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Original Research Paper

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A PROSPECTIVE STUDY OF ENDOMETRIAL CAUSES OF POSTMENOPAUSAL BLEEDING AND THE ROLE OF HYSTEROSCOPY IN A TERTIARY CARE CENTRE

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ABSTRACT

Background: Postmenopausal bleeding (PMB) is one of the common symptoms that a menopausal woman presents to the gynecologists. PMB, being anominous symptom, needs proper evaluation in order to exclude malignancy. As incidence of malignancy in the postmenopausal period is very high, it requires early diagnosis, follow-up, and prompt treatment. The objective of this study was to establish various endometrial causes of postmenopausal bleeding and to evaluate various risk factors in developing endometrial cancer. **Methodology:** In this study, spanning from June 2022 to June 2023, 90 cases of postmenopausal bleeding were collected from Vijaya Hospital, Chennai, Tamil Nadu, and were evaluated with transvaginal ultrasound and endometrial sampling done by either hysteroscopy-guided biopsy, fractional curettage, or pipelle biopsy. The data thus collected was analyzed. A chi-square test or Fisher's exact test was used to assess differences in categorical data. The p value of < 0.05 was considered significant. **Results:** Based on the histopathological reports, the causes of postmenopausal bleeding in our study population were atrophic endometrium (17.7%), endometrial polyps (26.6%), endometrial malignancy (13.3%), cervical cancer (0%), endometrial hyperplasia with atypia (12.2%), endometrial hyperplasia without atypia (14.4%), disordered proliferative endometrium (6.6%), ovarian cancers (0%), and other benign conditions like proliferative/secretory/unspecified diagnosis constituting another 8.8%. Risk factors like diabetes, body mass index, and endometrial thickness were statistically significant with a p value less than 0.05. **Conclusion:** The postmenopausal bleeding is an important symptom and requires careful and timely assessment to eliminate the possibility of malignancy as soon as possible. Strengthening public awareness about changing lifestyles and maintaining healthy weight and reducing the risk factors for developing pre-malignant and malignant lesions. Hysteroscopy has a major role , and can be used as the main diagnostic modality if feasible.

KEYWORDS : postmenopausal bleeding, malignancy, pelvic ultrasound, hysteroscopy, endometrial sampling.

INTRODUCTION:

Menopause is defined retrospectively as the time of the final menstrual period followed by 12 months of amenorrhea. [1] The average age of menopause for Indian women is 46 years. [2] Postmenopausal bleeding is bleeding from the reproductive system that occurs one year or more after menstrual periods have stopped. Any bleeding following menopause needs to be evaluated to rule out pathological causes. Incidence of postmenopausal bleeding: 3%. [2] Even without amenorrhea or irregularity, menstruation continuing after the age of 55 years should be investigated. [3] The main objective in the diagnostic workup in postmenopausal women presenting with uterine bleeding is to detect or rule out endometrial cancer or atypical hyperplasia, further referred to as (pre)malignancy of the endometrium. As most cases are found to be benign, the goal of clinical management is to achieve an accurate diagnosis. [4]

The principal aim of investigation of PMB is to identify or exclude endometrial pathology, most notably endometrial carcinoma. Women with PMB may be assessed initially with TVS and an endometrial biopsy.

Endometrial thickness is measured as the maximum anteroposterior thickness of the endometrial echo on a long-axis transvaginal view of the uterus. Women with PMB with an endometrial thickness of 3-5 mm in the transvaginal scan do not require endometrial sampling unless they are at a high risk for EC or bleeding is episodic. In an asymptomatic early postmenopausal woman, an endometrial thickness of >11 should prompt an endometrial biopsy. [2]. . An endometrial thickness of more than 3–5 mm in TVS is considered endometrial sampling. The sensitivity for detecting EC at 3 mm is 98%, at 4 mm is 95%, and at 5 mm is 90%. In women with homogeneous and normal morphology, those on MHT, and hypertensive medication, the acceptable combined thickness is 6 mm. A focal increased echogenicity or a diffuse heterogeneity in the endometrium even in a thin endometrium warrants further investigations.[2] Outpatient endometrial sampling devices such as pipelle in low-risk women and with global pathology may be used. Outpatient hysteroscopy is the preferred method for endometrial sampling. If the endometrial biopsy tissue is reported as insufficient for diagnosis and the endometrial thickness on TVS is < 4 mm, follow-up is sufficient. Recurrent episodes warrant further investigation.

