

Correlation of Histological Findings with Clinical and Ultrasonographic Features in Postmenopausal Bleeding Observational Study

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ABSTRACT

Background: Postmenopausal bleeding is generally regarded as an ominous alarm of genital pathologies, which requires a thorough evaluation clinically and pathologically to exclude carcinoma as the cause and ensure a benign pathology. This study aims to determine whether clinical diagnosis and ultrasonographic features can serve as reliable parameters for diagnosing the causes and whether the findings correspond with histopathology reports.

Methods: A total of eighty postmenopausal women presenting with bleeding were enrolled in this observational study. A detailed history was taken and a clinical examination was conducted. All patients underwent transvaginal ultrasonography. Patients with clinically visible lesions on the cervix and vulva were subjected to biopsy, and the rest underwent fractional curettage, and a sample was sent for histopathological examination. Finally, the histopathology report was compared with clinical and ultrasonographic findings.

Results: On physical examination, the most common findings in the cervical, vaginal, and uterine areas were a healthy cervix (76.25%), a healthy vagina (95%), and a normal uterus (58.75%), respectively. On USG examination, the most common cervical and uterine findings were normal normal-sized cervix (71.25%) and a normal uterus (41.25%), with the most frequent ET ranging from 47mm (75%). The most common PAP smear results were negative for malignancy (47.5%) and inflammatory smear (41.25%). On endometrial biopsy, the most common findings were benign (85%), followed by malignant (10%) and pre-malignant lesions (5%). On cervical and endometrial biopsy findings, Pre-malignant and malignant lesions were significantly associated with advancing age ($p < 0.05$).

Conclusion: We have concluded that clinical findings and ultrasonographic features do not correlate statistically with histopathological findings of postmenopausal bleeding cases.

Key-words: Postmenopausal bleeding, Ultrasonography, Clinical findings, Histopathology

INTRODUCTION

Menstruation ceases for 12 months or longer at menopause, a normal life change for women that typically occurs between the ages of 45 and 55, marking the end of ovarian function and fertility ^[1]. Postmenopausal bleeding (PMB) is one of the most serious issues that women should be aware of when going through the menopause. With a 10% incidence, postmenopausal bleeding is a prevalent clinical problem

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[2]. Benign disorders such as endometrial or vaginal atrophy, cervical polyps, endometrial polyps, and decubitus ulcer in cases of utero-vaginal prolapse, neglected pessary, or a forgotten intrauterine device are present in 80% to 90% of women who present with PMB. Leukemia, thrombocytopenia, chronic endometritis of tuberculosis, anticoagulant usage, and secondary coagulopathy from liver illness are a few rare benign causes of PMB [3]. Even though benign illnesses are the most common causes of PMB, it's crucial to rule out malignant causes. A cervical smear test, pelvic sonography to determine the endometrial thickness (ET), diagnostic hysteroscopy, and biopsy from the potential bleeding location are all viable clinical assessment procedures in each PMB case [4]. Following a comprehensive clinical history and examination, transvaginal ultrasonography is advised by the American College of Obstetricians and Gynecologists [5]. "PMB indicates malignancy unless proven otherwise," goes the rule. Over the past 20 years, corpus uteri cancers have been on the rise, according to the Indian Cancer Registry [6]. To evaluate atrophic vaginitis and rule out cervix, vaginal, vulva, or cervical polyp tumors, a clinical evaluation should involve abdominal, per speculum, and bimanual examination. Ultrasonography can detect a visible cavitory lesion or an abnormally thin or thick endometrium. Endometrial biopsy is generally deemed unnecessary in perimenopausal and postmenopausal women with irregular bleeding when the endometrial thickness is less than 4 or 5 mm, as the risk of endometrial hyperplasia or malignancy is low. A biopsy is recommended when the clinical history reveals long-term unopposed estrogen exposure. An endometrial stripe of 5 mm thickness has been linked to an exceedingly low incidence of endometrial hyperplasia or cancer [7]. Women with an endometrial thickness of more than 5 mm should be further evaluated with saline infusion sonography or an endometrial biopsy [8]. Sonography, followed by histological examination, is the cornerstone of diagnosis. Histopathological examination (HPE) is necessary to rule out malignancy in PMB [9]. Women with PMB with increasing ET should be encouraged to obtain an endometrial biopsy to rule out underlying cancer. However, females with a thin endometrium but postmenopausal bleeding should not be left untreated [10].

