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Original Research Article

Clinicopathological evaluation of patients with postmenopausal bleeding in a tertiary care center

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ABSTRACT

Background: Postmenopausal bleeding (PMB) is frequent finding in 5-10% of women in gynaecology clinic. About 10% of these patients have primary or secondary malignancy. PMB requires complete assessment to ensure the absence of malignancy and to identify and treat high risk patients such as those with endometrial hyperplasia.

Aim: The aim of this study is to investigate the clinical significance and endometrial pathology in patients with PMB.

Materials and Methods: A retrospective study on postmenopausal women visiting a tertiary care center between 2016 January to 2017 December was taken up for study. About 80 patients with PMB were selected and these patients were evaluated by pelvic USG, Endometrial biopsy and Endometrial histopathology.

Results: Maximum patients with PMB belonged to age group of 46-50 years (31.25%). 57.5% were multiparous (parity>2). About 53.75% had PMB 1 to 5 years after menopause. Endometrial thickness (ET) was > 4mm in 86.25%. Majority had ET between 5-10mm (58.75%).

Histopathological analysis of endometrial curettings showed Proliferative phase in 35%, disordered proliferative phase in 17.5%, Atrophic Endometrium in 13.75% and endometrial carcinoma in 11.25%.

Conclusion: Postmenopausal bleeding is an important symptom which requires evaluation to eliminate possibility of malignancy. Transvaginal sonography (TVS) is the first mode of investigation for PMB but Histopathology of Endometrium serves as gold standard for definitive diagnosis.

1. Introduction

WHO defines menopause as permanent cessation of menstruation resulting from loss of ovarian activity.[1] Postmenopausal women constitute 1% of female population.[2] The average age of menopause is around 45-50years.[2] Postmenopausal bleeding [PMB] is defined as abnormal uterine bleeding after 1 year of menopause.[1] The incidence of PMB in postmenopausal women is 10%.[3] PMB is a common presentation due to increased longevity and increase incidence of obesity.

Significant endometrial pathology is detected in 10% of postmenopausal women.[4] A woman not on Hormone replacement therapy (HRT), who bleeds after menopause has a 10% risk of having genital malignancy and further 10% risk of significant pathology.[2] Therefore PMB should be always be evaluated.[2] PMB is often associated with benign conditions but there is 10% risk of having genital malignancies such as cervical, Endometrial, vaginal, ovarian and carcinoma of vulva.[5]

1.1. Etiology of postmenopausal bleeding

1. Non gynaecological causes

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(a) Trauma
(b) Bleeding disorder
(c) Use of HRT
(d) Thrombocytopenia, leukemia
(e) Use of anticoagulants

2. Gynaecological causes

(a) Benign causes
   i. Proliferative or atrophic EM
   ii. EM polyp
   iii. Cervical polyp
   iv. EM hyperplasia (simple, complex with or without atypia)
   v. Chronic endometritis of TB

(b) Malignant causes
   i. Ca endometrium, uterine sarcoma
   ii. Ca cervix
   iii. Estrogen secreting ovarian tumours
   iv. Vaginal and vulval carcinoma

Most frequent causes of PMB are usually benign conditions but has to be evaluated thoroughly to rule out Endometrial Carcinoma. In developed countries risk of EM Ca in PMB women is high were as risk of Ca cervix is higher in developing countries.[6] Premalignant and malignant lesions of cervix also present as PMB.[3] Atypical EM hyperplasia has higher risk of malignant transformation.

EM Ca present earliest with warning symptoms of PMB, so women seek medical advice early and detection at early stages of cancer which improve chances of cure rate and therefore reduce Mortality.[5] Early diagnosis of EM Ca increases the 5-year survival rate up to 95%.[7]

Evaluation of endometrium includes various modalities such as TVS, Hysteroscopy and guided biopsy, Dilatation and curettage, CT, MRI. But histopathology is the gold standard for definitive diagnosis.

2. Materials and Methods

This study was a retrospective observational study conducted in department of obstetrics and gynaecology in Kasthurba Gandhi Hospital Chennai in 2016-2017. All women with PMB from Jan 2016 to Dec 2017 who fulfilled inclusion and exclusion criteria were included in the study.

