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Prevalence and Associated Factors of Endometrial Hyperplasia and Endometrial Cancer in Women with Abnormal Uterine Bleeding and Body Mass Index less than 30 kg/m^2 at Charoenkrung Pracharak Hospital

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ABSTRACT

Objectives: The primary objective was to determine the prevalence and the associated risk factors of endometrial hyperplasia and endometrial cancer in women with abnormal uterine bleeding (AUB) and body mass index (BMI) less than 30 kg/m^2

Materials and Methods: A cross-sectional retrospective study was conducted. The medical records of women with AUB and BMI less than 30 kg/m^2 who underwent endometrial sampling or fractional curettage or hysteroscopy with endometrial biopsy from January 1, 2018 to December 31, 2023 were reviewed. The demographic data included age, parity, BMI, menopause, diabetes mellitus, hypertension, tamoxifen used and histopathological reports were collected. The data were analyzed to determine the prevalence of endometrial hyperplasia and endometrial cancer, and multivariate logistic regression were utilized to identify associated risk factors.

Results: Of all 226 women were recruited. The prevalence of endometrial hyperplasia and endometrial cancer was total 9.2%. In multivariate logistic regression analysis, postmenopause (adjusted odds ratio (aOR) 9.39, 95% CI 1.56, 56.71, p = 0.015) and woman older than 60 years old (aOR 12.27, 95% CI 1.93, 78.20, p = 0.008) were independently associated with endometrial hyperplasia and endometrial cancer.

Conclusion: Postmenopause was an important factor for endometrial hyperplasia and endometrial cancer in women with AUB and BMI less than 30 kg/m^2, risk increasing significantly in those aged over 60 years. Early detection strategies should be considered.

Keywords: prevalence, risk factors, body mass index less than 30 kg/m^2, endometrial hyperplasia, endometrial cancer.

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ความชุกและปัจจัยที่มีความสัมพันธ์กับภาวะเยื่อบุโพรงมดลูกหนาตัวผิดปกติและมะเร็งเยื่อบุโพรงมดลูก ในสตรีที่มีเลือดออกผิดปกติจากโพรงมดลูกและมีดัชนีมวลกายน้อยกว่า 30 กก./ม^2 ณ โรงพยาบาลเจริญกรุงประชารักษ์

จิดาภา ฉันทวานิช, ปิยธิดา ทองรอง, จิรพร เหลืองเมตตากุล

บทคัดย่อ

วัตถุประสงค์: *เพื่อศึกษาความชุกและปัจจัยที่มีความสัมพันธ์ของภาวะเยื่อบุโพรงมดลูกหนาตัวผิดปกติและมะเร็งเยื่อบุโพรงมดลูก ในสตรีที่มีเลือดออกผิดปกติจากโพรงมดลูกและมีดัชนีมวลกายน้อยกว่า 30 กก./ม^2*

วัสดุและวิธีการ: *การศึกษาข้อมูลแบบย้อนหลัง โดยทบทวนเวชระเบียนของสตรีที่มาด้วยอาการเลือดออกผิดปกติจากโพรงมดลูกและมีดัชนีมวลกายน้อยกว่า 30 กก./ม^2 ที่ได้รับการเก็บตัวอย่างชิ้นเนื้อจากโพรงมดลูกด้วยวิธีดูดเก็บเยื่อบุโพรงมดลูก หรือขูดมดลูกแบบแยกส่วน หรือการวินิจฉัยโดยใช้กล้องส่องโพรงมดลูกและเก็บตัวอย่างเยื่อบุโพรงมดลูกส่งตรวจ ตั้งแต่วันที่ 1 มกราคม พ.ศ. 2561 ถึง 31 ธันวาคม พ.ศ. 2566 รวบรวมข้อมูลพื้นฐานของผู้ป่วย ประกอบด้วย อายุ จำนวนการคลอดบุตร ดัชนีมวลกาย ภาวะวัยหมดประจำเดือน โรคเบาหวาน โรคความดันโลหิตสูง ประวัติการใช้ยา tamoxifen และรายงานทางพยาธิวิทยาของเยื่อบุโพรงมดลูกที่ได้รับการตรวจ จากนั้นนำข้อมูลมาวิเคราะห์หาความชุกของภาวะเยื่อบุโพรงมดลูกหนาตัวผิดปกติและมะเร็งเยื่อบุโพรงมดลูก รวมถึงวิเคราะห์แบบถดถอยโลจิสติกพหุตัวแปรเพื่อหาปัจจัยที่มีความสัมพันธ์ในการเกิดโรค*

