RESEARCH ARTICLE

Body Mass Index and Breast Cancer Risk among Thai Premenopausal Women: a Case-Control Study

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Abstract

Background: Breast cancer (BC) is the leading malignancy in women with high incidence and mortality worldwide. Obesity is one of several established risk factors for chronic diseases including cancer. The objective of this research was to determine the association of body mass index (BMI) with BC among Thai premenopausal women (TPW). **Materials and Methods:** A case-control study was conducted among TPW attending the National Cancer Institute in Bangkok, with 257 cases and 257 controls in 2013-2014. Cases and controls were matched by age (± 5 years), residential area and duration of attending. Data were collected with a questionnaire comprising 2 parts: part 1 socio-demographic characteristics, and part 2 health risk behavior and reproductive factors and BMI. The obtained data were analyzed using descriptive and analytic statistics with a computerized statistical package. **Results:** The study participants were mainly 40-44 years old (60 %) with an average age of 39 years. The major type of BC was the invasive ductal carcinoma (91.8%). On univariate analysis, risk factors for BC among the TPW were family history of BC, history of benign breast tumors, younger age at menarche, parity, miscarriage, contraceptive use, passive smoking, multivitamin use, and BMI ($p<0.05$). Multivariable conditional logistic regression analysis, controlling for possible confounding factors, revealed that a BMI 25-29.9 and ≥ 30 kg/m2 increased the risk of BC by a factor of 2.09 and 2.37 times, respectively (OR=2.09, 95%CI =1.09-3.97; OR=2.37, 95%CI =1.24-10.06). **Conclusions:** A surveillance system of obesity should be conducted in cooperation with information regarding physical activities and weight control among TPW as an essential measure to reduce BC risk.

Keywords: Body mass index- breast cancer- Thai premenopausal women

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Introduction

At present, it is well established that BC is the most commonly diagnosed invasive cancer and the leading cause of cancer death among women worldwide including in Thailand (Siegel et al., 2015; National Cancer Control Committee, 2013; Bureau of Policy and Strategies, 2010; Bureau of Policy and Strategies, 2011; Bureau of Policy and Strategies, 2015). Currently, the Global BC statistics showed an increasing trend in most countries, including Europe, Latin America, Asia, and Africa (DeSantis et al., 2015). In Thailand, we found an increasing trend of BC death rate over 10 years, as shown in Figure 1 (Bureau of Policy and Strategies, 2010; Bureau of Policy and Strategies, 2015). Causes of being BC are likely to be multifactorial. The association between BMI and BC risk has been examined in numerous studies, mainly in western countries. Although the incidence of BC in the Asian population still remains lower than that in the Western population (Wada et al., 2014). However, these studies were comparatively few among Asian population. The effects of BMI on BC have remained unclear among premenopausal women. In Thailand, there are quite very few studies of this association among TPW. The present study was carried out to assess the association between BMI and BC occurrence among TPW.

Materials and Methods

Study Design, Sample Size and Sampling Technique

A hospital based matched case-control study (1:1) was performed at the National Cancer Institute in Bangkok during November 2013 - December 2014 to identify the effect of BMI and BC risk among TPW. A total of 257 BC cases and 257 controls were included in the study. The cases were newly diagnosed with breast cancer by pathologists. The controls were healthy TPW who had annual health check-up. Cases and controls were matched (1:1) by age (±5 years), residential area and duration of attending. Of the 514 women were both premenopausal and aged <45 years at the time of study. Both cases and controls used the same questionnaire to obtain data

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collection. The sample size was calculated by the formula (Lwanga and Lemeshows, 1991). Where Po(0.32) and P1 (0.68) were the proportions of exposure in controls and cases (Umpan, 2004); Zα/2 = 1.96 at α = 0.05; Zβ = 0.84 at β = 0.20; and P = 0.5. The calculated sample size in each group was at least 256.

Tool and Measurements

Data collection was obtained by a self-administered questionnaire, any suspicion upon questionnaire items would be guided by research assistants. The questionnaire comprised socio-demographic factors, health risk behaviors, reproductive factors, obesity and cancer status. While BC information was collected by laboratory and pathological results, namely, TNM classification, stage of disease, hormone receptor test, and date of diagnosis with BC.