MATERIALS AND METHODS

This prospective observational study was performed in the Department of Obstetrics and Gynecology, Jawaharlal Nehru Hospital and Research Center, Bhilai, Chhattisgarh, over a period of 18 months, i.e. from June 2022 to December 2023.

Inclusion criteria

- ✓ All postmenopausal women presenting with postmenopausal bleeding
- ✓ Women who willing to participate in the study

Exclusion criteria

- ✓ Women who were known cases of bleeding disorders
- ✓ Women with liver disease and women treated for genital malignancy
- ✓ Women on anticoagulant therapy or hormonal therapy
- ✓ Women who are not willing to participate in the study

Methodology- Data were collected from all the study patients, are age, body mass index (BMI), socioeconomic status based on the modified Kuppuswamy scale, Age of menopause, duration of menopause, and menstrual pattern one year before menopause. Findings on physical examination of the cervix, vagina, and uterus were evaluated to rule out the etiology of postmenopausal bleeding (PMB).

PAP smear findings, ultrasonographic (USG) examination of cervix, uterus, and endometrial thickness; endometrial cytology findings; endometrial biopsy findings; and cervical biopsy findings were recorded.

The patients were clinically evaluated by detailed history and examination, and a provisional diagnosis was made. Patients with clinically visible local lesions on the cervix and vulva were subjected to biopsy for histopathological examination.

Statistical Analysis- Data was collected and graphics were designed by Microsoft Office Excel 2019. Descriptive statistics were used. The categorical and continuous variables are represented as frequency (percentage) and mean (standard deviation, SD), respectively. A p-value less than 0.05 is considered statistically significant.

RESULTS

A total of 80 PMB women were enrolled and analysed in the present study. On physical examination, most patients had a healthy cervix (76.25%), while cervical erosion was present in 21.25%. Vaginal examination showed normal findings in 95% of women, with rectocele

and cystocele observed in only 2.5% each. Uterine findings revealed that 58.75% had a normal uterus, 21.25% were atrophic, and 20% were bulky, indicating that atrophic and bulky changes are common in postmenopausal women (Table 1).

Table 1: Distribution of patients according to physical examination findings of the genital tract

Physical examination findings		Frequency (N=80)	Percentages (%)
Cervical findings	Healthy	61	76.25
	Erosion	17	21.25
	Mass	2	2.5
Vaginal findings	Healthy	76	95
	Rectocele	2	2.5
	Cystocele	2	2.5
Uterine findings	Normal	47	58.75
	Atrophic	17	21.25
	Bulky	16	20

On ultrasonography, the cervix was of normal size in 71.25% of patients and bulky in 28.75%. Uterine findings showed normal size in 41.25%, a bulky uterus in 36.25%, and an atrophic uterus in 22.5%. Endometrial thickness

was between 4 and 7 mm in the majority of cases (75%). These findings highlight that endometrial thickening is a frequent observation among women presenting with postmenopausal bleeding (Table 2).

Table 2: Distribution of patients according to findings on USG examination

USG examination		N (=80)	Percentages (%)
Cervix	Normal size	57	71.25
	Bulky	23	28.75
Uterus	Normal	33	41.25
	Bulky	29	36.25
	Atrophic	18	22.5
Endometrial thickness	<4 mm	7	8.75
	4–7 mm	60	75
	>7 mm	13	16.25

Histopathological evaluation revealed benign lesions in 85%, premalignant in 5%, and malignant in 10% of cases. Malignant and premalignant lesions were more common in women above 50 years. Higher BMI (25–29.9 kg/m²) was strongly associated with malignant and premalignant pathology. Almost all patients were

multiparous, and comorbidities were present in 75% of benign, 100% of premalignant, and 87.5% of malignant cases. This suggests that increasing age, higher BMI, longer duration of menopause, and comorbidities may increase the risk of malignant changes (Table 3).

