Original Article

Association of Postmenopausal Bleeding with Gynaecological Malignancy: A Clinicopathological Study

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ABSTRACT:

Background: As the worldwide burden of gynaecological malignancy continues to rise, early detection strategies focused on women with postmenopausal bleeding (PMB), have the potential to identify genital malignancies at an early treatable stage.

Objective: The objective of this study is to investigate the association of PMB and its clinico-pathological risk factors with the prevalence of gynaecoloical malignancies.

Material and methods: This is a prospective cross-sectional study for a period of 1 year over 100 women with PMB.

Results: Benign lesions are accounted for 71% of the cases of PMB and malignant lesions are for 29% cases. Endometrial polyps are the most frequent cause (22%) followed by cervical malignancy (17%), Leiomyoma (14%), Endometrial atrophy (13%), Endometrial malignancy (10%), Endocervical polyp (8%), Endometrial hyperplasia (5%), Endometritis with pyometra (4%) and Ovarian malignancy (2%). Among the malignancies, Cervical carcinoma (58.62%) is the commonest malignancy followed by endometrial carcinoma (34.48%) and ovarian carcinoma (6.89%). Endometrial cancer shows a significant association with increasing age (p = 0.008). On the other hand, Cervical Cancer exhibits significant association with lower socioeconomic status (p = 0.001), higher parity (5 and above) (p = 0.029), normal body weight categories (p = 0.007) and decreased ET up to 4 mm (p = 0.019). Endometrial Polyps and Endometrial Cancer have significant associations with increased ET (Endometrial Thickness), with p-values 0.016 and 0.007, respectively. On comparison between Benign and Malignant group, clear span is significantly greater in the Malignant group (p = 0.022). So, evaluation of risk factors of PMB in our study has showed significant association of Malignancies with increasing age, BMI, socioeconomic status, parity, clear span and endometrial thickness (ET).

Conclusion: Our study represents an important and timely evaluation of the risk with the prevalence rate and pattern of gynaecological malignancies in women with PMB in our country.

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Background

Postmenopausal bleeding (PMB) refers to any episode of vaginal bleeding that occurs 12 months or more after the cessation of menstruation [1]. Globally, its prevalence is estimated to be around 10% [2]. Among the various causes of PMB, malignancies of the female genital tract represent one of the most significant concerns. In women not receiving HRT, the occurrence of bleeding after menopause carries approximately a 10% probability of underlying genital tract malignancy and another 10% likelihood of serious pathology [2]. Therefore, even minimal or short-lived bleeding in postmenopausal women warrants thorough evaluation. More than 90% of women with endometrial carcinoma present with PMB as the initial symptom [3]. Endometrial cancer ranks among the most frequent gynecological malignancies worldwide, second only to cervical cancer in incidence [4]. Other non-endometrial malignancies such as cervical, vaginal, and vulvar cancers must also be considered in the differential diagnosis of PMB. The underlying risk patterns vary geographically—endometrial cancer is more prevalent among postmenopausal women in developed nations, whereas cervical cancer remains more common in developing countries [5]. Nearly 70% of cervical cancer patients in low-resource settings seek medical attention at advanced stages, resulting in a five-year survival rate of only 50% [6]. In contrast, early detection of both cervical and endometrial malignancies markedly improves cure rates, with endometrial cancer showing an overall five-year survival rate of about 75% [7]. Hence, timely identification and management of PMB are crucial to rule out precancerous and malignant lesions and ensure early treatment for better outcomes. Unfortunately, in many developing regions, including Bangladesh, limited awareness, lack of screening initiatives, and insufficient healthcare infrastructure often lead to delayed diagnosis, with patients presenting at advanced stages. Although numerous studies on PMB have been reported globally, data from Bangladesh remain scarce. Our study results will represent a reliable reference of existing causes of PMB in our country with prevalence rate and pattern of genital malignancies and risk factors in comparison to other countries.

Material and Methods

This cross-sectional study was conducted in Combined Military Hospital (CMH) Dhaka, Bangladesh from May 2023 to April 2024. Study included 100 patients with postmenopausal bleeding excluding Premature menopause, Surgical Menopause, Radiation Menopause, Chemotherapy induced Menopause, HRT, Anticoagulant therapy, Coagulation disorders, Injuries to genital tract. Data were collected, tabulated, and analysed using STATA (version17).