ผลการศึกษา: *จากสตรีทั้งหมด 226 ราย พบความชุกของภาวะเยื่อบุโพรงมดลูกหนาตัวผิดปกติและมะเร็งเยื่อบุโพรงมดลูกคิดเป็นร้อยละ 9.2 จากการวิเคราะห์แบบถดถอยโลจิสติกพหุตัวแปรพบว่า ภาวะวัยหมดประจำเดือน (adjusted odds ratio (aOR) 9.39, 95% CI 1.56, 56.71, p = 0.015) และ อายุมากกว่า60 ปี (aOR 12.27, 95% CI 1.93, 78.20, p = 0.008) เป็นปัจจัยที่มีความสัมพันธ์กับการเกิดภาวะเยื่อบุโพรงมดลูกหนาตัวผิดปกติและมะเร็งเยื่อบุโพรงมดลูก*

สรุป: *ภาวะวัยหมดประจำเดือนเป็นปัจจัยที่มีความสำคัญในการเกิดภาวะเยื่อบุโพรงมดลูกหนาตัวผิดปกติและมะเร็งเยื่อบุโพรงมดลูก ในสตรีที่มีเลือดออกผิดปกติจากโพรงมดลูกและมีดัชนีมวลกายน้อยกว่า 30 กก./ม^2 ความเสี่ยงเพิ่มขึ้นอย่างมีนัยสำคัญตามอายุ โดยเฉพาะอายุมากกว่า 60 ปี ดังนั้นควรพิจารณาแนวทางการค้นหาตั้งแต่ระยะแรก*

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Introduction

Abnormal uterine bleeding (AUB) is defined as bleeding from the uterine cavity with abnormal volume, duration, frequency, or regularity of menstrual cycles[1]. It is a common gynecologic condition, affecting approximately 10–30% of women[2]. AUB has multiple various etiologies, including structural causes such as endometrial polyps, endometrial hyperplasia, and endometrial carcinoma, while non-structural causes include hormonal imbalance. Endometrial hyperplasia and carcinoma have been reported in up to 20% of women with AUB[3-5].

The International Agency for Research on Cancer (IARC), GLOBOCAN 2022, reported 420,368 new cases of endometrial cancer and 97,723 deaths worldwide. In Thailand, it is the second most common gynecologic malignancy after cervical cancer, with 4,248 new cases and 1,301 deaths annually[6]. Endometrial cancer most frequently occurs in women aged 60–70 years, with about 95% diagnosed after the age of 40[7]. Endometrial hyperplasia, often resulting from hormonal imbalance such as unopposed estrogen, is recognized as a precursor lesion with potential progression to endometrial carcinoma[8].

Previous studies have shown varying prevalence and associated risk factors of endometrial hyperplasia and endometrial carcinoma (EH/EC) in women with AUB. Obesity (body mass index (BMI) more than 30 kg/m²) has consistently been identified as an important risk factor. However, several reports demonstrated that even among women with BMI less than 30 kg/m², the prevalence of EH/EC ranged from 4% to 15.7%[9-16]. Most studies focused on low risk or premenopausal populations, and few specifically examined women with BMI less than 30 kg/m² [9,12]. This group remains underrecognized despite its clinical importance. Moreover, no such study has been conducted in hospitals under the Bangkok Metropolitan Administration (BMA).

Charoenkrung Pracharak Hospital is a tertiary-care center. Women presenting with AUB would be evaluate using various modalities, including endocervical sampling, fractional curettage, office hysteroscopy, and hysteroscopy with biopsy. Treatment was provided by general gynecologists, gynecologic oncologists and gynecologic endoscopist allowing early specialist evaluation for appropriate management of AUB.

