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**Original Research Article**

# Association of postmenopausal bleeding with endometrial cancer

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## ABSTRACT

**Background:** Uterine cancer, also clinically referred to as endometrial cancer, stands out as the most prevalent cancer within the reproductive system of women. Notably, approximately 80% of women experiencing postmenopausal bleeding (PMB) with an endometrial thickness of ≥4 mm exhibit localized pathological lesions in the uterine cavity. This study aimed to assess the association of PMB with endometrial cancer.
**Methods:** This prospective study was conducted at the department of obstetrics and gynecology, delta medical college and hospital, Dhaka, Bangladesh from July 2018 to June 2019. The study comprised 1000 patients selected through purposive sampling, adhering to specific inclusion and exclusion criteria. Microsoft office tools were employed for data processing and analysis. The analytical approach employed was descriptive in nature.
**Results:** The study revealed that the highest percentage of patients (20.20%) exhibited abnormal endometrial hyperplasia, followed by carcinoma cervix (19.2%) and endometrial cancer (16.7%). Additionally, a significant portion of the participants, constituting 40.30%, had co-existing hypertension, while 38.1% had diabetes mellitus, and 34.0% had dyslipidemia. Notably, 65.9% of patients diagnosed with endometrial carcinoma displayed an endometrial thickness exceeding 4 mm.
**Conclusions:** PMB is not statistically significant for endometrial cancer, but prompt evaluation is essential to exclude malignancy. Transvaginal ultrasonography (TVUS) is a reasonable first-line approach, and invasive sampling is recommended when the endometrial thickness exceeds 4 mm.

**Keywords:** PMB, Endometrial cancer, Transvaginal sonography, TVUS

## INTRODUCTION

Endometrial cancer is the most common gynecologic cancer in developed countries, constituting nearly 5% of cancer cases.[1] In contrast to most cancers, both the incidence of endometrial cancer and associated mortality rates have seen an increase in recent years. The likelihood of uterine malignancy in women with postmenopausal uterine bleeding rises with age, from less than 1% in women under 50 to 24% in those over 80.[2-6] Diagnosis often occurs at a localized stage, offering a high curability rate with surgery and a 5-year survival of around 95%. However, the 5-year survival for late-stage (stage IV) endometrial cancer ranges from 16% to 45%.[7-9] PMB is a common symptom, accounting for approximately two-thirds of gynecologic visits among perimenopausal and postmenopausal women. Women presenting with PMB typically undergo additional clinical testing, including TVUS, hysteroscopy, endometrial biopsy, and/or dilation and curettage. The diagnostic workup can vary widely across different healthcare settings.[10,11] Endometrial cancer is often diagnosed at stage I (73% of cases), with more than 90% of malignancies occurring in women over 50, and 95% presenting with abnormal uterine bleeding. Some authors propose using ultrasound examination of endometrial thickness in all postmenopausal women. Studies like the Nordic trial and Italian multicentric trial suggest that an endometrial thickness <4 mm in patients without hormonal replacement therapy (HRT) safely excludes endometrial cancer and accurately predicts atrophy. The primary goal of TVUS is to assess the

endometrium and exclude endometrial carcinoma. In cases of a thin endometrium, the likelihood of endometrial carcinoma is considered low, allowing for expectant management and avoiding invasive procedures like dilatation and curettage or office endometrial biopsy. International guidelines recommend transvaginal ultrasound measurement of endometrial thickness for PMB. If the thickness is increased, additional endometrial sampling is advised.[12] Some guidelines propose hysteroscopy for all patients, while others factor in risk factors to decide on obtaining histology after an initial insufficient tissue sample.[13] For patients on HRT with an endometrial thickness ≥4 mm, endometrial sampling is recommended.[14] Notably, asymptomatic patients with endometrial cancer tend to have a higher rate of well-differentiated tumors compared to those with PMB.[15] Although women with endometrial hyperplasia without atypia are generally considered to have a low risk for cancer, a study found a significant long-term risk of endometrial cancer following PMB.[16] The objective of this study is to assess the association of PMB with endometrial cancer.

