Review Article

# Association of Overweight and Obesity with Breast Cancer During Premenopausal Period in Asia: A Meta-Analysis

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## Abstract

**Background:** The association of overweight and obesity with breast cancer risk in premenopausal women and in different ethnicities remains in debate, especially among Asian women. The aim of this systematic review and meta-analysis was to determine the association of overweight and obesity with breast cancer during premenopausal period in Asian women. **Methods:** We performed a meta-analysis of research articles on the association of overweight and obesity with breast cancer during premenopausal period in Asian women published from January 2000 to July 2018 in article databases of EBSCO, PubMed, and ProQuest. Pooled odds ratios (ORs) were calculated by fixed and random-effect models. Publication bias was visually evaluated using funnel plots, and then statistically assessed using Egger's and Begg's tests. Review Manager 5.3 (RevMan 5.3) and Stata version 14.2 (Stata Corporation) were used to process the data. We reviewed 886 articles. **Results:** We found 15 studies conducted systematic review continued by meta-analysis of relevant data with 22,362 patients. There was significant association of obesity [OR = 1.36 (95% confidence interval (CI) 1.26–1.47, $P < 0.00001$)] and overweight [OR = 1.17 (95% CI 1.10–1.25, $P < 0.00001$)] with breast cancer during premenopausal period in Asian women. In this study, there was no significant publication bias for studies included in overweight and obesity with breast cancer during premenopausal in Asian women. **Conclusions:** This study suggested association of overweight and obesity with breast cancer during premenopausal period in Asian women.

**Keywords:** *Breast neoplasms, obesity, overweight, premenopause*

## Introduction

Breast cancer is the most frequent type of cancer found in women worldwide. It is estimated that 11.6% or 2,088,849 new cases and 6.6% or 626,679 cases are predicted to end with mortality with this cancer.[1] The etiology is multifactorial – one of the risk factors confirmed is high body mass index (BMI).[2-4]

A study, conducted by Women's Health Initiative Clinical Trial Participants on baseline BMI (kg/m$^2$) with a sample size of 67,142 respondents in the United States, confirmed that the incidence of breast cancer in patients with overweight was higher in White women with 82.7% and in obese White women it was 78.7%. In overweight Black women it was 8.9% and it was 13.2% for obese Black women. Furthermore, interestingly, it has been found that breast cancer in Asians who were overweight and obese was 2.1% and 1.8%, respectively.[5,6]

High BMI potentially increases the risk of breast cancer as the synthesis of estrogen in body fat correlates with the proliferation of breast tissue.[7] Adipose tissue has an essential role in the body by storing excess calories as fat and establishing endocrine control in other body sites. Furthermore, central distribution increase of body mass could produce a higher risk of breast cancer in women, particularly if the patient has family history of breast cancer.[7]

The correlation of high BMI with the increase in breast cancer risk in postmenopausal women showed constant evidence.[2-4] However, the correlation is still controversial in premenopausal women.[8,9] The association of BMI with breast cancer risk in premenopausal women from various ethnicities remains in debate, especially among Asian women.[3,10,11] Several studies in Asian premenopausal women from Japan, China, and Taiwan have suggested no association between BMI and breast cancer risk.[3,10,12-14] Yet, some studies in India, Thailand, Saudi Arabia, and Vietnam

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found significant correlation of BMI with breast cancer risk.[15-18]

Therefore, this study was held to determine the association of overweight and obesity with breast cancer during premenopausal period in Asian women through a meta-analysis study to draw a stronger strength of conclusion.

## Methods

### Study design and research sample

This research was quantitative which was conducted using meta-analysis study design. The meta-analysis followed PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) statement.[19] Meta-analysis was held to determine the association of overweight and obesity with breast cancer during premenopausal period in Asian women. The research samples included published research articles from January 2000 to July 2018 in article databases of EBSCO, PubMed, and ProQuest.