Saline infusion sonography and three-dimensional (3D) USG play a limited role in PMB evaluation. [2] In this study, all women who have attained natural menopause after 40 years of age, presenting with spontaneous postmenopausal bleeding, are being evaluated, and the outcome is being studied to know the incidence of various endometrial causes in our population.

Aims And Objectives

- **Primary objective:** To establish the various endometrial causes of postmenopausal bleeding through histopathological evaluation.
- **Secondary objective:** This study also evaluates the correlation between age, parity, transvaginal ultrasound endometrial thickness, body mass index, and medical disorders in women (hypertension, diabetes, and hypothyroidism) presenting with postmenopausal bleeding versus the risk of endometrial cancer.

Methodology:

MATERIALS AND METHODS

- Human study involving USG and HPE Study design: prospective, clinical observational study in PMB patients attending gynecology OPD in Vijaya hospital, Chennai.
- **Period of study:** June 2022 to June 2023 (12 months)
- **Sample size:** 90

Inclusion Criteria

All women who have attained natural menopause after 40 years of age, presenting with postmenopausal bleeding.

Exclusion Criteria

- Women with other obvious causes of bleeding from the cervix and vagina, for example cervicitis, vaginitis, cervical cancer,.
- Women with known cases of bleeding disorders
- Premature menopausal women.

All women with postmenopausal bleeding were recruited based on inclusion and exclusion criteria. Informed consent obtained. Data collection (by history and examination) is done using a structured protocol. Patients were subjected to transvaginal ultrasound and endometrial sampling. The etiology and correlation of various risk factors and endometrial thickness with histopathology will be studied.

Sample Size Calculation

The sample size of this study was calculated as 90. Our study had an assumption of 8% precision, a 5% level of significance, and a 95% confidence interval.

Formula

$$n = \frac{Z^2_{1-\alpha/2}\, p(1-p)}{d^2}$$

Where,

p : Expected proportion

d : Absolute precision

1- α/2 : Desired Confidence level

The required sample size is 90. Statistical Methods: Statistical analysis is going to done by the statistical software STATA 11.0. Continuous variables will be representing as 'Mean (SD)', and categorical variables are representing as 'Frequency (percentage)'. Chi-square test or Fisher's exact tests will be used to assess differences in categorical data. The p value of < 0.05 will be considered as significant.

RESULTS:

Table 1: Distribution of patients according to age

Age (years)	N	%
41-50	8	8.89
51-60	52	57.78
61-70	25	27.78
70-79	5	5.56
Total	90	100

It is evident from the above bar diagram, PMB seems to occur most commonly within the next few years of menopause (i.e.) at 51-60 years constituting 57.78% and the next peak after 60 years of age at 27.78%. The mean age of distribution of PMB was 58.7 years.

Table 2: Distribution of patients according to parity

Parity	N	%
0	2	2.22
1	15	16.67
2	55	61.11
3	14	15.56
4	1	1.11
5	1	1.11
6	2	2.22
Total	90	100

Multiparous women constituted 97.8%, whereas 2 women (2.22%) were nulliparous.

Table 3: Distribution of patients according to body mass index

BMI(cm/kg2)	N	%
<25	2	2.22
25-30	28	31.11
31-35	38	42.22
36-40	17	18.89
41-45	3	3.33
>45	2	2.22
Total	90	100

On considering the BMI, about 31.1% of our women were overweight, 42.22% obese and 18.89% morbidly obese. The mean BMI in our study population was 32 kg/m2.

Table 4: Distribution of patients according to medical co morbidities

Medical co morbidities	Yes	No
Diabetes	49	41
Hypertension	48	42
Thyroid disorders	25	65

Medical comorbidities like diabetes, hypertension, hypothyroid were found in 40% , 39% and 21% of our study women respectively.

Table 5: Distribution of patients according to Endometrial thickness(TVUS)

ET in mm	N	%
</= 4	5	0.05
5 to 10	47	52.2
11 to 20	30	43.33
21 to 30	6	33.3
>30	2	0.02
Total	90	100

Majority of patients (47 out of 90) presenting with postmenopausal bleeding had Endometrium thickness of 5-10mm through transvaginal ultrasound. Followed by 11-20mm in 30 cases.