Based on these data, the objective of the present study was to determine the prevalence and associated risk factors of EH/EC among women with AUB and BMI less than 30 kg/m².

Materials and Methods

This retrospective cross-sectional study was approved by the Bangkok Metropolitan Administration Human Research Ethics Committee (BMAHREC) (R007hc/67_EXP). We enrolled women who presented with AUB and BMI less than 30 kg/m², who underwent endometrial tissue diagnosis at Charoenkrung Pracharak Hospital from January 1, 2018 to December 31, 2023. The sample size was calculated for cross-sectional study using a 15.71% prevalence of EH/EC in women with AUB and BMI less than 30 kg/m², based on study in 2019(11), with a 95% confidence level, acceptable error 0.05 and an additional 10% adjustment for potential data loss, resulting in a required sample size of 226 participants.

Between 2018 and 2023, a total of 2,782 women presented with AUB at Charoenkrung Pracharak Hospital. Of these, 1,012 women with BMI less than 30 kg/m². Based on the sample size calculation described above, a total of 226 participants were required for the study. Systematic random sampling was employed in order to reduce selection bias.

The inclusion criteria were women aged from 20 to 80 years, presented with AUB and BMI less than 30 kg/m² who underwent endometrial evaluation including endometrial sampling, fractional curettage or hysteroscopy with biopsy and had confirmed histopathological results. In Charoenkrung pracharak

hospital, indications for endometrial evaluation included age more than 35 years, or age less than 35 years with one or more risk factors, including polycystic ovary syndrome, chronic anovulation, a family history of endometrial or colorectal cancer, persistent or recurrent AUB despite medical treatment, or tamoxifen used. Ultrasonography for endometrial assessment was not routinely performed in all women with AUB and was selectively performed according to clinical indications and patient risk stratification. The exclusion criteria were inadequate tissue for histopathological diagnosis, a prior diagnosis of EH/EC, and presence of other malignancies with uterine metastasis.

Data was collected using case record forms, coded without patient identifiers, and stored in a password-protected computer accessible only to the investigators. The variables collected included baseline characteristics (age, nationality, BMI, parity, menopausal status, history of tamoxifen use, diabetes mellitus, hypertension, smoking status, family history of breast or colorectal cancer), and pathological outcomes from endometrial sampling or fractional curettage or hysteroscopy with endometrial biopsy. Diagnoses of endometrial hyperplasia and endometrial cancer were independently reviewed by two pathologists in accordance.

Data analysis was performed using SPSS version 26. Continuous variables were presented as mean with standard deviation or median and interquartile range. Categorical variables were presented as number with percentage. Descriptive statistics were used to present the prevalence of EH/EC. Multivariable logistic regression analysis was used to analyze the associating factors and presented as adjusted odds ratios (aOR) and 95% confidence intervals (CI). A p value < 0.05 was considered statistically significant.

Results

From January 2018 to December 2023, 226 participants met the inclusion criteria. Of the total participants, 182 (80.5%) underwent endometrial sampling, 23 (10.2%) underwent fractional curettage and 21 (9.3%) underwent hysteroscopy with endometrial biopsy. Among them, 21 women were diagnosed with EH/EC, giving a prevalence of 9.2%. The demographic information is presented in Table 1. The average age was 46.6 ± 8.2 years, with the main age group of women being 41–50 years (58.8%). The average BMI was 23.4 ± 3.0 kg/m², with the majority of individuals (66.8%) being within the normal range of 18.5–24.9. Concerning medical comorbidities, 4.4% were diagnosed with diabetes mellitus and 12.8% with hypertension. A majority of women were multiparous (72.6%), whereas 18.6% were postmenopausal.

The Histopathological report is shown in Table 1. The findings revealed that the most common histopathological pattern was proliferative phase endometrium (58.9%) and followed by secretory phase endometrium (16.9%). Endometrial polyps were found in 9.7% of cases, while 5.7% had endometrial hyperplasia (with or without atypia). Endometrial carcinoma was identified in 3.5% of participants. Histological subtypes included endometrioid adenocarcinoma in 4 cases, serous carcinoma in 1 case, clear cell carcinoma in 1 case, and mixed cell adenocarcinoma in 2 cases.