### Operational definitions

The variables of this study were divided into two independent variables, that is, overweight (BMI 23.0–24.9 kg/m$^2$) and obese (BMI ≥25 kg/m$^2$),[20] and a dependent variable, that is, breast cancer.

### Research procedure

This study was held by collecting data by identification of published research articles on association of overweight and obesity with breast cancer during premenopausal period in Asian women in article databases of EBSCO, PubMed, and ProQuest [Figure 1].

Identification process of the 886 articles was conducted by reviewing the article titles, and then continued by reviewing the abstract and their full text. The exclusion criteria were as follows: (a) unrelevant to subjects of the study, (b) the study methods were neither cohort nor case–control study, and (c) the data provided in the study results' section were not proper for extraction.

### Data collection technique

Data collection was held by online search. The search was limited to English articles. The date of publication was limited from January 2000 to July 2018. The article type was limited to research articles. The research subject was limited to human subject research. The abstract of articles with relevant titles were assessed, while the irrelevant ones were excluded. Furthermore, the articles included were reviewed in full-text form; after that, irrelevant full-text articles were excluded. The inclusion criteria of this study sample were research on overweight and obesity for breast cancer risk with case–control and cohort study methods. The exclusion criteria were either the article was not available in full-text form or the criteria were unsatisfyingly

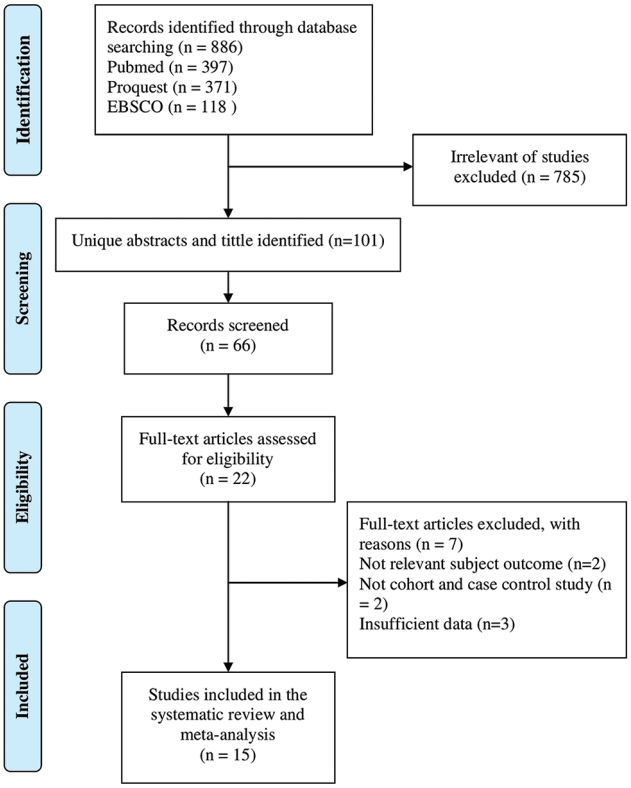


**Figure 1: Flow diagram research procedure**

fulfilled, or if the information provided was not proper for data extraction. These following data were obtained from the articles: name of first author and publication year, region of study location, study type, exposure, and total samples.

Two independent investigators carefully extracted information from all articles included in accordance with standardized protocol. Disagreements were resolved by three other investigators. Quality assessment was conducted by Newcastle–Ottawa Quality Assessment Scale (NOS). Articles with a total score of 0–3, 4–6, and 7–9 points were specified as poor, moderate, and high quality, respectively.[21]

### Data analysis

The analysis was performed to get the pooled odds ratio (OR) as combined OR from the articles. OR with corresponding 95% confidence intervals (CIs) were utilized to pool the results. Significant heterogeneity was indicated by $I^2$ > 50% as these tests presented minimal statistical power on cases with limited numbers of articles and sample sizes. A random-effect model was used when observing significant heterogeneity; otherwise, a fixed-effect model was utilized. *Review Manager* 5.3 (RevMan 5.3) was used to analyze the data.