Case sheets of 80 women admitted with PMB were studied.

2.1. Inclusion criteria

Postmenopausal women with complaints of bleeding PV.

2.2. Exclusion criteria

1. Bleeding disorders
2. Patients on HRT, Tamoxifen, Anticoagulants
3. Injuries to genital tract

Using proforma relevant history, clinical examination findings and investigation details were taken from case sheets. History included – Age, parity, age of menopause, age of PMB, duration of PMB, Medical history like diabetes, hypertension.

Clinical examination and investigation reports like Endometrial thickness (ET) from TVS and histopathology from endometrial biopsy were collected from the case sheets. Data were analyzed using MS office 2019.

3. Results

The age distribution, clinical presentation, ET by TVS, histological patterns of EM of 80 patients were studied.

Table 1: Age distribution of the patients

Age in years	No of cases (N=80)	Percentage%
40-45	6	7.5
46-50	25	31.25
51-55	18	22.5
56-60	13	16.25
>60	18	22.5

Age of the patients with PMB ranged from 44 years to 72 years with maximum of 41.25% in age group of 46-50 years.

Table 2: Postmenopausal years

Postmenopausal years	No of cases	Percentage %
1-5	43	53.75
6-10	12	15
11-15	9	11.25
16-20	11	13.75
>20	5	6.25

Table 3: Age of menopause

Age in years	No of cases	Percentage%
40-45	31	38.75
46-50	33	41.25
51-55	14	17.5
56-60	2	2.5

In our study 80% attained menopause before 50 years and 20% after 50years. Only 2 cases (2.5%) attained menopause after 55 years.

57.5% were multiparous (>2 parity). 28.75% of patients had diabetes and hypertension, 13.75% had hypothyroidism, hyperthyroidism in 1.25% and history of molar pregnancy in 1.25%.

TVS to measure endometrial thickness is easier. ET of 4-5mm is taken as cutoff in PMB women. In this study only 13.75% had ET < 4mm and 86.25% had ET > 4mm.

The common histopathological findings in our study was proliferative endometrium in 33.5% followed by

Table 4: Parity of the patients

Parity	No of cases	Percentage%
Nulli	6	7.5
Para (1-2)	28	35
>Para 2	46	57.5

Table 5: Medical disorders in patients with PMB

Medical disorder	No of cases	Percentage%
Diabetes	23	28.75
Hypertension	23	28.75
Hypothyroid	11	13.75
Hyperthyroid	1	1.25
Previous Molar Pregnancy	1	1.25

Table 6: Distribution of cases according to ET in TVS

ET in mm	No of cases	Percentage%
<4mm	11	13.75
5-10mm	47	58.75
11-15mm	14	17.5
16-20mm	6	7.5
>20mm	2	2.5

Table 7: Histopathology of endometrium

Histopathology	No of cases	Percentage%
Atrophic endometrium	11	13.75
Proliferative	24	33.5
Disordered proliferative	14	17.5
Simple hyperplasia without atypia	7	8.75
Simple hyperplasia with atypia	4	5
Complex Hyperplasia without atypia	5	6.25
Complex hyperplasia with atypia	3	3.75
Adeno carcinoma	9	11.25
Secretory Endometrium	3	3.75

disorderly proliferative endometrium in 17.5% and atrophic endometrium in 13.75%. Endometrial adenocarcinoma accounted for 11.25%.

4. Discussion

Endometrium reflects hormonal status in women with Abnormal Uterine Bleeding. PMB contributes to 5% of all gynaec outpatients, is considered as abnormal and needs evaluation.[5] PMB is a common presentation due to increased longevity, increased obesity and widespread use of hormonal therapy. Incidence of premalignant and malignant disorders increase in postmenopausal age group, Significant EM pathology is detected in 10% of postmenopausal women.[4] The EM evaluation includes TVS, Hysteroscopy, EM biopsy by Pipelle, Dilatation & curettage, CT and MRI. Histopathology is the gold standard for definitive diagnosis. Accurate histological diagnosis is essential as the treatment modality differs in benign and malignant pathology.[5] Evidence has shown that early detection of EM Carcinoma improves the cure rate and decrease mortality.[3]