Variable definitions

TPW were defined as Thai women who aged ≤ 45 years and still having menstrual cycles at the time of study (Chaveepojnkamjorn et al, 2017).

BMI was calculated as (weight in kg)/(height in m)2 and it was categorized according to the Asian's criteria (Steering Committee, 2000).

BC was defined as code C50 according to the International Classification of Diseases and Health Related Problem, 10th Revision.

Ethical Considerations

The present study was reviewed and approved by the Ethics Committee for research of National Cancer Institute, Ministry of Public Health (148/2556) and the Ethics Committee for Research in Human Subjects of the Faculty of Public Health, Mahidol University (Ref No. MuPH 2014-090) and agreed with the Helsinki declaration. All participants are willing to participate in this study. Informed consent to participate in the study was obtained from participants after informing them the details of study. Information was collected by a self-administered questionnaire with the help and supervision of research assistants. Confidentiality was well kept throughout the study using anonymous technique (respondents were identified by code numbers to ensure confidentiality and the results were analyzed as a whole group).

Statistical Analyses

The data were analyzed with the statistical software STATA (Release 12, StataCorp LP, College Station, TX, Serial number: 4012044037). For better understanding, the information was tabulated by means of descriptive statistics, univariate analysis, and multivariate analysis. Categorical variables were given as a frequency and percentage, crude odds ratio, 95 % confidence interval (CI) of OR and p-value. The numerical variables were expressed as mean, median, minimum and maximum, and standard deviation (SD). Univariable conditional logistic regression analysis was performed to differentiate proportional exposures between BC patents and controls for categorical variables. Adjusted odds ratio and the 95 % CI of OR were calculated from multivariable conditional logistic regression to examine associations between BMI and BC occurrence, adjusted for potential confounding factors of reproductive factors and health risk behaviors. A p-value of <0.05 was considered statistically significant in the analyses.

Results

Demographic Characteristics of subjects at baseline

A total of 514 TPW participated in the case-control study. The average age of subjects was 39 years. Table 1

Table 1. General Characteristics of Cases and Controls

Characteristics	Cases		Controls		p-value[a]
	No.	%	No.	%	
Age gr. (yrs)					0.981
≤ 29	10	3.9	11	4.3	
30-34	30	11.7	28	10.9	
35-39	63	24.5	61	23.7	
40-44	154	59.9	157	61.1	
Mean (SD)	39.20 (4.39)		39.30 (4.41)		
Min-Max	25-44		25-44		
Marital status					0.07
Single	68	26.5	84	32.7	
Married	159	61.8	156	60.7	
Widowed/Divorced	30	11.7	17	6.6	
Education					0.068
No formal education	10	3.9	8	3.1	
Primary school	67	26.1	52	20.2	
Secondary school	78	30.3	65	25.3	
Higher education	102	39.7	132	51.4	
Religion					0.689
Buddhism	248	96.5	247	96.1	
Islam	7	2.7	6	2.3	
Christianity	2	0.8	4	1.6	
Residence					1
North	1	0.4	1	0.4	
Northeast	11	4.3	11	4.3	
Central	176	68.5	176	68.5	
East	16	6.2	16	6.2	
West	48	18.7	48	18.7	
South	5	1.9	5	1.9	
Occupation					0.668
Office employee	92	35.8	87	33.8	
Entrepreneur	77	30	85	33.1	
Government officer	73	28.4	75	29.2	
Agriculture	15	5.8	10	3.9	
Monthly family income (baht)					0.066
< 10,000	38	14.8	34	13.2	
10,000-15,000	52	20.2	48	18.7	
15,001-30,000	138	53.7	124	48.2	
>30,000	29	11.3	51	19.9	
Mean	22,740.08		24,174.32		
(SD)	(9,311.92)		(13,541.38)		
Min-Max	7,000-70,000		7,800-95,000		

[a], Chi-square test

Table 2. Univariable Conditional Logistic Regression Analysis of Characteristics associated with BC among TPW