Results:

Table Ia. The socio-demographic distribution of the participants

General Characteristics	Measurement	
	Range	Mean ± SD
Age (years)	49-80	59.76±7.39
Parity (Nos)	1-7	3.13±1.43
BMI (kg/m^2)	18.55- 44.69	27.45±4.87
Age of Menopause(years)	47- 57	50.36±3.21

Table Ib. The socio-demographic distribution of the participants

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General Characteristics	Frequency	Percentage
Age group (yrs)		
59 and below	54	54
60 to 69	34	34
70 and above	12	12
Socioeconomic status *Bangladesh Bureau of Statistics (June 2021)		
Lower middle class (9148-35,978tk/mo)	39	39
Upper middle class (>35978-1,11,235tk/mo)	26	26
Higher income class (>1,11,235tk/mo)	35	35
Parity category		
1 to 2	34	34
3 to 4	47	47
5 and above	19	19
BMI category (kg/m^2)		
Normal weight	33	33
Overweight	43	43
Obese	24	24
Comorbidities		
No morbidity	28	28
Multi morbidity	57	57
HTN	64	64
DM	61	61
Family History of malignancy	4	4
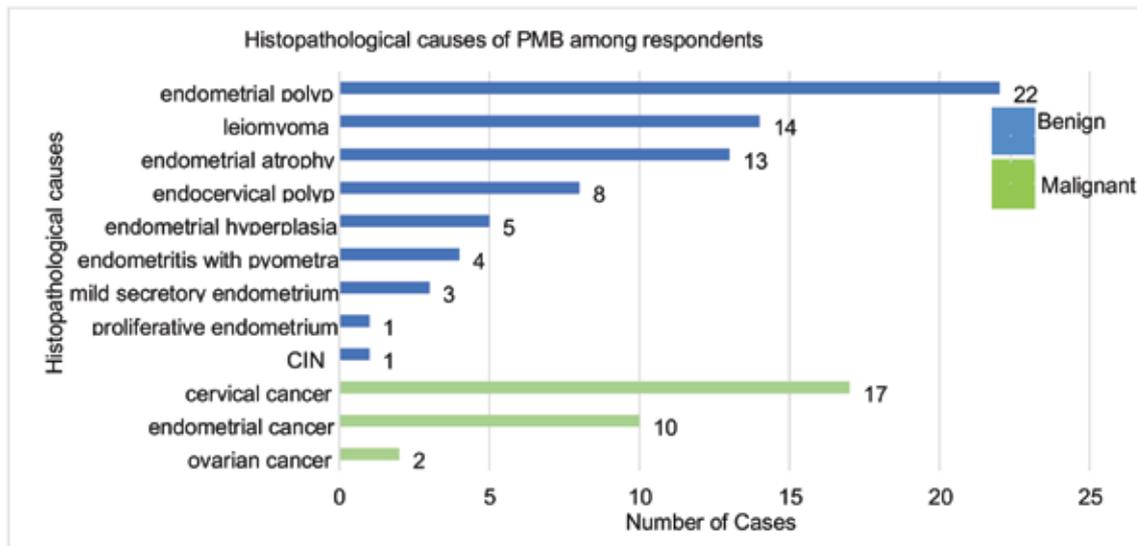
Figure I. Distribution of etiologies of PMB

Table-II denotes that Leiomyomas are notably more prevalent in higher socioeconomic group and Endometrial polyps are more prevalent in overweight and obese patients, but none of which is statistically significant.