### *Objectives*

*General objective*

General objective was to assess the association of PMB with endometrial cancer.

*Specific objectives*

Specific objectives examine respondent age distribution, investigate histopathology findings in subjects and assess co-morbid conditions presence, endometrial thickness, tumor stage in carcinoma-positive cases, and PMB pattern.

## METHODS

This was a prospective study that was conducted at the department of obstetrics and gynecology, delta medical college and hospital, Dhaka, Bangladesh, from July 2018 to June 2019. The study population comprised postmenopausal patients attending the outpatient department (OPD) and those admitted to the respective department due to abnormal uterine bleeding. The selection process involved choosing a total of 1000 patients as study subjects, using a purposive sampling technique based on specific inclusion and exclusion criteria.

### *Inclusion criteria*

Postmenopausal women. Women of 50-80 years old and patients who had given consent to participate in the study.

### *Exclusion criteria*

Patients receiving HRT and patients who did not give consent to participate in the study.

All patients in the study underwent ultrasonographic evaluation of endometrial thickness, outpatient hysteroscopy, and endometrial biopsy, along with additional necessary investigations. Data were collected through face-to-face interviews and retrieved from laboratory reports, then organized into a structured questionnaire. Microsoft office tools were used for data processing and analysis. The analysis employed a descriptive method, and statistical significance was determined with a $p<0.05$. Results were presented in tables and diagrams. Informed written consent was obtained from all study subjects.

## RESULTS

In this series, the majority of patients (62.4%) belonged to the 50-60 years age group, followed by (35.5%) in the 61-70 years age group (Table 1). It was observed that most of the patients (202, 20.20%) had abnormal endometrial hyperplasia, followed by, carcinoma cervix (192, 19.2%), endometrial cancer (167, 16.7%). However, 180 (18.0%) patients had other diagnoses according to histopathology findings (Table 2). In this study, the majority (64.10%) of the patients having PMB didn't show malignant uterine condition, whereas endometrial cancer constituted 16.7% (Figure 1). In this study, a significant majority of the subjects (792, 79.2%) had various co-morbidities (Figure 2). Among them, the predominant co-existing conditions were hypertension in 403 patients (40.3%), diabetes mellitus in 381 patients (38.1%), dyslipidemia in 340 patients (34.0%), chronic kidney disease in 112 patients (11.2%), and hypothyroidism in 90 patients (9.0%) (Figure 3). Observing patients with endometrial carcinoma, it was noted that a majority (659, 65.9%) exhibited an endometrial thickness >4 mm (Table 3). In terms of cancer staging, a significant proportion (93, 9.3%) had stage I cancer, followed by 54 patients (5.4%) at stage II (Table 4). Examining the pattern of PMB, 433 patients (43.3%) had a longer duration of menopause, 297 patients (29.7%) experienced a prolonged bleeding episode, 576 patients (57.6%) reported a higher amount of bleeding, and 168 patients (16.8%) had recurrent bleeding episodes (Table 5).

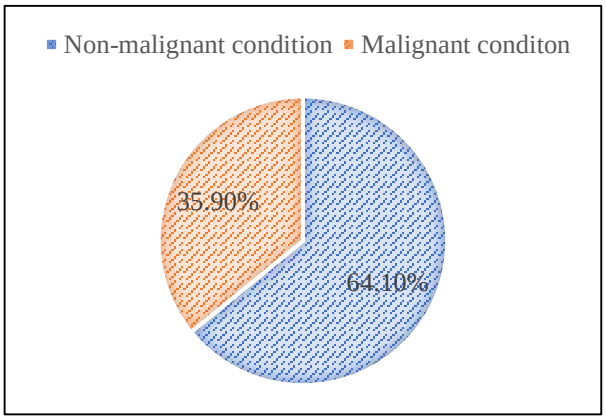


**Figure 1: Distribution of patients with PMB having malignant and non-malignant conditions, (n=1000).**

**Table 1: Distribution of patients according to age, (n=1000).**

| Age (In years) | N | Percentages (%) |
|---|---|---|
| **50-60** | 624 | 62.4 |
| **61-70** | 335 | 35.5 |
| **71-80** | 289 | 28.9 |