Characteristics	Cases		Controls		OR_c	95%CI	p-value[a]
	No.	%	No.	%			
Family history of BC							
No	211	82.1	249	96.9	1		
Yes	46	17.9	8	3.1	6.43	2.89-14.25	<0.001*
History of benign breast tumor							
No	209	81.3	235	91.3	1		
Yes	48	18.7	22	8.6	2.37	1.39-4.05	0.001*
Age at menarche (yrs)							
≥14	83	32.3	140	54.5	1		
<14	174	67.7	117	45.5	2.54	1.74-3.72	<0.001*
Parity							
No	193	75.1	172	66.9	1		
Yes	64	24.9	85	33.1	0.68	0.46-1.00	0.051
Miscarriage							
No	186	72.4	214	83.3	1		
Yes	71	27.6	43	16.7	1.93	1.24-3.00	0.003*
Contraceptive use							
No	90	35	162	63	1		
Yes	167	65	95	37	3.32	2.22-4.96	<0.001*
Active smoking							
No	248	96.5	251	97.7	1		
Yes	9	3.5	6	2.3	1.5	0.53-4.21	0.437
Passive smoking							
No	153	59.5	198	77.1	1		
Yes	104	40.5	59	22.9	2.22	1.46-3.37	<0.001*
Alcohol consumption							
No	251	97.7	252	98.1	1		
Yes	6	2.3	5	1.9	1.2	0.32-4.61	0.761
Multivitamin use							
No	227	88.3	168	65.4	1		
Yes	30	11.7	89	34.6	0.26	0.16-0.42	<0.001*
BMI (kg/m2)							
18.5-22.9	89	34.7	122	47.4	1		
23.0-24.9	44	17.1	54	21	1.18	0.71-1.97	0.531
25.0-29.9	88	34.2	41	16	3.07	1.87-5.05	<0.001*
≥30.0	26	10.1	10	3.9	3.68	1.64-8.25	<0.001*
<18.5	10	3.9	30	11.7	0.44	0.22-0.95	0.036*

[a], Univariable analysis performed on 257 matched pairs; BC, Breast Cancer; OR_c, crude odds ratio; CI, confidence interval; *, Significant at p-value <0.05.

outlined the socio-demographic characteristics of them. To summarize majority of them were aged 40-44 years (59.9%, 61.1%), married (61.8%, 60.7), education higher than secondary school (39.7%, 51.4%), buddhism (96.5%, 96.1), living in central region (68.5%), office employee (35.8%, 33.8%), and had monthly family income between 15,000-30,000 baht (53.7%, 48.2%). As shown in Table 1, there was no significant difference regarding demographics at baseline among TPW (p>0.05).

BC and Risk Factors

Using a univariable conditional logistic regression analysis, we found that possible risk factors of developing BC among TPW were family history of BC, history of benign breast tumor, younger age at menarche, miscarriage, contraceptive use, passive smoking, multivitamin use and BMI (p<0.05), as shown in Table 2. Using a multivariable conditional logistic regression analysis, BMI showed the association with BC occurrence after controlling for possible confounding factors (family history of BC, history of benign breast tumor, younger age at menarche, miscarriage, contraceptive use, passive smoking, and multivitamin use), higher BMI was significantly associated with increased risk of BC. Risks

Table 3. Multivariable Conditional Logistic Regression Analysis of BMI associated with BC among TPW

Variables	OR_c	95%CI	OR_{adj}	95%CI	p-value
BMI (kg/m^2)					
18.5-22.9	1		1		
23-24.9	1.18	0.71–1.97	0.9	0.44–1.84	0.77
25-29.9	3.07	1.87–5.05	2.09	1.09–3.97	0.025*
≥30.0	3.68	1.64-8.25	2.37	1.24-10.06	0.018*
<18.5	0.44	0.20-0.95	0.3	0.09-1.08	0.065

OR_c, crude OR; OR_{adj}, Adjusted OR for family history of BC, history of benign breast tumor, age at menarche, miscarriage, contraceptive use, passive smoking, and multivitamin use; *, Significant at p-value <0.05.

of developing BC with BMI 25-29.9 and ≥ 30 kg/m2 were 2.09 and 2.37 times respectively when compared with those of BMI 18.5-22.9 kg/m2 (ORadj= 2.09, 95%CI=1.09-3.97; ORadj= 2.37, 95%CI=1.24-10.06), as shown in Table 3.

