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Original Research

Prevalence of Endometrial Cancer and Correlation between Body Mass Index and Histopathological Finding of Endometrial Tissue for Prediction of Endometrial Cancer: Retrospective Analysis of Electronic Medical Records

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Introduction: Aim of the study was to investigate the prevalence and correlation of body mass index (BMI) and histopathological finding of the endometrium for prediction of endometrial hyperplasia/ endometrial cancer (EH/EC) in women with abnormal uterine bleeding (AUB).

Materials and methods: This retrospective cohort study was conducted at the outpatient clinic, department of obstetrics and gynecology, Bhumibol Adulyadej Hospital, Royal Thai Airforce, Thailand from January 2021 through December 2024. The subjects were female who presented with AUB and underwent endometrial biopsy (EB). Demographic data was collected and analyzed.

Results: A total of 1,408 cases were recruited. Mean age of participants were 49.9 years old. There were 430 and 978 cases of age less (A1) and more than (A2) 45 years old. Subjects A2 group had significantly more parity (74.9% vs 59.3%), diabetes mellitus (10.2% vs 0.9%), hypertension (20.6% vs 3.5%) and dyslipidemia (13.1% vs 1.6%) than those in A1 group. Polycystic ovarian syndrome was commonly found among subjects in A1 group than A2 group (2.8% vs 0.2%, p-value < 0.001). Prevalence of EC was 3.5 (54/1, 540) percent. Percentage of EH/EC was 14.2 (200/1,408). Among subjects in A1 group, the cut point of BMI for predicting EH/EC was 32 kg/m^2. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy were 48.9, 85.7, 28.6, 93.5, and 81.9 percent, respectively.

Conclusions: BMI ≥ $32kg/m^2$ was significantly associated with EH/EC among women age less than 45 years old with abnormal uterine bleeding.

Introduction

Endometrial hyperplasia (EH) is an abnormal proliferation of the endometrium tissue. EH with

cellular atypia is defined as endometrial intraepithelial neoplasia (EIN). Estrogen stimulates endometrium during proliferative phase. Progesterone is secreted from corpus luteum after ovulation. Anovulation condition namely polycystic ovarian syndrome (PCOS), obesity, early menarche, and late menopause cause unopposed estrogen to endometrium [1]. Excessive exposure to unopposed estrogen without the protective effect of progesterone leads to endometrial hyperplasia or cancer development [2].

According to World Health Organization (WHO), both EH and EIN were associated with endometrial cancer (EC) with 1-3 and 23-40 percent, respectively [3]. EC is one of the most common malignancies of the female reproductive tract [4]. In Thailand EC is in the 6th most common malignancy of the female reproductive tract which has a prevalence 1.5 to 5.3 per 100,000 female population [5]. The most leading symptom of EH and EC (90 percent) was abnormal uterine bleeding (AUB) such as spotting, or heavy menstrual bleeding, and post-menopausal bleeding [6].

According to WHO, obesity is defined as body mass index (BMI) 30.0 kg/m^2 or greater. However, Thai department of health defined obesity for Thai female population at 25 kg/m^2 or greater [7]. Obesity causes chronic ovulation and unopposed estrogen. Adipose tissue converts androstenedione to estrone, which is mostly found in obese patients. Estrone (E3) is one of the lowest potent of estrogen [2, 8, 9].

To make a diagnosis of EH, EIN or even EC, histopathology is the gold standard. Endometrial tissue is obtained from endometrial biopsy (EB) either by blind or hysteroscopic guided endometrial biopsy, and dilation and curettage (D&C). EB can be performed at the outpatient clinic without the need for anesthesia. D&C is a procedure that needs to be an in-patient status which requires anesthesia and operative setting. Correlation of EB and D&C ranged between 97 and 98 percent, respectively [10]. EB is the most cost-effective biopsy strategy compared to D&C for EC diagnosis.

