperplasia; 15(55.55%) cases were associated with heavy menstrual bleeding, 1(3.77%) case with inter menstrual bleeding. Amongst 44 cases of endometrial hyperplasia, Pilli found heavy menstrual bleeding to be present in 11 cases (25%) and 8 patients (18.2%) had inter menstrual bleeding.¹² Jyotsna et al found that hyperplastic endometrium was most commonly associated with heavy menstrual bleeding (52.94%) cases followed by inter menstrual bleeding in 3 (17.64%) cases.¹⁴

Zlatkov V et al found endometrial hyperplasia in 46.10% cases out of which simple hyperplasia was present in 91 (39.6%) cases and atypical hyperplasia was present in 15 (6.5%) cases.²⁴ Muzaffar et al found endometrial hyperplasia in 64 (24.7%) cases. Simple hyperplasia constituted 39 (15%), complex 22 (8.51%) and atypical 3(1.2%).²⁵

Bolde SA et al reported that in endometrial hyperplasia, maximum number of cases showed simple hyperplasia without atypia of endometrium (84.61%) and only 2 cases (3.08%) showed atypical endometrial hyperplasia.¹⁹ Cornițescu et al in their study revealed endometrial hyperplasia seven cases (2.7%) of which simple hyperplasia without atypia with squamous metaplasia – three cases (1.2%) and complex hyperplasia with atypia – four cases (1.6%).⁹ Forae, and Aligbe in their study on 231 peri and post-menopausal women found endometrial hyperplasia in 17% of women out of which 58.8% was simple endometrial hyperplasia and 41.2% was complex endometrial hyperplasia. In reproductive and peri-menopausal age groups, complex endometrial hyperplasia was present in 5/231 cases (2.2%) out of which 3/231 (1.3%) showed atypia.²⁶ In a study by Singh P et al, 44 out of 212 (3.3%) cases showed hyper plastic

changes. Of all these cases 11/3% showed simple, 7.09% showed complex and 0.94% showed atypical hyperplasia.²⁷

In the study done by Babbar K et al out of 19.8% of cases of endometrial Hyperplasia, 16.8% of cases were simple hyperplasia without atypia and 1% each of cases of complex hyperplasia with and without atypia.⁶

Hence in present study we had a larger number of hyperplasia cases even though the incidence of atypia is similar in most studies.

Ca Endometrium

Endometrial carcinoma can occur as a result of excess estrogenic stimulation and developing against a background of endometrial hyperplasia or de novo combined with insufficient progesterone levels. Endometrioid endometrial carcinoma is the most common form of endometrial cancer.²⁸ In our study the total no of cases of endometrial Carcinoma were 2 and both were in 55-59-year age group.

Bolde S et al found the incidence of endometrial carcinoma in their study to be 1.49%.¹⁸ Singh P et al in 0.94% of cases, Kavita Babbar et al in 1% of cases.^{6,27} Zlatkov V et al in 7 (3.1%) cases Chandoul et al in 1.34% cases.^{25,29} The findings of present study are in concordance with other studies.

CONCLUSION

This study of endometrial patterns of Perimenopausal bleeding was conducted on 100 women in the age group of 40-59 years who had come to our tertiary care centre for evaluation of abnormal uterine bleeding. The commonest clinical presentation was heavy menstrual bleeding (53%) and maximum no. of cases of abnormal uterine bleeding were seen in age group of 40-44 years. (47%). A clinical diagnosis of fibroid uterus was made in 45% cases, AUB in 36% cases, Polyp in 8% cases, Adenomyosis in 9% cases and Ca endometrium in 2% cases.

The commonest association between menstrual abnormality and clinical disorder was of heavy menstrual bleeding. Dilatation and curettage, endometrial suction aspiration and hysteroscopy techniques were utilized in assessing the uterine cavity to determine various endometrial bleeding patterns.

Amongst the different histological patterns proliferative type of endometrium was found in 43% cases, secretory type of endometrium in 18% cases and endometrial hyperplasia in 37% cases. Out of these 37% cases, 72.9% constituted simple hyperplasia, 21.6% constituted complex hyperplasia and 5.4% constituted atypical hyperplasia. Carcinoma endometrium also constituted 2% of cases. With respect to histopathology and abnormal

uterine bleeding, cases with simple hyperplasia had all bleeding patterns followed by complex hyperplasia and secretory endometrium in equal proportion.

In the present study, there was good correlation between abnormal uterine bleeding, clinical diagnosis and histopathological findings. In terms of symptomatology, the perimenopause may be even more important than either early or late menopause. An early diagnosis and appropriate line of management in these cases can not only give symptomatic relief to the patient but may also help in diagnosis of malignancies at an early stage. Hence by heeding the evidence based approaches to evaluation and treatment described therein, clinicians can improve the health and lives of their Perimenopausal patients.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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