

RECURRENT POSTMENOPAUSAL BLEEDING: PATHOLOGICAL FINDINGS AND  
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## ABSTRACT

**Background:** Postmenopausal bleeding (PMB) is a common but abnormal symptom requiring urgent evaluation. Atrophy is the leading cause, though postmenopausal bleeding might signal endometrial cancer. Early detection improves outcomes, emphasizing timely diagnosis and management to prevent malignancy progression. **Objectives:** The study aims to determine the prevalence of endometrial pathology in women with recurrent postmenopausal bleeding, identify predictive clinical and demographic factors, and assess the diagnostic accuracy of imaging and biopsy methods. **Methods:** This is a prospective observation study conducted at Al-Hakeem Teaching Hospital, Misan City, for the duration from 1<sup>st</sup> of September 2024 till 1<sup>st</sup> of September 2025 in Iraq. The study included 100 women aged  $\geq 45$  years with a complaint of recurrent postmenopausal bleeding. Data collection included demographic, gynecological, medical history, BMI, and findings of physical examination. All participants underwent transvaginal ultrasound for endometrial thickness, followed by outpatient endometrial sampling by Pipelle for histopathological evaluation in those with  $\geq 4$ mm endometrial thickness to identify the prevalence and types of endometrial pathology. **Results:** This study of 100 women with recurrent postmenopausal bleeding found a mean age of  $62.5 \pm 7.3$  years. Histopathology revealed pathology in 62%, including 9% carcinoma. Significant associations were identified between endometrial pathology and older age ( $p=0.001$ ), longer menopausal duration ( $p=0.041$ ), greater number of bleeding episodes ( $p=0.006$ ), and increased endometrial thickness  $\geq 4$  mm on ultrasound ( $p=0.001$ ). **Conclusions:** Significant predictors included older age, longer menopausal duration, multiple bleeding episodes, and endometrial thickness  $\geq 4$  mm, underscoring key diagnostic and risk factors.

**KEYWORDS:** Basrah, Pathological Findings, Postmenopausal, Predictive Factors, Recurrent Bleeding.

## 1- INTRODUCTION

Menopause is defined as the total cessation of menstrual periods, occurring when a female has no remaining ovarian follicles, and is clinically recognised after one year of amenorrhoea. The mean age of menopause in the United States is 51 years.<sup>[1]</sup> Postmenopausal bleeding, defined as bleeding occurring after menopause, is deemed abnormal and accounts for nearly two-thirds of all gynaecologic office visits among postmenopausal women.<sup>[2,3]</sup>

The differential diagnosis for postmenopausal bleeding (PMB) includes several disorders. While atrophy of the lower reproductive tract is the predominant cause of

postmenopausal bleeding (PMB), 90% of postmenopausal women diagnosed with endometrial carcinoma had vaginal haemorrhage.<sup>[4]</sup>

Endometrial cancer ranks as the fifth leading cause of cancer-related mortality in the United States and is the fourth most prevalent cancer among females.<sup>[5]</sup> In addition, endometrial cancer accounts for 92% of uterine cancer cases and is the most often diagnosed malignancy in women. More than 90% of postmenopausal women diagnosed with endometrial cancer have postmenopausal bleeding (PMB).<sup>[6]</sup>

In women under 50, less than 1% of postmenopausal bleeding is attributable to endometrial cancer. The prevalence of postmenopausal bleeding attributable to endometrial cancer rises to 24% in women over the age of 80.<sup>[7]</sup>

The rising prevalence of endometrial cancer risk factors, including obesity and late menopause, is the main cause of the rising incidence of endometrial cancer worldwide. By 2030, it is projected that the number of people with endometrial cancer will have doubled.<sup>[2,8]</sup>

A study conducted in Iraq involving 140 women with PMB found that 10% of those with recurrent bleeding were diagnosed with endometrial cancer. The most common cause identified was endometrial hyperplasia, accounting for 45% of cases.<sup>[9]</sup>