Obesity represents an important risk factor for EC. According to Onstad's study, women with a BMI ≥ 30 kg/m^2 presented 2-4 times higher basic risk for endometrial cancer, while WHO ASEAN population, defined obesity as BMI ≥ 25 kg/m^2 [2, 7, 11].

This study aimed to investigate the prevalence and correlation of BMI and histopathological finding of the endometrial biopsy for the prediction of endometrial hyperplasia and cancer (EH/EC) in Thai women.

Materials and methods

This retrospective cohort study was conducted at the outpatient clinic, department of obstetrics and gynecology, Bhumibol Adulyadej Hospital (BAH), Royal Thai Airforce, Thailand between January 2021 and December 2024. The present study was approved by the BAH Ethic Committee (IRB number 58/68) in the year 2025.

The subjects were AUB cases who underwent outpatient EB with histopathology report. EB was performed by using Pipelle (Pipelle De Cornier, Laboratories CCD, Paris, France), or sharp curettage, or both. If >1 biopsy was performed within 6 months, the one resulting in the most serious diagnosis was considered as the outcome. We recruited the medical information and recorded it via the medical electronic database of BAH. ICD-9 No 6816 code was used for medical term searching. Exclusion criteria were cases with one or more of the following, lack of clinical data, known case of EC or EIN prior to January 2021, or insufficient tissue for diagnosis. Subjects were divided into two groups namely A1 (age less than 45 years old) and A2 (age equal or more than 45 years old). Demographic characters included age, body weight, height, BMI, parity, underlying diseases, and hormonal used. Histopathology of EB was also collected. We used the prevalence of the EC as 9 percent, according to meta-analysis study of Clarke et al in year 2018

[12]. We set alpha and beta errors at a level of 0.05 and 0.1, respectively. Sample size was at least 1,399 cases. A total sample size of 1,540 cases was needed after the addition of 10 percent. A p-value of 0.05 was considered statistically significant (Figure 1).

Figure 1. Flow Chart of Participants. EB, endometrial biopsy; EC, endometrial carcinoma.

Current guidelines discussion about the role of endometrial histopathology examination was suggested to those with AUB aged equal or more than 45 years old, obese, and unopposed to estrogen [13]. Subjects were further divided into two groups according to age less and more than 45 years old. Cut point of obesity for Asian population was equal to or more than 25kg/m^2 [7].

The statistical analysis was performed using SPSS version 18.0. Demographic data of participants were determined, frequency and percentage for categorical data while mean, standard deviation, median and interquartile range were used for continuous data. Comparisons between groups were performed using independent t-test, Mann-Whitney U test, chi-square test or Fisher's exact test as appropriated. Multivariable analysis by multiple logistic regression was used in determining independent risk factors, adjusting for potential confounders. Data were analyzed using the discrimination ability and optimal cutoff value of BMI. Highest sensitivity and specificity were determined by receiver operating characteristic (ROC) curve analysis.

Results

During the study period, a total of 1,408 cases were recruited as shown in Figure 1. Mean age of participants were 49.9 years old. There were 430 and 978 cases of participants aged less and more than 45 years old. Subjects older than 45 years old had higher parity (74.9% vs 59.3%), diabetes mellitus (DM 10.2% vs 0.9%), hypertension (HT: 20.6% vs 3.5%) and dyslipidemia (DLP: 13.1% vs 1.6%) than those younger than 45 years old with statistical significance. PCOS was commonly found among subjects younger than 45 years old than those older than 45 years old (2.8% vs 0.2%, p-value < 0.001). History of hormonal contraception, tamoxifen usage, BMI and enlarged uterus (fibroid/adenomyosis) of both groups were comparable as shown in Table 1. There were 54 cases of EC in this study. The prevalence of EC was 3.5 (54/1,540) percent. The percentage of EH/EC was 14.2 (200/1,408) without statistical significance between both groups as shown in Table 1.