**Table 2: Distribution of respondents according to histopathology finding, (n=1000).**

| Finding | N | Percentages (%) |
|---|---|---|
| **Carcinoma cervix** | 192 | 19.2 |
| **Endometrial cancer** | 167 | 16.7 |
| **Abnormal endometrial hyperplasia** | 202 | 20.20 |
| **Cystic glandular hyperplasia** | 113 | 11.3 |
| **Senile endometriosis** | 91 | 9.1 |
| **Atopic vaginitis** | 34 | 3.4 |
| **Tubercula endometriosis** | 21 | 2.1 |
| **Other diagnosis** | 180 | 18.0 |
| **Total malignant condition** | | 35.90 |
| **Total non-malignant condition** | | 64.10 |

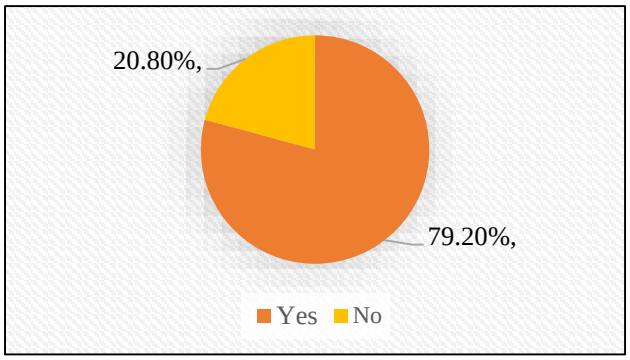


**Figure 2: Distribution of patients according to the presence of co-morbidity, (n=1000).**

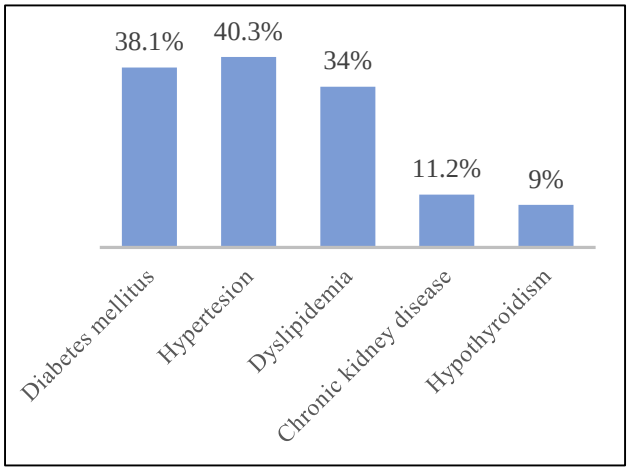


**Figure 3: Distribution of respondents according to co-morbidities, (n=1000)**

**Table 3: Distribution of patients according to endometrial thickness in cancer patients, (n=1000).**

| Endometrial thickness (mm) | N | Percentages (%) |
|---|---|---|
| **≤4** | 341 | 34.1 |
| **>4** | 659 | 65.9 |

**Table 4: Distribution of patients according to stages of endometrial cancer, (n=167).**

| Stages | N | Percentages (%) |
|---|---|---|
| **Stage I** | 93 | 9.3 |
| **Stage II** | 54 | 5.4 |
| **Stage III** | 12 | 1.2 |
| **Stage IV** | 8 | 0.8 |

**Table 5: Pattern of PMB, (n=1000).**

| Patterns | N | Percentages (%) |
|---|---|---|
| **Longer duration of menopause** | 433 | 43.3 |
| **Longer lasting bleeding episode** | 297 | 29.7 |
| **Higher amount of bleeding** | 576 | 57.6 |
| **Recurrent bleeding episodes** | 168 | 16.8 |