Using noninvasive techniques such as TVS is preferable at first instance for detecting EM lesions followed by invasive techniques like hysteroscopy and D&C. ET of 4-5mm is taken as cut off in postmenopausal age group.[4] The main aim of investigating these women is to rule out EM carcinoma and its precursor lesions – Endometrial hyperplasia.[8] The probability of EM carcinoma in PMB is 10% and for Endometrial hyperplasia is 15%.[8] Even though the most frequent causes of PMB are benign conditions it is important to exclude atypical hyperplasia and EM Carcinoma by thorough investigations.[3] Advanced age, obesity, early menarche, late menopause, HT, DM, nulliparity can increase risk of having EM carcinoma.[3] USG is the appropriate first line procedure to identify which women with PMB is at higher risk of EM carcinoma. Thicker the endometrium higher the probability of important pathology. Measurement of ET by TVS having a cutoff of >4mm yields sensitivity of 98% for Detection of EM carcinoma.[3] ET <4mm has a 99% negative predictive value.[9] Vaginal bleeding is the presenting sign in more than 90% of PM women with EM Ca.[9] In our study 80 patients with PMB were analysed. Patients presented with age ranging from 44 to 72 years with maximum of 31.25% in age group of 46-50 years. This is similar to study by Parvathavarthini Krishnamoorthy et al,[7] Kothapally et al.[10] Of these patients 57.5% were multiparous (parity >2), this is in accordance with study by Kothapally et al, Parvathavarthini Krishnamoorthy et al, Jyothsna Sravanthi et al.[3] Regarding presentation of symptoms after menopause, maximum patients (53.75%) presented with PMB within 1 – 5 years of menopause and 15% in 6-10 years.

In this study 28.75% had HT and DM compared to 20% HT and 11% DM in study by Jyothsna Sravanthi et al,[3] 36% HT and 13% DM in study by Radha Nair et al.[2]

Transvaginal sonography showed ET>4mm in majority of cases (86.25%) similar to findings in study by Kothapally et al,[10] Radha Nair et al,[2] Parvathavarthini Krishnamoorthy et al.[7] According to ACOG committee opinion no: 734, ET <4mm has a 99% negative predictive value for EM Ca.[9]

Sonographic measurement of ET has to be done first in PMB to decide whether further investigations are needed to rule out malignancy. D&C is an invasive procedure and is associated with complications.

Of the histopathology of the endometrium of the 80 patients with PMB, the commonest finding was Proliferative endometrium seen in 33.5% similar to study by Kothapally et al.[10] Proliferative endometrium suggests high level of

unopposed estrogen stimulation which can lead to rapid progression to Endometrial hyperplasia or endometrial carcinoma.

17.5% had disordered proliferative endometrium. 13.75% had atrophic endometrium compared to 16.6% in study by Kothapally et al.[10] and 13% in study by Jyothsna Sravanthi et al.[3] Exact cause of bleeding from atrophic endometrium is not known but is postulated to be due to anatomic vascular variations or local abnormal haemostatic mechanism.

23.75% had Endometrial hyperplasia which is in accordance with study by Pushpa Singh et al which showed 23.3%.[11] Adenocarcinoma was seen in 11.25% similar to findings in study by Pushpa et al. which showed 13%[11] and 10% in study by Parvathavarthini et al. and Kothapally et al.[7,10]

In our study 9 patients had Endometrial carcinoma, their age group ranged from 49 to 67 years. 1 patient was nulliparous and other 8 patients were multiparous (parity>2).

ET ranged from 6mm to 33mm with mean of 15 mm which was similar to study by Parvathavarthini Krishnamoorthy et al.[7]

5. Conclusion

It can be concluded that benign lesions and carcinoma endometrium are commonly seen in postmenopausal women with complaints of PMB. Early diagnosis can improve quality of life and reduce morbidity and mortality. TVS can be used as first mode of investigation for PMB for predicting endometrial hyperplasia and endometrial carcinoma. Histopathological evaluation is mandatory for excluding malignancy by Endometrial biopsy.

6. Limitations

This study had limitations as it was a retrospective study, the extraction of information was from case sheets and short time of follow up.

7. Source of Funding

None.

8. Conflict of Interest

None.

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