Publication bias was visually evaluated using funnel plots and statistically assessed through Egger's and Begg's

tests. Meta-analysis was carried out in Stata version 14.2 (StataCorp, College Station, Texas, USA. A two-tailed *P* value <0.05 was considered statistically significant.

## Results

The selection of studies was conducted to obtain 15 studies related to the association of overweight and obesity with breast cancer during premenopausal period in Asian women [Table 1].[1,15-18,22-31]

Meta-analysis study was performed to determine the association of overweight with breast cancer during premenopausal period in Asian women [Figure 2]. Figure 2 shows meta-analysis of association of overweight with breast cancer during premenopausal period in Asian women with OR = 1.17 (95% CI 1.10–1.25, $P < 0.00001$). Heterogeneity in studies for overweight with breast cancer during premenopausal period in Asian women ($P_{heterogeneity} = 0.02$; $I^2 = 49\%$) showed a variation in homogeneous research on the occurrence of breast cancer. Funnel plots to identify publication bias among studies on the association of overweight with breast cancer during premenopausal period in Asian women are shown in Figure 3.

In Figure 3, we found that there was no significant publication bias for the studies on association of overweight with breast cancer during premenopausal in Asian women included in Egger's test ($P = 0.958$) and Begg's test ($P = 0.400$).

This meta-analysis study was also conducted to determine the association of obesity with breast cancer during premenopausal period in Asian women [Figure 4]. Figure 2 shows meta-analysis of association of obesity with breast cancer during premenopausal period in Asian women with OR = 1.36 (95% CI 1.26–1.47, $P < 0.00001$). Heterogeneity in studies for obesity with breast cancer during premenopausal period in Asian women ($P_{heterogeneity} = 0.11$; $I^2 = 37\%$) showed a variation in homogeneous research on the occurrence of breast cancer. Funnel plots to identify publication bias among studies on the association of obesity with breast cancer during premenopausal period in Asian women are shown in Figure 5.

In Figure 5, it can be seen that there was no significant publication bias for the studies on obesity with breast

**Table 1: Systematic review association of overweight and obesity with breast cancer during premenopausal period in Asia**

| First author, year | Region | Type of study | Exposure | No. of sample | | NOS |
|---|---|---|---|---|---|---|
| | | | | Cases | Control | |
| Nichols *et al*.[22] | Vietnam, China | Case-control | Overweight | 682 | 649 | 7 |
| Chow *et al*.[13] | Hong Kong | Case-control | Overweight<br>Obesity | 68 | 212 | 6 |
| Tian *et al*.[23] | Taiwan | Case-control | Overweight | 244 | 244 | 7 |
| Kim *et al*.[24] | South Korea | Case-control | Overweight<br>Obesity | 690 | 1380 | 7 |
| Shin *et al*.[25] | China | Case-control | Overweight<br>Obesity | 2080 | 1962 | 8 |
| Singh *et al*.[15] | India | Case-control | Overweight<br>Obesity | 128 | 128 | 6 |
| Sangrajrang *et al*.[16] | Thailand | Case-control | Overweight<br>Obesity | 636 | 744 | 7 |
| Elkum *et al*.[17] | Saudi Arabia | Case-control | Overweight<br>Obesity | 264 | 484 | 7 |
| Tamaki *et al*.[26] | Japan | Case-control | Overweight<br>Obesity | 378 | 1206 | 8 |
| Li *et al*.[27] | China | Case-control | Overweight<br>Obesity | 150 | 151 | 7 |
| Iqbal *et al*.[28] | Bangladesh | Case-control | Overweight | 129 | 129 | 6 |
| Nguyen *et al*.[18] | Vietnam | Case-control | Overweight | 195 | 190 | 7 |
| Chen *et al*.[29] | Taiwan | Cohort | Overweight<br>Obesity | 1571 | 6709 | 8 |
| Trieu *et al*.[30] | Vietnam | Case-control | Overweight | 121 | 324 | 7 |
| Chaveepojnkamjorn *et al*.[31] | Thailand | Case-control | Overweight<br>Obesity | 257 | 257 | 7 |
| No. of samples | | | | 7,593 | 14,769 | |