Current guidelines recommend endometrial biopsy or transvaginal ultrasound as initial investigations, depending on patient risk factors.<sup>[6]</sup> An endometrial thickness  $>4$  mm on ultrasound is considered a threshold for further evaluation.<sup>[10]</sup> As with most cancers, early detection and intervention result in a markedly improved prognosis. Consequently, every postmenopausal woman experiencing vaginal bleeding must undergo immediate and thorough evaluation via a full clinical examination and diagnostic procedures, including endometrial biopsies and imaging investigations. Management often relies on a determined aetiology. Given the prevalence of postmenopausal bleeding among clinicians, healthcare professionals must possess advanced knowledge in choosing suitable diagnostic tests, addressing the aetiology, and promoting effective interprofessional collaboration to enhance patient outcomes in this prevalent condition.<sup>[11]</sup>

The aims of this study are to investigate the prevalence of endometrial pathology in women with recurrent postmenopausal bleeding, to identify clinical and demographic factors that predict the presence of endometrial pathology and to evaluate the diagnostic accuracy of various imaging modalities and endometrial biopsies.

## 2-PATIENTS AND METHODS

This is a prospective observation study conducted at Al-Hakeem Teaching Hospital, Misan City/ Iraq, to investigate the prevalence of endometrial pathology in women with recurrent postmenopausal bleeding, to identify clinical and demographic factors that predict the presence of endometrial pathology and to evaluate the diagnostic accuracy of various imaging modalities and endometrial biopsies. For the duration from 1<sup>st</sup> of September 2024 till 1<sup>st</sup> of September 2025.

The study included one hundred women presented with recurrent postmenopausal bleeding (RPB), defined as two or more episodes of vaginal bleeding occurring after 12 months of amenorrhea in women aged 45 years and

above. Participants will be recruited consecutively as they present to the centers during the study period.

The study included women aged 45 years or older, postmenopausal status ( $\geq 12$  months of amenorrhea), patients with history of recurrent postmenopausal bleeding (at least two episodes) and women with willingness to participate and provide informed consent. While, the study excluded pre-menopausal woman with abnormal uterine bleeding, women with known diagnosis of endometrial or cervical cancer before enrollment, women with bleeding due to causes other than pelvic pathology like, coagulopathy, urinary or gastrointestinal tract causes and women who refused to undergo an endometrial biopsy.

The data was collected from 100 women with RPB through a special questionnaire, the questionnaire includes the following parts. Part one for patients' sociodemographics such as women's age, occupation residency, marital status and educational level. Part two for women's gynaecological and obstetric history as women's parity, menopausal duration, number of RPB, duration, time between intervals, any associated symptoms, and usage of hormonal replacement therapy. Part three for medical and surgical history like any chronic medical condition, previous gynaecological surgery and anticoagulant treatment. Part four for women's anthropometric measurements, including weight, height, and BMI. Calculation of BMI: the body mass index was calculated by dividing weight by height in centimetres squared. Part five the findings of the physical examination, including an assessment of systemic health, pelvic examinations, such as per speculum inspection and bimanual palpation. Part six for women's transvaginal ultrasound findings, including an evaluation of the endometrial thickness, uterine morphology and the presence of any focal lesion such as polyps or myoma. Endometrial thickness was measured in the sagittal plane. The findings will be categorized as normal, thickened ( $>4$  mm), or the presence of structural abnormalities.

Participants with endometrial thickness of ( $\geq 4$  mm) and those of less than that but have a high risk for endometrial cancer underwent an endometrial biopsy using an office-based Pipelle device or equivalent. Biopsy specimens were sent for histopathological examination to determine the presence or absence of endometrial pathology and the type of pathology (for example atrophic endometrium, hyperplasia without atypia, hyperplasia with atypia, endometrial carcinoma). The study received formal approval from the Misan Health Directorate. Before participation, verbal informed consent was obtained from all women enrolled in the study.

Data analysis was conducted using the Statistical Package for Social Sciences (SPSS) version 26. Continuous variables were presented as mean  $\pm$  standard

deviation, while categorical variables were reported as frequencies and percentages. Relevant statistical tests were applied as appropriate, with a p-value of  $\leq 0.05$  considered indicative of statistical significance.

### 3-RESULTS

The study included 100 women. The study population had a mean age of  $62.5 \pm 7.3$  years, with a predominance

of urban residents (61%) and married women (82%). A large proportion were unemployed (68%). These data are presented in Table 1.