		Age (year)		p-value
	Total	< 45	≥ 45	
Age (years)	49.9 ± 11.5	38.2 ± 4.9	55.1 ± 9.7	<0.001
BMI (kg/m2)	25.7 ± 5.5	26.1 ± 6.5	25.5 ± 5.0	0.12
Nulliparity	421 (29.9)	175 (40.7)	246 (25.1)	<0.001
DM	104 (7.4)	4 (0.9)	100 (10.2)	<0.001
PCOS	14 (1)	12 (2.8)	2 (0.2)	<0.001
Fibroid	88 (6.3)	21 (4.9)	67 (6.9)	0.09
Adenomyosis	72 (5.1)	18 (4.2)	54 (5.2)	0.18
HT	217 (15.4)	15 (3.5)	202 (20.6)	<0.001
DLP	136 (9.7)	7 (1.6)	129 (13.1)	<0.001
SLE	14 (1)	5 (1.2)	9 (0.9)	0.43
Anemia	10 (7.1)	3 (0.7)	7 (0.7)	0.63
Tamoxifen usage	26 (1.8)	4 (0.9)	22 (2.2)	0.06
Post-menopause	403 (28.6)	5 (1.2)	398 (40.7)	<0.001
Hormonal used	230 (16.3)	72 (16.7)	158 (16.2)	0.42
ET (mm)	7.4 ± 5.1	7.5 ± 5.2	7.4 ± 5.0	0.83
EH/EC	200 (14.2)	62 (14.4)	138 (14.1)	0.07

Table 1. Characteristics of Participants who were Aged less (n=430) and more than 45 years (n=978).

BMI: body mass index, DM: diabetes mellitus, PCOS: polycystic ovarian syndrome, HT: hypertension, DLP: dyslipidemia, SLE: systemic lupus erythematosus, ET: endometrial thickness, EH: endometrial hyperplasia, EC: endometrial carcinoma

ROC for BMI in predicting EH/EC was generated among both groups (age < 45 and ≥ 45 years old). Area under curve (AUC) of BMI predict EH/EC were 0.67 and 0.56 among subjects with age less and equal or more than 45 years old, respectively as shown in Figure 2.

Figure 2. Receiver Operating Curve (ROC) for BMI in Predicting Endometrial Hyperplasia and Cancer, Stratified by Age Group (<45 Years and >45 Years). BMI, body mass index; ROC, receiver operating curve.

Among subjects younger than 45 years old, the cut point of BMI for predicting EH/EC was 32 kg/m^2. Diagnostic performance of BMI at levels of 25, 30, and 32 kg/m^2 were analyzed and presented inf Table 2.

			<45			
	> 25	95%CI	> 30	95%CI	> 32	95%CI
Sensitivity (%)	68.9	53.4-81.8	51.1	35.8-66.3	48.9	33.7-64.2
Specificity (%)	57.4	52.3-62.4	79.7	75.4-83.6	85.7	81.8-89.1
PPV (%)	15.9	11.1-21.8	22.8	15-32.2	28.6	18.8-40
NPV (%)	94	90.2-96.7	93.3	90.1-95.8	93.5	90.4-95.8
LR+	1.6	1.3-2	2.5	1.8-3.6	3.4	2.3-5
LR-	0.5	0.3-0.8	0.6	0.5-0.8	0.6	0.4-0.8
Accuracy (%)	58.6	53.9-63.3	76.5	72.8-80.7	81.9	78.2-85.5
			>45			
	>25	95%CI	>25.8	95%CI	>30	95%CI
Sensitivity (%)	59.4	51.2-67.2	52.3	44.1-60.3	19.4	13.5-26.5
Specificity (%)	53	49.5-56.4	61.8	58.3-65.1	83.8	81.1-86.3
PPV (%)	19.2	15.8-23.1	20.5	16.6-24.8	18.4	12.8-25.2
NPV (%)	87.3	84.1-90.1	87.3	84.3-89.9	84.6	82-87
LR+	1.3	1-1.5	1.4	1.2-1.6	1.2	0.8-1.7
LR-	0.8	0.6-0.9	0.8	0.7-0.9	1	0.9-1
Accuracy (%)	54	50.9-57.1	60.2	57.2-63.3	73.6	70.8-76.3

Table 2. Diagnostic Performance for BMI Thresholds in Subjects Aged Less and Equal or more than 45 Years.