## DISCUSSION

In this series, the majority of patients (624, 62.4%) were in the 50-60 years age group, followed by 335 patients (35.5%) in the 61-70 years age group. This age distribution aligns with findings in other studies.[17,18] Endometrial cancer is rare before the age of 45 but sees a significant increase in risk among women in their late 40s to middle 60s.[19] A significant proportion of the study subjects (792, 79.2%) had different co-morbidities. Among them, the majority of patients (403, 40.30%) had co-existing hypertension, 381 (38.1%) had diabetes mellitus, 340 (34.0%) had dyslipidemia, 112 (11.2%) had chronic kidney disease, and 90 (9.0%) had hypothyroidism. Obesity, a strong risk factor for endometrial cancer, contributes to 40% to 50% of all U.S. cases. Women with obesity-associated conditions such as diabetes, hypertension, and polycystic ovary syndrome also face an elevated risk, with obesity being a common factor linking these relationships.[20-25] Metabolic syndrome has been associated with a significant elevation in risk, although to a lesser extent than obesity.[26] Within the study, the majority of patients (202, 20.20%) had abnormal endometrial hyperplasia, followed by carcinoma cervix (192, 19.2%), and endometrial cancer (167, 16.7%). However, 180 patients (18.0%) received other diagnoses based on histopathology findings. Endometrial cancer exhibits a high incidence globally, ranking as the fourth most commonly diagnosed cancer and the seventh most common cause of cancer-related deaths among U.S. women. A U.S. report indicated an increasing rate of new

endometrial cancer cases from 1999 to 2015.[27] Notably, in the present study, a majority of patients with endometrial carcinoma (659, 65.9%) showed an endometrial thickness >4 mm. Some previous studies suggest using a cutoff level of 3-4 mm to exclude endometrial carcinoma in women with PMB.[28,29] Another study reported that women with initial hyperplasia without atypia exhibited a significantly increased risk of developing endometrial cancer during the first four years of follow-up. Interestingly, none of the women with endometrial thickness >4 mm and no or insufficient histology at the first presentation developed endometrial cancer.[30] Regarding the pattern of PMB in this study, 433 patients (43.3%) had a longer duration of menopause, 297 patients (29.7%) experienced a prolonged bleeding episode, 576 patients (57.6%) reported a higher amount of bleeding, and 168 patients (16.8%) had recurrent bleeding episodes. These findings were somewhat similar to the present study.[31] In the current study, a majority of the patients (93, 9.3%) had stage I cancer, followed by 54 patients (5.4%) at stage II. According to another study, the risk of endometrial cancer ranged from 0% to 48% in stage I, yielding an overall pooled estimate of 9% (95% CI, 8%-11%), with moderate variability observed between studies. They also estimated that the proportion of PMB was 84% in stages II to IV tumors.[32] This study revealed that approximately 34% of patients experiencing PMB had a malignant uterine condition, although this finding did not reach statistical significance. This contradicts a study by Salman et al., where they found that about 90% of women with PMB would ultimately be diagnosed with a non-malignant condition.[31] Additionally, according to Clarke et al only 9% of women with PMB were diagnosed with endometrial cancer.[32] The discrepancy in these findings highlights the variability in outcomes across different studies.

### *Limitations*

Due to the study being conducted in a single hospital for a brief duration, there is a potential limitation in the generalizability of the results to the broader community. The findings may not accurately reflect the characteristics and trends present in the entire population, emphasizing the need for caution when extrapolating the study outcomes to the larger community context.

## CONCLUSION

This study concludes that while PMB is not statistically significant with endometrial cancer, prompt evaluation is essential to exclude it. TVUS is recommended as a first-line approach, with invasive sampling needed for endometrial thickness above 4 mm. All women with post-menopausal bleeding, a common symptom of endometrial cancer, should undergo further evaluation, including clinical examination, cervical smear, transvaginal ultrasound, and mandatory outpatient hysteroscopy with biopsy. The study suggests the need for larger-scale research involving multiple centers.

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