Table 6: Distribution of patients according to sampling method used

Sampling Method	N	%
Hysteroscopic D and C	82	91.11
Pipelle biopsy	1	1.11
Dilatation and curettage	7	7.78
Total	90	100

Hysteroscopic dilatation and curettage was done in almost 82 cases out of 90 cases. Dilatation and curettage done in 7 cases. In our study the major modality for post menopausal evaluation used was hysteroscopy

Table 7: Distribution of patients according to histopathology

Histopathology	N	%
Benign endometrial polyp	24	26.6
Atrophic endometrium	16	17.7
Benign adenomatous polyp	4	4.4
Scanty proliferative endometrium	3	3.3
Disordered proliferative endometrium	6	6.6
Endometrial hyperplasia with atypia	11	12.2
Endometrial hyperplasia without atypia	13	14.4
EECA-grade-1	6	6.6
EECA-grade-2	5	5.5
Mucinous adenocarcinoma	1	1.1
Blood clots only ,no endometrial tissue	1	1.1

The above table 7 lists the various endometrial causes of post menopausal bleeding. With atrophic endometrium contributing to 17.7%, endometrial carcinoma 13.2 %, premalignant causes 26.6%. The most comman cause in our centre was Benign endometrial polyp which contributes to 26.6%. Second most comman cause being Atrophic endometrium.

Table 8: Correlation of clinical variables of postmenopausal bleeding with risk of endometrial cancer

Characteristics of women	Frequency (n) %	Endometrial carcinoma	P value
Age			
41-50	8(8.9)	0	
51-60	52(57.8)	7(7.7)	
61-70	25(27.9)	5(5.5)	
71-79	5(5.6)	0	0.761
Parity			
Nulligravida	2(2.2)	0	
Multigravida	88(97.7)	12(12.1)	0.922
Body mass index			
<25	2(2.2)	1(1.1)	
25-30	28(31.1)	0	
31-35	38(42.2)	6(6.6)	
36-40	17(18.9)	4(4.4)	
41-45	3(3.3)	1(1.1)	
>45	2(2.2)	0	<0.001
Diabetes			
Yes	49	9(9.9)	
No	41	3(3.3)	<0.028
Hypertention			
Yes	48	8(8.8)	
No	42	4(4.4)	0.387
Hypothyroid			
Yes	25	4(4.4)	
No	65	8(8.8)	0.131
Endometrial thickness			
</=4	5(5.6)	0	
5-10	47(52.2)	1(1.1)	
11-20	30(33.3)	5(5.5)	
20-30	6(6.7)	4(4.4)	
>30	2(2.2)	2(2.2)	<0.001

DISCUSSION:

Postmenopausal bleeding (PMB) is one of the common symptoms for which a menopausal woman presents to the gynecologists. PMB, being anominous symptom, needs proper evaluation in order to exclude malignancy. It is being estimated that the risk of endometrial cancer increases with age, which is 1% at the age of 50 years and 25% at 80 years. The incidence of malignancy in the postmenopausal period is very high. Hence, it requires early diagnosis, strict follow-up, and prompt treatment. Based on the histopathological reports, the causes of postmenopausal bleeding in our study population are listed in Table 7. Among these causes, benign etiologies constituted 52.22%, and premalignant and malignancies constituted 47.77%.

The incidence of Ca endometrium in postmenopausal bleeding is 13.3% in our study, which is almost the same the same as the incidence according to the Clinical Practice Guidelines on Menopause by Indian Menopausal Society, 2016 [2], which is 15%. And the incidence is the same as in the study done by Pushpa et al. (13.2%) [3].

The most common cause of postmenopausal bleeding in our study was endometrial polyp, with an incidence of 26.6%, which is high compared to the incidence of endometrial polyp in other studies. The incidence of atrophic endometrium was 14%, 44%, 24%, and 34.6% in studies done by Sreelatha et al. [4], Bhangalae SV et al. et al. [5], Paul et al. [6], and Ubeja et al. [7], respectively. In our study the incidence of atrophic endometrium was 17.7%.