Table 3: Association of Socio-demographic parameters and endometrial biopsy findings

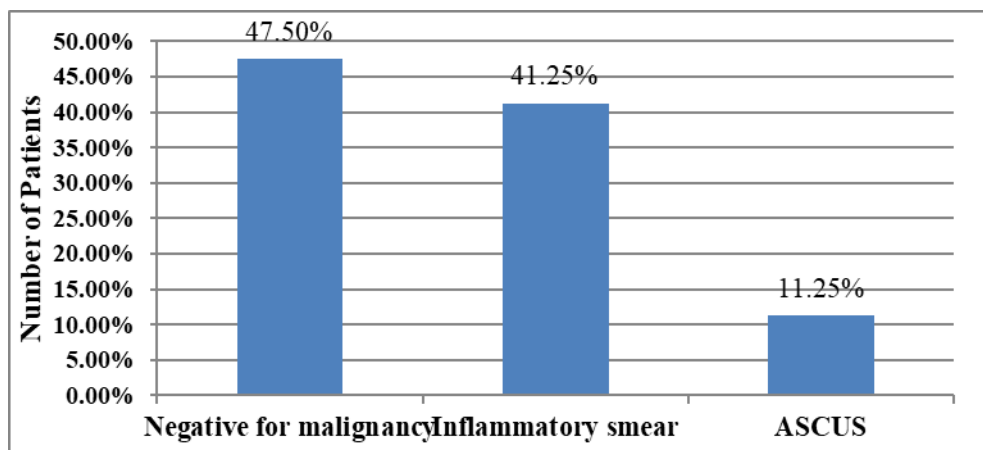
Socio-demographic parameters		Benign (n=68)	Pre-malignant (n=4)	Malignant (n=8)
Age groups	41-50 years	16 (23.53%)	1 (25%)	1 (25%)
	51-60 years	38 (55.88%)	1 (25%)	3 (37.5%)
	61-70 years	11 (16.18%)	1 (25%)	3 (37.5%)
	71-80 years	3 (4.41%)	1 (25%)	1 (12.5%)
BMI (kg/m ²)	18.5-24.9	10 (14.71%)	1 (25%)	2 (25%)
	25-29.9	51 (75%)	3 (75%)	4 (50%)
	30-34.9	7 (10.29%)	0 (0%)	2 (25%)
Parity	Primiparous	2 (2.94%)	0 (0%)	0 (0%)
	Multiparous	66 (97.06%)	4 (100%)	8 (100%)
Comorbidities	Yes	51 (75%)	4 (100%)	7 (87.5%)
	No	17 (25%)	0 (0%)	1 (12.5%)

Malignant changes were more frequent in women with a menopause duration of more than 10 years. Women with abnormal menstrual patterns (such as menorrhagia, oligomenorrhea, or hypomenorrhea) one year before

menopause showed a higher risk of premalignant and malignant findings compared to those with normal cycles (Table 4).

Table 4: Association of menopausal variables and endometrial biopsy findings

Menopausal variables		Benign (n=68)	Pre-malignant (n=4)	Malignant (n=8)
Duration of menopause	1-10 years	56 (82.35%)	2 (50%)	5 (62.5%)
	11-20 years	9 (13.24%)	1 (25%)	2 (25%)
	21-30 years	3 (4.41%)	1 (25%)	1 (12.5%)
Menstrual pattern 1 year before menopause	Normal	30 (44.12%)	1 (25%)	3 (37.5%)
	Oligomenorrhea	23 (33.82%)	1 (25%)	2 (25%)
	Hypomenorrhea	9 (13.24%)	0 (0%)	2 (25%)
	Menorrhagia	6 (8.82%)	2 (50%)	1 (12.5%)