Table II. Distribution of demographic variables in benign causes

General Characteristics		n	%	endometrial hyperplasia	endometrial polyp	endocervical polyp	leiomyoma	endometritis with pyometra	CIN	Endometrial atrophy	mild secretory endometrium	proliferative endometrium
Age group	59 and below	54	54	5.56	20.37	9.26	18.52	1.85	0.00	14.81	5.56	1.85
	60 to 69	34	34	5.88	23.53	8.82	11.76	2.94	2.94	11.76	0.00	0.00
	70 and above	12	12	0.00	25.00	0.00	0.00	16.67	0.00	8.33	0.00	0.00
	p-value			0.697	0.908	0.551	0.222	0.056	0.375	0.805	0.268	0.650
Socioeconomic status	Low	37	37	8.11	10.81	10.81	10.81	8.11	0.00	16.22	0.00	0.00
	Middle	24	24	0.00	25.00	4.17	4.17	4.17	4.17	12.50	0.00	0.00
	High	39	39	5.13	30.77	7.69	23.08	0.00	0.00	10.26	7.69	2.56
	p-value			0.365	0.102	0.644	0.086	0.197	0.202	0.740	0.089	0.454
Parity category	1 to 2	34	34	8.82	26.47	5.88	17.65	5.88	2.94	8.82	2.94	2.94
	3 to 4	47	47	2.13	14.89	8.51	12.77	4.26	0.00	19.15	4.26	0.00
	5 and above	19	19	5.26	31.58	10.53	10.53	0.00	0.00	5.26	0.00	0.00
	p-value			0.393	0.247	0.823	0.731	0.573	0.375	0.212	0.656	0.375
BMI cat	Normal weight	33	33	9.09	9.09	6.06	9.09	9.09	0.00	9.09	0.00	0.00
	Overweight	43	43	4.65	27.91	9.30	16.28	2.33	2.33	13.95	2.33	2.33
	Obese	24	24	0.00	29.17	8.33	16.67	0.00	0.00	16.67	8.33	0.00
	p-value			0.296	0.091	0.873	0.610	0.170	0.512	0.682	0.180	0.512
Comorbidities	No morbidity	28	28	3.75	28.57	10.71	10.71	3.75	0.00	10.71	0.00	0.00
	Single morbidity	15	15	6.67	6.67	13.33	20.00	13.33	0.00	13.33	0.00	0.00
	Multi-morbidity	57	57	5.26	22.81	5.26	14.04	1.75	1.75	14.04	5.26	1.75
	p-value			0.897	0.249	0.487	0.705	0.125	0.683	0.921	0.311	0.683

Statistical test: Chi-square; *Indicates level of significance at 5%

In Table-III Endometrial cancer shows a statistically significant association with increasing age of 70 years and above (p = 0.008). Cervical cancer being more prevalent among patients from lower socioeconomic backgrounds (p = 0.001), higher parity (5 and above) (p = 0.029) and normal BMI (p = 0.007)

Table III. Distribution of demographic variables and comorbidities among malignant causes

General Characteristics		n	%	Cervical Cancer %	Endometrial Cancer %	Ovarian Cancer %
Age group	59 and below	54	54	16.67 17.65	3.70	1.85
	60 to 69	34	34	16.67	11.76	2.94
	70 and above	12	12		33.33	0.00
	p value			0.992	**0.008***	0.817
Socioeconomic status	Low	37	37	27.03	5.41	2.70
	Middle	24	24	29.17	12.50	4.17
	High	39	39	0.00	12.82	0.00
	p value			**0.001***	0.502	0.481
Parity category	1 to 2	34	34	8.82	8.82	0.00
	3 to 4	47	47	14.89	14.89	4.26
	5 and above	19	19	36.84	0.00	0.00
	p value			**0.029***	0.181	0.361
BMI cat	Normal weight	33	33	33.33	12.12 6.98	3.03
	Overweight	43	43	11.63	12.50	0.00
	Obese	24	24	4.17		4.17
	p value			**0.007***	0.681	0.442
Comorbidities	No morbidity	28	28	25.00 6.67	3.75	3.75
	Single morbidity	15	15	15.79	20.00	0.00
	Multimorbidity	57	57		10.53	1.75
	p value			0.292	0.227	0.731

Statistical test: Chi-square; *Indicates level of significance at 5%

Table IV. Association between different etiologies and clear span

Diagnosis	n=100	Clear span Below 5yr %	Clear span 5yr to 10yr %	Clear span above 10yr %	P value
Endometrial hyperplasia	5	40.00	40.00	20.00	00753
Endometrial polyp	22	9.09	50.00	40.91	0.100
Endocervical polyp	8	37.50	62.50	0.00	0.128
Leiomyoma	14	50.00	50.00	0.00	0.013*
Endometritis with pyometra	4	0.00	25.00	75.00	0.150
CIN	1	0.00	0.00	100.00	0.342
Endometrial atrophy	13	46.15	23.08	30.77	0.201
Mild secretory endometrium	3	66.67	33.33	0.00	0.242
Proliferative endometrium	1	100.00	0.00	0.00	0.255
Cervical cancer	17	17.65	35.29	47.06	0.320
Endometrial cancer	10	0.00	40.00	60.00	0.057
Ovarian cancer	2	50.00	50.00	0.00	0.579

Statistical test: Chi-square; *Indicates level of significance at 5%

Clear span is the duration between a woman's final period and the first instance of postmenopausal bleeding.