BMI: body mass index, PPV: positive predictive value, NPV: negative predictive value, LR+: positive likelihood ratio, LR-: negative likelihood ratio

Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy were 48.9, 85.7, 28.6, 93.5, and 81.9 percent, respectively with 32 kg/m^2 cut point.

Discussion

Women who had AUB and were older than 45 years old were recommended to undergo EB according to ACOG recommendation in year 2012 [13]. However, women with AUB younger than

45 years old still underwent EB with high-risk condition namely unopposed estrogen condition, PCOS, and obesity [13-16]. Study from USA in 2020, Kahn reported the prevalence of EC/ EH at 0.08 percent among subjects with AUB. Kahn's subjects had average age of 35 years old with PCOS at 36 percent [14]. Chen reported from China in year 2022 among women with AUB and average age of 32 years old. Chen's subjects had an average BMI at 33.5kg/m^2 and one quarter (26/102) of subjects has an underlying of PCOS [15]. Another report from USA in year 2023, Beavis reported endometrial histopathology in women with AUB who had BMI more than 50kg/m^2 with mean age of 39 years old [16].

Most of EC cases were counselled to undergo surgical staging. In case of inoperable condition namely severe life-threatening medical conditions or morbid obesity. Concurrent chemoradiation was alternative option for unsuitable for surgery. Robotic surgery was recommended in morbid obesity [2]. How ever, the cost of robotic surgery was still expensive in Thailand (low-middle income country).

Subjects in the current study consisted of women with AUB with average age of 49.9 years old and BMI at 24.8kg/m^2. One-third (430/1408) of subjects were younger than 45 years old. EH/EC occurrence in the present study was 14.4 (62/430) percent.

Prevalence of EC from previous studies ranged from 0.08 to 9 percent [12, 14, 16-18]. Beavis reported EC prevalence at 4 percent. Their subjects had average age of 39 years old with obesity at 48 percent [16]. Prevalence of EC in the current study was 3.5 percent. The average age of the current study was 49.9 years old with obesity around 47.7 percent. The findings from the current study were similar to Beavis' study [16].

Report from Singapore by Lei showed prevalence of EC at only 0.37 percent. Lei's subjects had average age 56.8 years old. However, the obesity rate of Lei's subjects was only 9 percent [18]. Reported from USA by Kahn, the prevalence of EC was 0.08 percent among women with average age 35 years old. Two-thirds of Kahn's subjects were classified as obesity [14]. Wise's study from New Zealand, prevalence of EC was around 1.4 percent. Half of Wise's subjects were obesity [17]. Prevalence of EC was associated with higher age and obesity [2]. The prevalence of the current study supported the result from the previous studies [12, 14, 16-18]. Comparison of the current work to previous studies was summarized and presented in Table 3.

	Present	Stachowicz	Wise	Lei	Beavis	Chen	Thoprasert	Zhao	Kahn
Year	2025	2021	2016	2022	2023	2022	2023	2021	2020
Country	Thailand	Poland	NZ	SG	USA	China	Thailand	China	USA
Population (n)	1,408		916	34,028	3,175		304		11,569
EC/EH (n)	54/146	236/158	12/29		30/105	62/40	1.2/7.5	72/156	10/12
Prevalence (%)	3.5		1.4	0.37	4				0.08
Status	Pre/Peri/M	Peri/M	Pre	Peri/M	Pre	Pre	Peri	Peri/M	Pre
Menopause	28.6	73.3						41.2	
Age (yr)	49.9	60.3	42.9	56.8	39	32	44.7	48.7	35
BMI (kg/m^2)	25.7	30.4			29.7	33.5	27.5	24.3	
Nulliparity (%)	29.9		14.8	6.9		77.5	20.8	12.2	95
DM (%)	7.4		9.7		7	8.8	3.9	19.4	9
Obesity (%)	47.7	46	49.2	9	48	100			68
Hormonal use (%)	16.3		36.1	26.1	29				32
Tamoxifen (%)	1.8								