Our second aim is to study the various risk factors in association with endometrial hyperplasia and endometrial cancer. In the study by Begum and Samal et al. [8], the age at presentation was 45–75 years with a mean age of 57.17 ± 7.11, the age at menopause was 42–58 years with a mean age of 49.18 ± 3.69 years, and the mean year since menopause was 7.95 ± 6.52 years. The results are in accordance with the study done by Lidor et al. [9] in 226 PMB cases and revealed that the ages of patients ranged from 40 to 81 years, with a mean of 56 years. Whereas in a similar study done by Ubeja and Singh in 100 PMB cases, it was observed that the age of presentation was 41–70 years with a mean age of 54.51 years and the mean year since menopause was 7.20 years, which was similar to our study where the age at which there was the first episode of bleeding in women with endometrial hyperplasia/malignancy was between 51–60 years, when compared to that of benign conditions, 41–50 years in my study. Mean menopause age was 49.8 years, and time since menopause was between 5 and 10 years. There was no statistical difference in age, age at menopause, or time since menopause in my study.

A study by Katagiri R, Iwasaki M, Abe SK, et al. [10] in the Asian population concluded that late menarche, early menopause, and a higher number of deliveries were significantly associated with a lower risk of endometrial cancer because of reduced levels of estrogen, but in my study only 2 cases of nulliparous women were there; both of them had non-malignant causes of bleeding. Hence, risk could not be determined. [10].

In a study by Sebastian A et al. [11], 65% of endometrial cancers were seen in women with a BMI > 25 kg/m2. Univariate analysis using BMI showed that the risk of endometrial cancer was three times higher in those with a BMI of 31 kg/m2 compared to those with a BMI of <31 kg/m2.

The results of this meta-analysis by Saed et al. BMC cancer [12] showed that women with diabetes had a 72% increased risk of endometrial cancer compared to those without diabetes. Also, other studies [13, 14] have shown that diabetes increased the risk of endometrial cancer, which is in line with the results of the present study with a significant p value of 0.028.A meta-analysis by Aune D, Sen A, Vatten LJ et al. [15] suggests an increased risk of endometrial cancer among patients with hypertension [15]. But hypertension for endometrial malignancies had no statistical significance in my study.

In our study, 5 cases had ET less than 5 mm, which were evaluated and found to be benign, except one with disordered proliferative endometrium. There were no cases of malignancy in ET less than 5 mm, which is consistent with ACOG Committee Opinion No. 734 [16]:

The Role of Transvaginal Ultrasonography in Evaluating the Endometrium of Women with Postmenopausal Bleeding. And hysteroscopic dilatation and curettage was used in our study to evaluate the cause of postmenopausal bleeding in the majority of cases (91.1%); hence, the endometrial pathology was able to be evaluated with good accuracy. As described previously, hysteroscopy is superior to endometrial biopsy, D&C, and ultrasonography for the identification of structural lesions of the endometrium, such as endometrial polyps. Hysteroscopy has good diagnostic accuracy for structural lesions, such as polyps and leiomyomas, whether or not performed in an office setting, and good patient acceptability in either setting.[17,18,19,20]. Similarly, in our study, there were 23 cases of benign endometrial polyps that have been diagnosed with hysteroscopy. Furthermore, in cases of recurrent bleeding in postmenopausal women with endometrial thickness less than 4 mm, direct visualization of endometrium with hysteroscopy was done and malignancy was ruled out.

CONCLUSION

All women with postmenopausal bleeding should be evaluated, even if it is the first episode of bleeding if ET > 4 mm. Initial evaluation using transvaginal ultrasound is necessary in all cases of postmenopausal bleeding, as it is

necessary to determine the endometrial thickness irrespective of other associated risk factors.

Like many other accepted studies, in our study we found that endometrial thickness >=4mm correlates well with malignancy in our Indian woman too. Hence we suggest that, in a woman with the first episode of postmenopausal bleeding with endometrial thickness of < 4 mm, irrespective of the risk factors, further invasive tests like endometrial sampling/biopsy are not required. But in cases of recurrent postmenopausal bleeding, endometrial sampling is mandatory because of the risk of developing type 2 endometrial cancers.

For any postmenopausal bleeding evaluation, hysteroscopic dilatation and curettage would be the best method, considering its negative predictive value in ruling out cancers. And more benign pathology like benign endometrial polyp can be ruled out, and patients can be reassured. Hence, if hysteroscopy is feasible, it is the best diagnostic modality.

Obesity, diabetes, and hypertension are the triad of endometrial cancer. Strengthening public awareness about changing lifestyles and maintaining healthy weight, early diagnosis and treatment of hypertension and diabetes mellitus can decrease morbidity and mortality due to endometrial cancer.

Limitations Of Study

Sample size is less

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