Table-IV presents a significant association of Leiomyoma

with clear span up to 10 years group (P = 0.013). Endometrial cancer shows a borderline significant association (P = 0.057) with longer clear spans, primarily above 10 years (60%).

Table-V shows that Endometrial polyps and endometrial cancer have significant associations with increased ET, with p-values 0.016   and 0.007, respectively. Cervical cancer also shows a significant association with decreased ET (p = 0.019), with most cases (76.47%) having an ET up to 4 mm

Table V. Distribution of ET with various benign and malignant causes

Diagnosis	n	Endometrial thickness (mm) Up to 4 %	>4 to 10 %	>10 to 15 %	>15 to 20 %	above 20 %	P value
Endometrial hyperplasia	5	20.00	20.00	20.00	20.00	20.00	0.656
Endometrial polyp	22	13.64	13.64	31.82	9.09	31.82	0.016*
Endocervical polyp	8	50.00	12.50	12.50	0.00	25.00	0.791
Leiomyoma	14	42.86	14.29	28.57	14.29	0.00	0.323
Endometritis with pyometra	4	50.00	25.00	25.00	0.00	0.00	0.881
CIN	1	100.00	0.00	0.00	0.00	0.00	0.835
Endometrial atrophy	13	69.23	15.38	15.38	0.00	0.00	0.175
Mild secretory endometrium	3	33.33	0.00	66.67	0.00	0.00	0.407
Proliferative endometrium	1	0.00	100.00	0.00	0.00	0.00	0.258
Cervical cancer	17	76.47	11.76	11.76	0.00	0.00	0.019*
Endometrial cancer	10	0.00	20.00	20.00	10.00	50.00	0.007*
Ovarian cancer	2	50.00	50.00	0.00	0.00	0.00	0.664

Statistical test: Chi-square; *Indicates level of significance at 5%

Table VI compares the clinical characteristics of patients with benign and malignant gynecological conditions. However, the clear span is significantly greater in the malignant group compared to the benign group, with a p-value of 0.022. This suggests that among the clinical characteristics studied, clear span is a notable predictor of malignancy.

Table VI. Comparison of clinical characteristics in benign and malignant groups

Characteristics	Benign		Malignant		P value
	Mean	SD	Mean	SD	
Age (years)	58.97	7.13	61.69	7.80	0.095
BMI (kg/m²)	27.99	4.71	26.12	5.07	0.081
Parity	3.16	1.43	3.66	1.40	0.124
Endometrial thickness (mm)	10.96	9.24	10.03	9.19	0.651
Clear span (years)	8.30	6.47	11.69	9.06	**0.022***
Duration of PMB (months)	17.52	45.18	29.79	53.27	0.245

Statistical test: Two sample t-test; *Indicates level of significance at 5%

Discussion

In our study, mean age of menopause was 50.36 ± 3.21, which corresponds previous studies [8,9,10,16]. [Table-Ia] Mean age of presenting PMB was 59.76 ± 7.39 years. [table- 1b]. This is in correlation with various studies [11,12,13,14]. But it was remarkably higher (63.6 years) in a study by Escoffery et al. [15] and lower (51.4 years) in the study by Sreelatha et al. [16].

We found that 57% of the patients with PMB had multiple comorbidities and 28% had no comorbidities, which correspond previous Bangladeshi study by Rahman et al. [17]. But Talwar et al. [9], Begum and Samal [11] found about 35% of the patients had no comorbidities, where Singh et al. [18] found 65% had no comorbidities. These results showed increased prevalence rate of risk factors in our society.

Most of the studies on PMB [7,8,9,10,12,14,16,17,19,20,21] show higher frequencies of benign lesions like us, but in a few studies [18,22,23] frequency of genital tract malignancies was more than benign. Common benign lesions in our study were Endometrial polyps, Leiomyoma and Endometrial atrophy, respectively, which was similar to Pavani et al. [12], but Contrast to other studies [10,17,18,21]. On the other hand, Talwar et al. [9], Al Turiahi et al. [8] and Naher et al. [19] had endometrial hyperplasia as the commonest benign lesion in their study cases. But Lavanya et al. [7] and Sreelatha et al. [16] had found proliferative endometrium as common benign cause in their studies followed by atropic endometrium.