Table 2 shows the univariate analysis of risk factors for EH/EC. After using univariable logistic regression with significance defined at $p < 0.1$ for crude odds ratio calculation, women aged over 60 (crude OR 20.00, 95% CI 5.62, 71.15, $p < 0.001$), postmenopausal status (crude OR 7.78, 95% CI 3.02, 20.05, $p < 0.001$). DM (crude OR 4.71, 95% CI 1.12, 19.82, $p = 0.034$) and HT (crude OR 3.17, 95% CI 1.12, 8.97, $p = 0.030$) showed significant increased risk of EH/EC. Other variables including BMI subgroup, nationality, parity, tamoxifen use, smoking, and family history of breast or colorectal cancer were not significantly associated with EH/EC.

Table 1. Baseline characteristic of participants (n = 226).

Baseline characteristic	n (%)
Age (years), mean ± SD	46.61 ± 8.18
- ≤ 40	41 (18.2)
- 41-50	133 (58.8)
- 51-60	40 (17.7)
- > 60	12 (5.3)
BMI (kg/m2), mean ± SD	23.38 ± 3.01
- < 18.5	9 (4.0)
- 18.5-24.9	151 (66.8)
- 25-29.9	66 (29.2)
Nationality	
- Thai	207 (91.6)
- Non-Thai	19 (8.4)
Underlying disease	
- Diabetes mellitus	10 (4.4)
- Hypertension	29 (12.8)
Parity	
- Nulliparity	62 (27.4)
- Multiparity	164 (72.6)
Menopausal status	
- Premenopause	184 (81.4)
- Postmenopause	42 (18.6)
Tamoxifen used	5 (2.2)
Smoking	2 (0.9)
History of breast cancer in family	4 (1.8)
History of colorectal cancer in family	2 (0.9)
Histopathology result	
- Proliferative phase endometrium	133 (58.9)
- Secretory phase endometrium	38 (16.9)
- Atrophy endometrium	12 (5.3)
- Endometrial polyp	22 (9.7)
- Endometrial hyperplasia without atypia	12 (5.3)
- Endometrial hyperplasia with atypia	1 (0.4)
- Endometrial cancer	8 (3.5)

BMI: body mass index, SD: standard division
Histopathology results from endometrial sampling or fractional curettage or hysteroscopy with endometrial biopsy.

Table 2. Factors associated with endometrial hyperplasia and endometrial carcinoma.

Variables	Endometrial hyperplasia and Endometrial carcinoma		Crude OR (95% CI)	p value
	No n = 205	Yes n = 21		
Age (years)				
- ≤ 60	200 (97.6)	14 (66.7)	Ref	-
- > 60	5 (2.4)	7 (33.3)	20.00 (5.62,71.15)	< 0.001*
BMI (kg/m^2)				
- < 18.5	9 (4.3)	-	-	0.999
- 18.5-24.9	135 (65.9)	16 (76.2)	Ref	-
- 25-29.9	61 (29.8)	5 (23.8)	0.69 (0.24,1.97)	0.491
Nationality				
- Thai	186 (90.7)	21 (100.0)	-	0.998
- Non-Thai	19 (9.3)	-	Ref	-
Diabetes mellitus	7 (3.4)	3 (14.3)	4.71 (1.12,19.82)	0.034*
Hypertension	23 (11.2)	6 (28.6)	3.17 (1.12,8.97)	0.030*
Parity				
- Nulliparity	57 (27.8)	5 (23.8)	0.81 (0.28,2.32)	0.696
- Multiparity	148 (72.2)	16 (76.2)	Ref	-
Menopausal status				
- Premenopause	175 (85.4)	9 (42.9)	Ref	-
- Postmenopause	30 (14.6)	12 (57.1)	7.78 (3.02,20.05)	< 0.001*
Tamoxifen used	5 (2.4)	-	-	0.999
Smoking	2 (1.0)	-	-	0.999
History of breast cancer in family	4 (2.0)	-	-	0.999
History of colorectal cancer in family	2 (1.0)	-	-	0.999

Values are presented as number (%). BMI: body mass index, OR: odds ratio, CI: confidence interval
* significant at p < 0.05 using univariable logistic regression for crude odds ratio calculation.