NOS: Newcastle-Ottawa Quality Assessment Scale

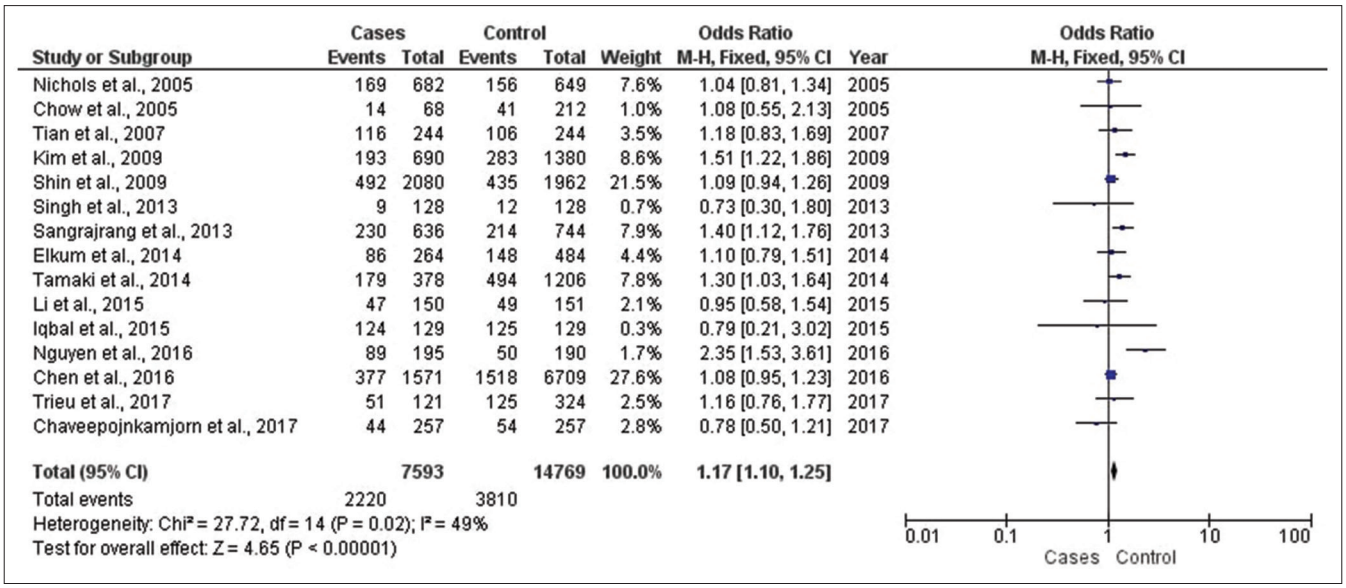


**Figure 2: Forest plots' association of overweight with breast cancer during premenopausal period in Asia**

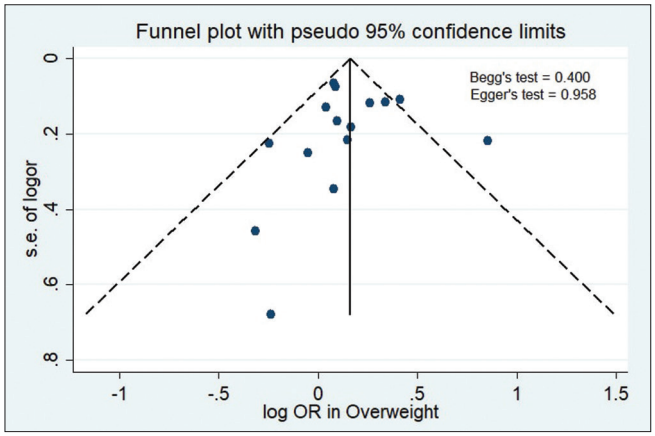


**Figure 3: Funnel plots' association of overweight with breast cancer during premenopausal period in Asia**

cancer during premenopausal in Asian women included in Egger's test ($P$ = 0.213) and Begg's test ($P$ = 0.540).