**Table 1: Sociodemographic characteristics of women with recurrent postmenopausal bleeding (number = 100).**

Variables		Number	Percent
Age	Mean± SD Range	62.5± 7.3 (45 -76)	
Residency	Rural	39	39.0
	Urban	61	61.0
Marital status	Married	82	82.0
	Single	8	8.0
	Widow and divorced	10	10.0
Occupation	Employed	32	32.0
	Unemployed	68	68.0
Total		100	100.0

Table 2 shows the clinical and medical history of study participants. Most women were multiparous, with 58% having 1–4 children. The majority (87%) had been menopausal for  $\geq 2$  years, with a mean menopausal duration of  $7.12 \pm 4.5$  years. Notably, 40% of the women

reported no chronic medical conditions, while diabetes (23%) and hypertension (31%) were the most prevalent comorbidities. A minority had undergone previous gynecological procedures. Regarding body mass index, 46% were overweight and 30% were obese.

**Table 2: Clinical and medical history of study participants (number = 100).**

Variables		Number	Percent
Parity	Nullipara	11	11.0
	1-4	58	58.0
	>5	31	31.0
Menopausal duration	Mean± SD	7.12 ±4.5	
	<2 years	13	13.0
	$\geq 2$ years	87	87.0
History of medical conditions	Diabetes mellitus	23	23.0
	Hypertension	31	31.0
	Thyroid disorders	11	11.0
	None	40	40.0
Previous gynecological procedures	Dilatation and Curettage (D&C)	21	21.0
	Hysteroscopy	10	10.0
	Endometrial ablation	5	5.0
	None	62	62.0
BMI	Normal	24	24.0
	Overweight	46	46.0
	Obese (grade 1)	22	22.0
	Obese (grade 2)	8	8.0
Total		100	100.0

Table 3 shows the characteristics of recurrent postmenopausal bleeding. The mean number of bleeding episodes was  $3.5 \pm 1.23$ , each lasting around  $4.2 \pm 1.53$  days, with inter-episode intervals of about 2.91 months.

Pain (27%) and vaginal discharge (15%) were the most common associated symptoms, while systemic symptoms were infrequent.

**Table 3: Characteristics of recurrent postmenopausal bleeding (number = 100).**

Variable		Number	Percent
Number of RPB	Mean± SD	3.5 ±1.23	
Duration of each bleeding episode (days)	Mean± SD	4.2 ±1.53	
The time interval between episodes (months)	Mean± SD	2.91 ± 1.8	
Associated symptoms	Pain	27	27.0
	Vaginal discharge	15	15.0
	Systemic symptoms (e.g., fever, malaise)	9	9.0

The mean endometrial thickness was 6.7 ± 3.0 mm, with 69% of women having thickness ≥4 mm, a recognized threshold for further diagnostic work-up. As shown in table 4.

**Table 4: Transvaginal Ultrasound Findings in Women with RPB (number = 100).**

Variables		Number	Percent
Endometrial thickness	Mean± SD	6.7 ±3.0	
	< 4 mm	31	31.0
	≥ 4 mm	69	69.0

Histopathology revealed that 38% of patients had no detectable pathology, while 62% had abnormal findings, including endometrial hyperplasia with or without atypia, polyps, and carcinoma (9%). These data are presented in Table 5.

**Table 5: Histopathological Findings from Endometrial Biopsy (number = 100).**

Histopathological findings	Number	Percent
No detected pathology	38	38.0
Atrophic endometrium	21	21.0
Endometrial hyperplasia without atypia	16	16.0
Endometrial hyperplasia with atypia	5	5.0
Endometrial polyp	11	11.0
Endometrial carcinoma	9	9.0
Total	100	100.0

Table 6 shows the association between sociodemographic variables and the presence of endometrial pathology. A significant association was found between age and endometrial pathology (p=0.001), with affected women being older on average. No statistically significant associations were observed with residency or marital status.

**Table 6: Association between sociodemographic variables and presence of endometrial pathology (number = 100).**

Variables		Detected pathology (n=62)	No detected pathology (n=38)	P-value
Age	Mean± SD	65.3± 4.2	60.12± 5.3	<b>0.001</b>
Residency	Rural	26 (41.9)	13 (34.2)	<b>0.442</b>
	Urban	36 (58.1)	25 (65.8)	
Marital status	Married	52 (83.9)	30 (78.9)	<b>0.324</b>
	Single	4 (6.5)	4 (10.5)	
	Widow and divorced	6 (9.7)	4 (10.5)	

Table 7 shows the association between reproductive, hormonal, and medical History and Endometrial Pathology. Longer menopausal duration (p=0.041) was significantly associated with endometrial pathology.