Characteristics of BC Patients

Cases were the newly patients with BC diagnosed by pathological confirmation and laboratory testing during November 2013-December 2014 (incidence cases). Majority of them were weight 55-64 kg (40.5%) and height 150-159 cm (65.7%). Considering on body size, 60.7% showed overweight and obesity. Location of BC, mostly in both sides (52.2%). Most of study cases were diagnosed as IDC-NOS (91.8%) and duration of stage II (45.5%).

Discussion

Findings from the present study, TPW participants were mostly aged 40-44 years (60%). Socio-demographic characteristics of cases and controls were quite alike. When controlled by health risk behaviors and reproductive factors, obesity measurement by BMI and criteria for Asians (Steering Committee, 2000), found that obese group was risky being BC higher than normal group. Our findings indicated that women with BMI >25 kg/m2 had a higher risk for BC. Obesity plays a major role in the etiology of BC. When considering for Asian premenopausal women, it showed positive association between BMI and BC (Wada et al., 2014; Suzuki et al., 2013; Iwasaki et al., 2007; Kuriyama et al., 2005; Wu et al., 2006). A study showed the BMI of higher than 27 kg/m2 was the borderline-significant positive association between BMI and BC among premenopausal women (Wada et al., 2014). The results differed from the findings from western studies (Cheraghi et al., 2012; Renehan et al., 2008; Reeves et al., 2007; Lahmann et al., 2004; Michels et al., 2006; Tehard et al., 2004; World Cancer Research Fund/American Institute for Cancer Research, 2007) which showed a significant inverse association. Some studies found this association only in the postmenopausal women (Carpenter el al., 2003; Eliassen et al., 2006; Mahoney et al., 2008; Emaus et al., 2014), while a study found the association in both pre and post menopausal women (Wada et al., 2014). The reason to support the association why obesity increased BC risk, it could explain that an increasing of BMI would enhance the risk of estrogen receptor and progesterone receptor-positive tumors (Enger et al., 2000; Ahm et al., 2006). Therefore, weight control is the crucial factor to reduce risk of BC, namely, dietary control with both quantity and quality, and proper physical activities level, it will support the cardiorespiratory function and improve vigor and vitality (Schmitz et al., 2005; Voege et al., 2015). In addition, the benefits of regular physical exercise affect healthy body and mind, normal function, increase flexibility and quality of life (American Cancer Society, 2007; Kolden et al., 2002). WHO recommends persons aged 18-64 years should have physical activities in moderate (150 minute/wk) and vigorous intensity (75 minutes/wk). For Thais, campaign of women aged ≥ 20 years to examine by themselves, they should be aware of advantages and limitations of this technique, support breast feeding after give birth 6 months, reduce alcohol consumption and reduce obesity (National Cancer Control Committee, 2013). For women ≥ 40 years should be checked up with mammogram annually (Smith et al., 2003; American College of Radiology, 2013).

Advantages and limitation of the Study

There are some advantages of this case-control study. First, the National Cancer Institute is the specialized hospital for cancer patients. Second, they are easily identified, and provide sufficient numbers. Finally, cases are newly BC patients diagnosed and confirmed by pathologists, which lead to the reduction in classification bias. Some limitations of this study should be noted. First, the study was a hospital based matched case-control study, therefore, the representative of target population couldn't be mentioned. Second, it was very difficult to select the suitable controls. However, we matched cases and controls by age, residence and duration of attending. In summary, it should be the surveillance system of obesity and campaign of proper regular exercise, healthy diet, weight control and basic methods for health lifestyle among risk groups (National Cancer Control Committee, 2013), it will minimize BC occurrence and reduce risks of developing BC extensively and wisely.

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