## Discussion

The results of this meta-analysis revealed that overweight and obesity during premenopausal period can increase the risk of breast cancer in Asian women. Obesity had higher OR for breast cancer risk [OR = 1.36 (95% CI 1.26–1.47)] than overweight [OR = 1.17 (95% CI 1.10–1.25)]. The higher the level of BMI, the higher the risk for incident breast cancer in women during premenopausal period.

Recent trends have shown an increase in breast cancer incidence, not only in postmenopausal but also in premenopausal women nowadays. A potential explanation for this increase is lifestyle change as a result of rapid economic improvement. In the past two decades, the levels of physical activity have reduced and food patterns have changed, leading to an increase in average population BMI.[32] Previous studies, which collected data on 42 developing countries in Asia, the Middle East, Africa, and Latin America, found that the growth of overweight and obesity was 0.7% annually, and there was an estimated 19% of rural women and 37.2% of urban women who were overweight or obese.[33,34]

Breast cancer is characterized by high prevalence in overweight and obese women, high percentage of body fat and central obesity, and unbalanced diet. Considering that in recent years the prevalence of obesity has increased significantly in both developed and developing countries, it is crucial to develop strategies to prevent this condition and its associated breast cancer risk factors.[32,35]

There was significant correlation between overweight and breast cancer during premenopausal and postmenopausal periods in Southeast Asia [OR = 1.61 (95% CI 1.43–1.80)].[4] A number of studies have shown an increase in breast cancer risk in premenopause and a positive correlation between obesity and breast cancer development.[9,36] Present BMI and BMI 5 years before diagnosis were poorly associated with breast cancer risk in both premenopausal and postmenopausal women.[13] Several studies in India, Thailand, Saudi Arabia, and Vietnam found association between BMI and breast cancer risk.[15-18]

According to data of all breast cancer diagnosed in women, approximately 7% of women with breast cancer were diagnosed before the age of 40 years, more than 40% of them were diagnosed as breast cancer in the age of 40 years, 20% in the age of 30 years, and more than 2% in the age of 20 years.[37] This finding explained that the risk of breast cancer can strike in all age groups. Compared to other ethnic groups, Asian women have been previously reported to show an increase in breast cancer risk associated with larger waist-to-hip ratio among