Table 3 presents the outcomes of the multivariate logistic regression analysis. The current analysis identified that age above 60 years (aOR 12.27, 95% CI 1.93, 78.20, p = 0.008) and menopausal state (aOR 9.39, 95% CI 1.56, 56.71, p = 0.015) were statistically significant independent predictors of the disease. The significant relationships seen for diabetes and hypertension in the univariable analysis disappeared after controlling for age and menopausal state.

Table 3. Multivariate logistic regression of factors associated with endometrial hyperplasia and endometrial Carcinoma.

Variables	Endometrial hyperplasia and Endometrial Carcinoma		Crude OR (95% CI)	Adjusted OR (95% CI)	p value
	No n = 205	Yes n = 21			
Age (years)					
- ≤ 60	200 (97.6)	14 (66.7)	Ref	Ref	-
- > 60	5 (2.4)	7 (33.3)	20.00 (5.62,71.15)	12.27 (1.93,78.20)	0.008*
Diabetes mellitus	7 (3.4)	3 (14.3)	4.71 (1.12,19.82)	1.30 (0.16,10.89)	0.810
Hypertension	23 (11.2)	6 (28.6)	3.17 (1.12,8.97)	0.55 (0.07,4.34)	0.571
Menopausal status					
- Premenopause	175 (85.4)	9 (42.9)	Ref	Ref	-
- Postmenopause	30 (14.6)	12 (57.1)	7.78 (3.02,20.05)	9.39 (1.56,56.71)	0.015*

Values are presented as number (%).
OR: odds ratio, CI: confidence interval
* significant at p < 0.05, significant after multivariate adjustment using multivariable logistic regression for adjusted odds ratio calculation.

Discussion

The prevalence of EH/EC among women with AUB and BMI less than 30 kg/m² in the present study was 9.2%. This prevalence was higher than that reported by Sattanakho et al[9], who found a prevalence of 4%, and by Jha et al[12], who reported a prevalence of 4.7% in women with AUB and BMI less than 30 kg/m². The lower prevalence observed in these 2 studies may be explained by both focused on low-risk, premenopausal women. In contrast, the present study included both premenopausal and postmenopausal women and incorporated additional risk factors, such as nulliparity and tamoxifen use, which may have contributed to the higher observed prevalence.

Age above 60 years and postmenopausal status were the most predictive factors for EH/EC in the present study, accounting for 58.3% of women aged more than 60 years and 28.0% of postmenopausal women. The findings aligned with the disease's epidemiology, which typically affects women aged 60–70 years[17]. The findings also aligned with the 2020 study by Clarke et al[13], which revealed a 17.7% risk of EH/EC in women over 60 years who presented with postmenopausal bleeding (risk 17.7%, 95% CI 13.0, 22.3%, p < 0.001). Similarly, in a study by Suwanwanich in 2019[11], postmenopausal status was also identified as a strong risk factor for EH/EC, with 68.52% of all postmenopausal women affected (RR 4.74, 95% CI 2.5, 9, p < 0.001). Consistent with the study by Sompratthana et al in 2024[18], which reported that aged over 60 years were independently associated with concurrent endometrial cancer, with an adjusted odds ratio of 4.37 (95% CI 1.04, 18.29, p = 0.04) among patients with endometrioid intraepithelial neoplasia (EIN). Although the study population differed from the present study, their results reinforced the importance of older age as a strong risk factor for endometrial cancer.

Diabetes and hypertension were significant in univariate analysis but lost significance after multivariate analysis. The lack of significance may be explained by the exclusion of women with a BMI more

than 30 kg/m² in the present study, which reduced the number of participants with diabetes and hypertension and limited their statistical impact. Compare with other studies such as Suwanwanich in 2019[11], which reported a relative risk of diabetes mellitus (DM) of 3.65 (95% CI 1.8, 7.3, p < 0.001) and HT of 3.33 (95% CI 1.7, 6.4, p < 0.001), and the study of Giannella et al in 2019[14], which highlighted DM as a strong risk factor for EH/EC with an adjusted odds ratio of 9.71 (95% CI 1.63, 57.81, p = 0.012), which may be because neither of the two studies controlled for obesity. By contrast, the study of Wise et al in 2016[15] reported diabetes and hypertension showed no effect, while BMI was a dominant predictor for EH/EC, possibly due to small subgroup numbers. As a result, some variables may have appeared nonsignificant; for example, young healthy women were not usually screened for diabetes.