Among the malignancies, Cervical carcinoma was the commonest malignancy followed by endometrial and ovarian carcinoma. These pattern of malignancy was found in some studies, eg: [16,17,18,23]. In contrast, endometrial carcinoma was the commonest followed by cervical, ovarian etc in other studies like [8,9,10,12,19,21].

Now, it is clearly observed in our discussion that carcinoma of cervix is the highest recorded malignancy among women presenting with PMB in Bangladesh, India, Pakistan etc. [7,17,18,20,23]. But in contrast to this, frequency of endometrial carcinoma was more in few other studies [8,9,10,12,13,14,19,21,22]. These results also reflect prevalence of cervical cancer is comparatively more common in this Indian subcontinent than Turkey, Jordan, Iraq where rate of genital malignancy in PMB is much less than us, even rate of cervical cancer was also very low. On the other hand, Thomas Gred Mark et al [24] in Sweden, Lidor A et al. [25] in Israel and Alberico S et al. [26] in Italy conducted multicentred studies with large study sample. They showed lowest frequency of genital tract malignancies in PMB, even without any cervical or endometrial malignancy in some studies. This is the sharp contrast with the industrialized world where the incidence of endometrial cancer and carcinoma of cervix has decreased due to the implementation of effective and well-organized screening program.

In our study, cervical cancer shows a significant association with moderate amount PMB [Table-2], where Endometrial cancer was significantly associated with severe bleeding in the study by Al-Turiahi et al. [8]. Leiomyoma shows a significant association with a clear span of below 5 years (P = 0.013) and endometrial cancer shows a borderline significant association (P = 0.057) with longer clear spans, primarily above 10 years (60%) [Table-IV], which correspond the finding of Turiahi et al. [8]

In our study, Endometrial cancer shows statistically significant association with increasing age (60 to 69 years) [Table-III], which finding is similar to Al-Turiahi et al. [8]. Lower Socioeconomic status, higher parity and normal body weight exhibit significant associations with cervical cancer. [Table-III]. Singh et al. [18] found multiparity has association with cervical cancer and diabetes mellitus, hypertension and obesity were found to be associated with endometrial hyperplasia and Carcinoma endometrium.

Bani-Irshaid and Al sumadi [10] showed that the risk of cancer increased with increasing age while the incidence of bleeding decreased with age.

Again, in our study, Cervical cancer shows a significant association with decreased ET up to 4 mm [Table-V]. On the contrary, endometrial polyps and endometrial cancer show significant associations with increased ET. Bruchim et al. [27] also found that the mean ET was significantly lower in the absence of endometrial carcinoma than in its presence.

Comparison of clinical characteristics in benign and malignant groups [Table-VI] showed no significant difference in the mean age of participants. But Talwar et al. [9] found a significant difference in age where malignant aetiology presenting at higher age. In present study, the patients with malignancies had a significantly longer clear span, which is like the study by Talwar et al. [9] and others [18,25]. But in the study by Talwar et al. [9] multiparity and BMI also shows correlation with increase chance of malignancy.

The differences between studies' results could be due to loco-regional and socioeconomic variations in the study populations. Overall, these factors highlight how demographic and clinical factors influence the prevalence of different types of malignant gynecological conditions in our country.

4.2 Conclusions

With increased life span the incidence of postmenopausal bleeding is on rise and any bleeding in that age group should be evaluated in the line of malignancy unless proved otherwise. In our study we encountered 29% of malignant lesions where majority were cervical carcinomas followed by endometrial carcinomas and ovarian carcinomas. Increased prevalence of the risk factors associated with genital malignancies were found in our study.

4.3 Limitations of study

1. The study included only a single centre which limits generalization.

2. A limited number of patients were included, so results cannot be generalized.

3. Duration of study was also very short.

4.5 Recommendations

1. Initiatives should be taken for increasing awareness among the general population about the alarming symptom of PMB and need for urgent medical evaluation.

2. Priority should be given at the government level to strengthen regular gynaecological screening program for early detection, referral and effective management of PMB.

3. Further multicentre based large cohort studies are necessary.

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