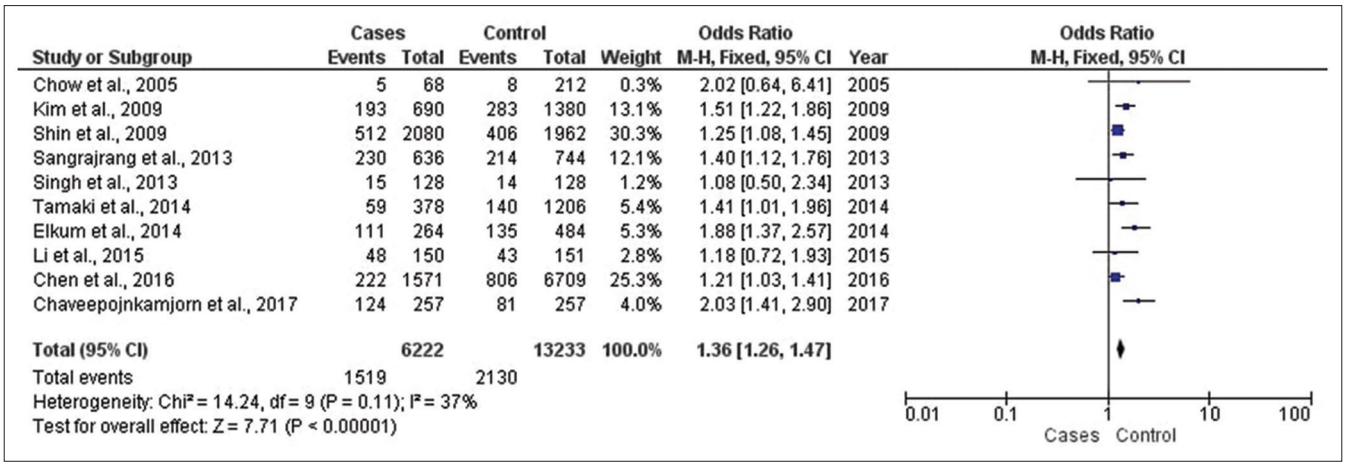


**Figure 4: Forest plots' association of obesity with breast cancer during premenopausal period in Asia**

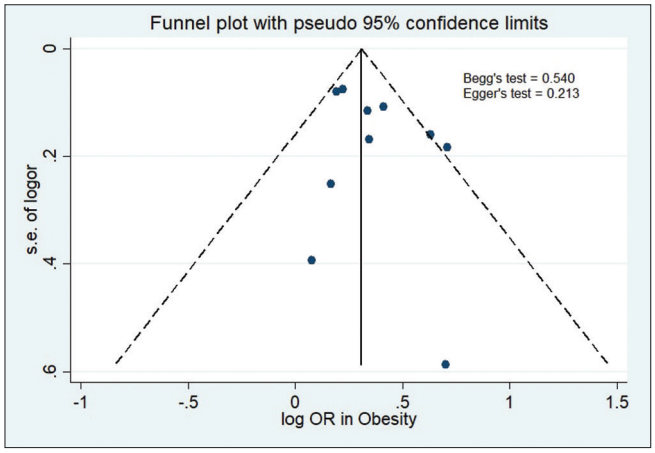


**Figure 5: Funnel plots' association of obesity with breast cancer during premenopausal period in Asia**

premenopausal and postmenopausal women,[38,39] which was smaller (increased risk of lower magnitude) in African and Caucasian women.[9]

The role of dietary factors in the risk of breast cancer may cause an increase in BMI. The environment can change the eating habits, contributing to increased risk of breast cancer. These results provided preliminary evidence indicating that exposure to environmental factors such as diet can change the risk of breast cancer later in life.[40] It has estimated that up to 35% of cases may be prevented by diet and lifestyle modification.[40]

The effects of favorable or unfavorable energy balance have been suggested to be mediated through the alteration of sex hormone and growth factor levels, and recently elevated insulin levels have been associated with bioavailability increase in both sex hormones and growth factors.[41] Lack of physical activity and a relatively high BMI are possibly associated with increased risk for premenopausal breast cancer.[39]

There were several limitations in this meta-analysis study. First, three studies seemed potentially eligible to be included in this meta-analysis, yet full texts could not be accessed. This issue might raise the possibility of selection bias. Second, the number of research sample in one study was relatively small,[13] which could reduce the statistical power.

This analysis confirmed the association of overweight and obesity with breast cancer during premenopausal period in Asian women. The results of this study recommend the need to maintain normal weight. Weight control in obese women should be an effective assessment for breast cancer prevention in premenopausal women. This study also suggests the need for education and counseling about eating habits and the importance of avoiding foods with high fat composition. Low physical activity and dietary intake especially high-fat diet could potentially increase BMI. Furthermore, women with overweight and obesity are suggested to promote physical activity to improve weight body.

## Conclusions

This analysis confirmed the association of overweight and obesity with breast cancer during premenopausal period in Asian women. The results of this study recommend the need to maintain normal weight and the need for education and counseling about eating habits, the importance of avoiding foods with high fat composition, and promoting physical activity.

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### Conflicts of interest

There are no conflicts of interest.

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