Nulliparity was not significantly associated with EH/EC in this present study (OR 0.81, 95% CI 0.28, 2.32, p = 0.696). A possible explanation was participants in this group had a mean age of 44.0 ± 7.3 years, and most were premenopausal women, which likely reduced the risk of EH/EC in this subgroup. Similarly, the study by Giannella et al[14] also reported that nulliparity was not significantly associated with EH/EC (OR 3.00; 95% CI 0.93, 9.67; p = 0.065). But contrast with Suwanwanich[14], which showed a relative risk of nulliparous 7.44 (95% CI 3.6, 15.6, p < 0.001). Because of 1. the exclusion of women with BMI > 30 kg/m² in our study removed a critical synergistic factor. Obesity drives peripheral aromatization of androgens to estrogens; without this substrate, nulliparity alone may be insufficient to generate the threshold of unopposed estrogen required for neoplastic transformation. 2. Our study was predominantly premenopausal with a mean age of 44 years. Unlike older studies where nulliparity reflects a lifetime of cumulative exposure, our participants retained cyclic progesterone protection (luteal phase) during regular menstrual cycles. This suggested that in non-obese, premenopausal women, nulliparity was not an independent predictor of EH/EC, whereas in older or obese populations (as likely seen in Suwanwanich), it served as a proxy for chronic anovulation and long-term estrogen exposure.

The analysis of tamoxifen usage in the current investigation was precluded by the limited number of cases, aligning with Suwanwanich in 2019[11] (RR 2.08, 95% CI 0.6, 7.2, p = 0.221), where the small cohort of patients administered tamoxifen restricted the capacity to formulate definitive findings. However, the current study differs from Chen et al[16], who concentrated on women with breast cancer undergoing tamoxifen treatment in comparison to non-users. The logistic regression analysis, conducted with a sufficiently enough sample size, established a significant correlation between tamoxifen usage and the incidence of endometrial cancer (OR 2.94; 95% CI 2.13, 4.06; p < 0.001). In contrast, a study of Suwanwanich in 2024[19], which assessed the risk of EH/EC in premenopausal women with AUB, identified tamoxifen (95% CI 1.33, 165.76; p=0.041) as significant predictors. This difference may be explained by variations in study population and methodology, as that study included obese women and incorporated endometrial thickness > 10 mm into the risk assessment model, thereby increasing the likelihood of detecting such associations.

The strength was that the present study focused specifically on AUB in patients with a BMI of less than 30 kg/m². All participants met the strict inclusion criteria, and diagnoses were confirmed by histopathological findings

This study was conducted in a single center, which may limit the generalizability of the findings to other populations. The retrospective design limited the analysis to variables available in medical records, and some relevant risk factors could not be fully assessed. The sample size was relatively small for evaluating uncommon exposures such as tamoxifen used, smoking, or family history of breast or colorectal cancer, thereby limiting the statistical power to detect associations. Furthermore, direct measures of body fat composition and distribution were not available, which may have led to underestimation of the true

effect of adiposity on endometrial pathology.

The study demonstrated that even among women with BMI less than 30 kg/m², the prevalence of EH/EC was considerable (9.2%). Age above 60 years and postmenopausal bleeding were independent predictors. These findings suggest that clinicians should prioritize early endometrial assessment in older and postmenopausal women presenting with AUB, regardless of BMI. Incorporating age and menopausal status into triage algorithms may improve timely diagnosis and patient outcomes.

Conclusion

The prevalence of EH/EC among women with AUB and BMI less than 30 kg/m² was 9.2%. Postmenopause was an important factor for the disease. The risk increased significantly with age, especially after being 60 years old. These findings suggest that early detection strategies should be considered, particularly in older and postmenopausal women presenting with AUB.

Potential conflicts of interest

The authors declare no conflicts of interest.

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