**Fig. 1:** Distribution of Patients according to Pap smear Findings

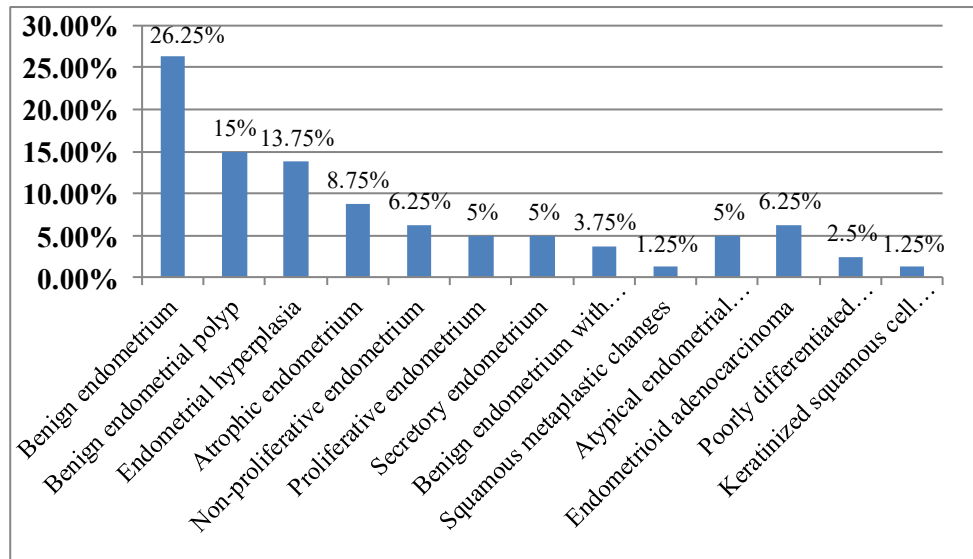


Fig. 2: Distribution of Patients according to Endometrial Biopsy Findings

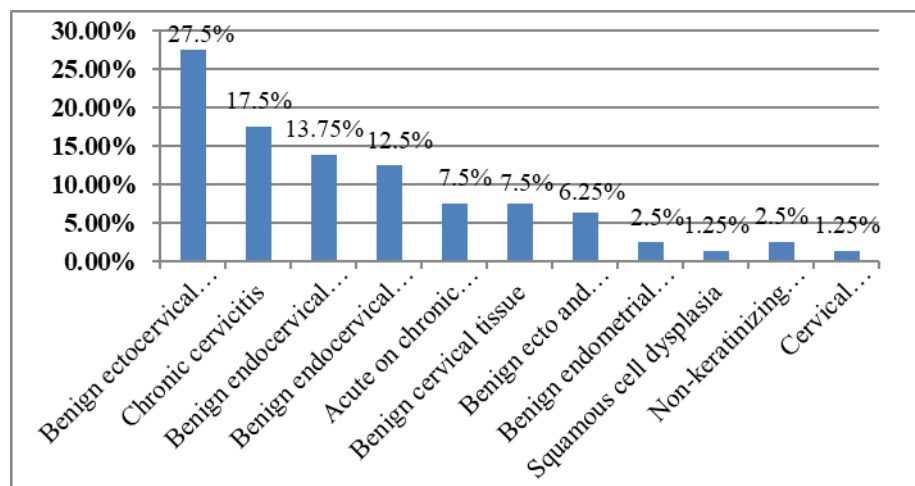


Fig. 3: Distribution of Patients according to Cervical Biopsy findings

Most cases with <4 mm endometrial thickness were benign. With 4–7 mm, both benign and premalignant lesions were detected, along with some malignancies. Endometrial polyps were particularly associated with

thickness >7 mm. Although statistical significance was not reached ($p=0.12$), a clear trend was observed showing that a thicker endometrium was more likely to harbor pathological changes (Table 5).

Table 5: Association of Endometrial Thickness and Endometrial Biopsy findings

Endometrial biopsy findings	Endometrial thickness		
	<4 mm (n=7)	4– 7 mm (n=60)	>7 mm (n=13)
Benign endometrium (n=21)	1 (14.29%)	20 (33.33%)	0 (0%)
Benign endometrial polyp (n=12)	1 (14.29%)	4 (6.67%)	7 (53.85%)
Endometrial hyperplasia (n=11)	1 (14.29%)	9 (15%)	1 (7.69%)
Atrophic endometrium (n=7)	0 (0%)	6 (10%)	1 (7.69%)
Non-proliferative endometrium (n=5)	1 (14.29%)	3 (5%)	1 (7.69%)
Proliferative endometrium (n=4)	0 (0%)	3 (5%)	1 (7.69%)
Secretory endometrium (n=4)	1 (14.29%)	2 (3.33%)	1 (7.69%)

Benign endometrium with cystic Changes (n=3)	0 (0%)	3 (5%)	0 (0%)
Squamous metaplastic changes (n=1)	0 (0%)	0 (0%)	1 (7.69%)
Atypical endometrial hyperplasia (n=4)	0 (0%)	4 (6.67%)	0 (0%)
Endometrioid adenocarcinoma (n=5)	1 (14.29%)	4 (6.67%)	0 (0%)
Poorly differentiated endometrial adenocarcinoma (n=2)	1 (14.29%)	1 (1.67%)	0 (0%)
Keratinized squamous cell carcinoma (n=1)	0 (0%)	1 (1.67%)	0 (0%)

Chi-square:4.127, p-value: 0.127

Cervical biopsy findings revealed benign lesions in 95%, premalignant in 1.25%, and malignant in 3.75%. Malignant lesions were more frequent among women aged ≥ 60 years and those with higher BMI (25–29.9 kg/m²). Almost all cases occurred in multiparous women (Table 6).