While comorbidities like diabetes and previous gynecological procedures showed trends toward higher risk, they did not reach statistical significance.

**Table 7: Association between reproductive, hormonal, and medical history and endometrial pathology (number = 100).**

Variables		Detected pathology (n=62)	No detected pathology (n=38)	P-value
Parity	Nullipara	8 (12.9)	3 (7.9)	0.490
	1-4	37 (59.7)	21 (55.3)	
	≥5	17 (27.4)	14 (36.8)	
Menopausal duration (years)	Mean± SD	8.0 ±4.8	6.2 ±3.9	<b>0.041</b>
History of medical conditions	Diabetes mellitus	18 (29.0)	5 (13.2)	0.067
	Hypertension	21 (33.9)	10 (26.3)	0.427
	Thyroid disorders	8 (12.9)	3 (7.9)	0.437
Previous gynecological procedures	Dilatation and Curettage (D&C)	15 (24.2)	6 (15.8)	0.320
	Hysteroscopy	7 (11.3)	3 (7.9)	
	Endometrial ablation	3 (4.8)	2 (5.3)	
	None	37 (59.7)	27 (71.1)	
BMI	Normal	12 (19.4)	12 (31.6)	0.12
	Overweight	29 (46.8)	17 (44.7)	
	Obese (grade 1)	15 (24.2)	7 (18.4)	
	Obese (grade 2)	6 (9.7)	2 (5.3)	

The association between bleeding episode characteristics and endometrial pathology is shown in Table 3.8. The number of RPB episodes was significantly higher among women with pathology (p=0.006), suggesting that

recurrent bleeding is an important clinical indicator. No significant association was found with bleeding duration or the interval between episodes.

**Table 8: Association between bleeding episode characteristics and endometrial pathology (number = 100).**

Variables		Detected pathology (n=62)	No detected pathology (n=38)	p-value
Number of RPB	Mean± SD	3.9 ±1.3	3.1± 1.1	0.006
Duration of each bleeding episode	Mean± SD	4.4± 1.4	3.9± 1.5	0.12
The time interval between episodes	Mean± SD	3.0 ±1.8	3.2 ±1.7	0.131
Associated symptoms	Pain	18 (29.0)	9 (23.7)	0.588
	Vaginal discharge	10 (16.1)	5 (13.2)	0.690
	Systemic symptoms (fever, malaise)	7 (11.3)	2 (5.3)	0.306

Table 9 shows the association between ultrasound findings and endometrial pathology detection. A statistically significant association was found between

increased endometrial thickness and pathology (p=0.001), with a higher proportion of women with pathology having thickness ≥4 mm.

**Table 9: Association between ultrasound findings and endometrial pathology detection (number = 100).**

Variables		detected pathology (n=62)	No detected pathology (n=38)	P-value
Endometrial thickness	Mean± sd	7.5 ±2.9	4.9 ± 2.1	0.001
	< 4 mm	13 (21.0)	18 (47.4)	
	≥ 4 mm	49 (79.0)	20 (52.6)	

#### 4- DISCUSSION

Postmenopausal bleeding (PMB) is a common clinical presentation that necessitates thorough investigation due to its potential association with serious underlying pathology, including endometrial carcinoma.<sup>[12]</sup> While a single episode of PMB is concerning, recurrent postmenopausal bleeding (RPB) poses an even greater diagnostic challenge, warranting robust clinical evaluation and targeted investigations.<sup>[13]</sup> This

prospective multicenter study aimed to determine the prevalence of endometrial pathology in women presenting with RPB and to identify key sociodemographic, clinical, and ultrasound predictors associated with pathological findings.