PCOS (%)	1				3	26	1.2		36
Endometriosis	5.1					5.9			9
Anovulation							59		
Hypothyroidism							1.9		18
HT	15.4				17			62.9	27
DLP	9.7							25.9	
CA-125 (mean)								20.5	
ET (mm)	7.4	8	12				8.3	10.1	
Smoker (%)			15.5		22				
Cut point BMI	32/25.8	30	30		50		8.3 (ET)		
Sensitivity	48.9/52.3						78.6		
Specificity	85.7/61.8						61.6		
PPV	28.6/20.5						13.2		
NPV	93.5/87.3						97.5		

Table 3. Comparation of the Current Study to the Previous Literatures in Prevalence of Endometrial Cancer.

EC: endometrial cancer, EH: endometrial hyperplasia, BMI: body mass index, DM: diabetes mellitus, PCOS: polycystic ovarian syndrome, HT:hypertension, DLP: dyslipidemia, ET: endometrial thickness, PPV: positive predictive value, NPV: negative predictive value

From the current study, cut point of BMI was generated for diagnostic power of EH/EC diagnosis. The sensitivity, specificity, PPV, NPV and accuracy of BMI at > 25 and > 32kg/m^2 were 68.9/48.9, 57.4/85.7, 15.9/28.6, 94.0/93.5 and 58.6/81.9 percent, respectively. NPV at the cut-point of BMI at > 25 and > 32kg/m^2 were comparable. According to WHO, the ASEAN population defined obesity as BMI ≥ 25 kg/m^2, while in European population was ≥ 30 kg/m^2 [7]. It meant that if there were subjects under 45 years old who have AUB with BMI more than 25 kg/m^2 then EB for histopathology should be performed. If the EB obtaining procedure was not complicated, then EB should be done. However, if the EB obtaining procedure cannot be done at out-patient clinic, then procedure should be performed in operation room under anesthesia.

From the current study, cut-point BMI for women younger than 45 years old was 32kg/m^2. The subjects younger than 45 years old with AUB with BMI between 25 and 32 kg/m^2 could be observed if the EB obtaining procedure was difficult. Even though the sensitivity of BMI cut point at 32kg/m^2 was less than BMI at 25kg/m^2 (48.9 vs 68.9%). The higher BMI cut point (32kg/m^2) value, the lower sensitivity would be result. The lower cut point (25kg/m^2) gave comparable high NPV to high BMI cut point (94.0 vs 93.5%). In addition to BMS, various other interventions have been introduced to improve outcomes and quality of life of in patients with cancer, which should be taken into consideration when interpreting the results of the present study [19-23].

The trend of non-invasive concepts found public favor. Those who had difficulty obtaining EB, women who were younger than 45 years old presented with AUB with BMI of less than 32kg/m^2 should be counseled that the risk of EH/EC was 5.1 percent (22/430). Closed observation might be benefit than trying to force endometrial obtaining procedure.

Strength of this study were synthesized literatures and large number of premenopausal women with AUB who undergone EB obtaining for tissue histopathology. Limitations of this study were unavailable confound from its retrospective design, molecular study (MMR, POLE, p53, and p16) and limited ethnic population.

In conclusion, in women younger than 45 years old presented with AUB and obesity (BMI > 25kg/m^2), an EB should be performed. However, closed follow-up protocol was justified for those who BMI between 25 and 32kg/m^2 and the EB was difficult to perform or would be painful. Counseling for clinical observation was an alternative option or hysteroscopy if possible.

Acknowledgments

Statement of Transparency and Principals:

• Author declares no conflict of interest

• Study was approved by Research Ethic Committee

of author affiliated Institute.

• Study's data is available upon a reasonable request.

• All authors have contributed to implementation of this research.

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