Table 6: Association of Socio-demographic parameters and cervical biopsy findings

Socio-demographic parameters		Benign (n=76)	Pre-malignant (n=1)	Malignant (n=3)
Age groups	41-50 years	18 (23.68%)	0 (0%)	0 (0%)
	51-60 years	41 (53.95%)	1 (100%)	0 (0%)
	61-70 years	13 (17.11%)	0 (0%)	2 (66.67%)
	71-80 years	4 (5.26%)	0 (0%)	1 (33.33%)
BMI (kg/m ²)	18.5–24.9	13 (17.11%)	0 (0%)	0 (0%)
	25–29.9	54 (71.05%)	1 (100%)	3 (100%)
	30–34.9	9 (11.84%)	0 (0%)	0 (0%)
Parity	Primiparous	2 (2.63%)	0 (0%)	0 (0%)
	Multiparous	74 (97.37%)	1 (100%)	3 (100%)

DISCUSSION

Postmenopausal bleeding (PMB) evaluation primarily aims to rule out malignancies and benign causes, including endometrial hyperplasia, atrophic vaginitis, as well as endometrial and cervical polyps, which are commonly encountered. This necessitates careful histologic examination to ensure comprehensive patient management.

On physical examination of cervix, vagina, and uterus, the most frequent findings were no pathology in the present study, in agreement with the Talwar *et al.* [2], whereas disagreement with the Kant *et al.* [11] report that only 45.7% patients had no pathology.

Ultrasonographic measurement of endometrial thickness is an important tool for the evaluation of postmenopausal bleeding.

In the current study, our findings are comparable with those of Narayanan *et al.* [12] and Vempalli *et al.* [13] observed that the maximum patients had endometrial thickness more than 4 mm.

In our study, the most common findings on PAP smear were negative for malignancy and inflammatory smear, while the least common finding was atypical squamous cells of undetermined significance. In consensus with the findings of Salih *et al.* [14].

We have found that the most common findings on endometrial biopsy were benign, followed by malignant and premalignant lesions in PMB women; similar results were found by many other studies [15,16].

The most common findings on cervical biopsy were benign ectocervical tissue, followed by chronic cervicitis, benign endocervical polyp, and benign endocervical

tissue. In contrast, the least common findings were squamous cell dysplasia and cervical adenocarcinoma, in the present study, comparable with the Rahman *et al.* [17], reported that cervical carcinoma (12%) as well as cervical polyp and cervical dysplasia (each 2%) were the most frequently histopathological findings. In our study, maximum endometrial malignancies were found in ET >4mm, in accordance with Reddy *et al.* [18] and Sujana *et al.* [19].

In the present study, pre-malignant and malignant lesions were significantly associated with advancing age ($p < 0.05$). At the same time, there was no significant association between pre-malignant and malignant lesions and BMI, parity, presence of comorbidities, duration of menopause, menstrual pattern 1 year before menopause, and ET ($p > 0.05$). Our results are consistent with those of Thomas *et al.* [20], whereas a study done by Paul *et al.* [21] reported no significant association of pre-malignant and malignant lesions with age, parity, BMI, and ET ($p > 0.05$).

CONCLUSIONS

We have concluded that on physical and USG examination, the most common cervical, vaginal, and uterine findings were normal. On endometrial and cervical biopsy, the most common findings were benign, followed by malignant and premalignant lesions. Correlation of ET with biopsy findings was not significant; various endometrial thicknesses show variable findings on histopathological examination. Pre-malignant and malignant lesions were significantly associated with advancing age. Despite various limitations, the findings provide valuable insights into the multifaceted nature of PMB, emphasizing the need for further research to validate and expand upon these observations.

CONTRIBUTION OF AUTHORS

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