The study involved 100 postmenopausal women (mean age 62.5 ± 7.3 years), primarily urban residents, married, and multiparous. A notable proportion (68%) were

unemployed, possibly contributing to delayed healthcare access. The average menopausal duration was over seven years, consistent with the natural decline in estrogen exposure over time, a factor often implicated in atrophic changes and bleeding risk as reported by Gold et al.<sup>[14]</sup>

Hypertension and diabetes were common (31% and 23%, respectively), both of which are known risk factors for endometrial hyperplasia and malignancy due to their association with chronic unopposed estrogen and metabolic syndrome, as reported by Chou et al.<sup>[15]</sup>

Participants averaged 3.5 bleeding episodes lasting 4 days, with a significant association between frequency and pathology ( $p=0.006$ ), reinforcing findings by Begum et al., who reported that the recurrence and frequency of bleeding episodes are strong clinical indicators warranting endometrial evaluation.<sup>[16]</sup>

Transvaginal ultrasound revealed a mean endometrial thickness of  $6.7 \pm 3.0$  mm, and 69% of participants had a thickness  $\geq 4$  mm, a critical threshold widely used to guide biopsy decisions. Notably, a statistically significant association was found between endometrial thickness and pathology ( $p=0.001$ ). Among women with endometrial pathology, 79% had a thickness  $\geq 4$  mm, consistent with international evidence suggesting that a cut-off of  $\geq 4$  mm yields high sensitivity for detecting endometrial disease in postmenopausal women, and this is in line with the findings from studies by Saccardi et al. and Quaranta et al.<sup>[17,18]</sup> While a minority of patients had a thickness  $< 4$  mm, pathology was still found in 21% of them, underscoring the limitation of using ultrasound alone for risk stratification, especially in cases of recurrent bleeding. These findings highlight the importance of combining clinical features, ultrasound results, and histopathology in the diagnostic process as per recommendations from Dimitraki et al.<sup>[19]</sup>

Histology revealed pathology in 62% of cases: 9% had carcinoma, 21% had hyperplasia (with or without atypia), and 11% had polyps, highlighting the spectrum of PMB causes. These results mirror a previous study by Singh et al. that reported endometrial cancer in 5–10% of women with PMB and reinforce the assertion that RPB is a significant red flag symptom.<sup>[20]</sup>

Pathology was significantly associated with older age ( $p=0.001$ ) and longer menopausal duration ( $p=0.041$ ), reflecting cumulative estrogen exposure. This aligns with known epidemiological data showing that the risk of endometrial cancer increases with advancing age, as reported by Sattanakho et al.<sup>[21]</sup>

No statistically significant associations were observed with parity, residency, marital status, BMI, or specific chronic illnesses such as diabetes and hypertension—though trends toward increased risk were noted, particularly in diabetic women ( $p=0.067$ ). These findings are consistent with prior work by Clarke et al. and Van

Doorn et al., who emphasized the importance of age and endometrial thickness as predictive factors for malignancy in women with postmenopausal bleeding.<sup>[2, 22]</sup> Moreover, while endometrial thickness remains a reliable screening tool, this study reinforces the notion that reliance on ultrasound alone can miss pathology in a notable minority, particularly in women with RPB, where histological confirmation is essential even if imaging is inconclusive.

This study highlights a high prevalence of endometrial pathology among women with recurrent postmenopausal bleeding, with significant associations found for older age, longer menopausal duration, increased endometrial thickness, and number of bleeding episodes. These findings support a comprehensive diagnostic approach that integrates clinical evaluation, ultrasound, and histopathology to ensure early detection of potentially serious conditions, including endometrial carcinoma.

## 5- RECOMMENDATION

All women presenting with recurrent postmenopausal bleeding (RPB) should undergo comprehensive endometrial evaluation, including transvaginal ultrasound and endometrial biopsy, irrespective of the severity of symptoms or initial imaging findings. While transvaginal ultrasound remains a valuable first-line diagnostic tool, an endometrial thickness of  $\geq 4$  mm should always prompt further investigation due to its strong association with underlying pathology. Women who experience multiple episodes of bleeding, are of advanced age, or have a longer duration since menopause should be prioritized for urgent diagnostic assessment, given their elevated risk for endometrial abnormalities, including malignancy. Importantly, endometrial biopsy should be performed routinely in all cases of RPB, even when ultrasound findings appear borderline or within normal limits, to reduce the risk of missed or delayed cancer diagnoses. In addition, there is a pressing need to educate both healthcare providers and postmenopausal women about the clinical significance of recurrent bleeding and the importance of early reporting, thorough evaluation, and timely intervention to improve outcomes and reduce morbidity associated with undiagnosed endometrial pathology.

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