

Original Research

## Central obesity increases risk of breast cancer irrespective of menopausal and hormonal receptor status in women of South Asian Ethnicity



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### **KEYWORDS**

Breast cancer; Central obesity; Menopausal status; Hormone receptor status; South Asian **Abstract** *Background:* Current evidence suggests that the relationship between obesity and breast cancer (BC) risk may vary between ethnic groups.

*Methods:* A total of 1633 BC cases and 1504 controls were enrolled in hospital-based case –control study in Mumbai, India, from 2009 to 2013. Along with detailed questionnaire, we collected anthropometric measurements on all participants. We used unconditional logistic regression models to estimate odds ratios (ORs) and 95% confidence interval (CI) for BC risk associated with anthropometry measurements, stratified on tumour subtype and menopausal status.

**Results:** Waist-to-hip ratio (WHR) of  $\geq 0.95$  was strongly associated with risk of BC compared to WHR  $\leq 0.84$  in both premenopausal (OR = 4.3; 95% CI: 2.9–6.3) and postmenopausal women (OR = 3.4; 95% CI: 2.4–4.8) after adjustment for body mass index (BMI). Premenopausal women with a BMI  $\geq 30$  were at lower risk compared to women with normal BMI (OR = 0.5; 95% CI: 0.4–0.8). A similar protective effect was observed in women who were postmenopausal for <10 years (OR = 0.6; 95% CI: 0.4–0.9) but not in women who were postmenopausal for  $\geq 10$  years (OR = 1.8; 95% CI: 1.1–3.3). Overweight and obese women (BMI: 25–29.9 and  $\geq 30$  kg/m<sup>2</sup>, respectively) were at increased BC risk irrespective of

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menopausal status if their WHR  $\geq$ 0.95. Central obesity (measured in terms of WC and WHR) increased the risk of both premenopausal and postmenopausal BCs irrespective of hormone receptor (HR) status.

*Conclusions:* Central obesity appears to be a key risk factor for BC irrespective of menopausal or HR status in Indian women with no history of hormone replacement therapy.

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#### 1. Introduction

Recent trends have shown marked increase in breast cancer (BC) incidence in India, with a larger increase in postmenopausal compared to premenopausal women [1]. A potential explanation for this increase could be changing patterns of lifestyle factors as a result of rapid economic transition. In the last two decades, levels of physical activity have reduced, and food patterns have changed, leading to an increase in the average population body mass index (BMI) [2]. The prevalence of central obesity is particularly high in Indian population; and Indians are reported to have a higher body fat percentage than Caucasians for the same BMI [3].

Higher  $(\geq 30 \text{ kg/m}^2)$  BMI has been consistently associated with increased risk of postmenopausal BC [4] but decreased risk of premenopausal BC in Caucasian and Asian populations [5]. Central obesity has been associated with increased risk of BC in postmenopausal women [6], but its effect on premenopausal BC seems to vary according to ethnic status. Markers of central obesity such as waist-to-hip ratio (WHR) appear to show strong positive association for premenopausal Asian women, but smaller (increased risk of lower magnitude) for African and Caucasian women [6]. The studies from Asia too have largely been limited to Japan, China, Taiwan and Thailand [6].

We performed a case—control study at the Tata Memorial Hospital (TMH), Mumbai, India, to evaluate the risk of premenopausal and postmenopausal BC in relation to different measures of body fatness (BMI, WC and WHR) stratified on hormone receptor (HR) status in a population which has not been exposed to hormone replacement therapy and has not undergone systematic community screening for BC.

#### 2. Material and methods

We conducted a hospital-based case—control study at TMH between January 2009 and September 2013. A total number of 1659 premenopausal (818 cases and 841 visitor controls) and 1478 postmenopausal women (815 cases and 663 visitor controls) were enrolled during the study period. The information on HR status, i.e., oestrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor 2 (HER2) was available on 1294 (79.0%) BC cases. The premenopausal and postmenopausal BC cases were further stratified into oestrogen receptor positive/progesterone receptor positive (ER+/PR+), oestrogen receptor negative/progesterone receptor negative (ER-/PR-) and triple negative breast cancer (TNBC). The study has been approved by TMH Institutional Review Board.

#### 2.1. Selection of cases

The cases were female BC patients coming to TMH. Only primary histologically confirmed BC cases aged 20–69 years were enrolled in the study with date of diagnosis not more than 6 months from the date of interview.

#### 2.2. Selection of controls

All female visitors with no history of cancer coming along with any site cancer patient (e.g. breast, head and neck, thoracic, urology, gynaecology, etc) aged 20–69 years were included in the study. Controls were frequency matched to cases on age  $(\pm 10 \text{ years})$  and region of residence (northern, western, central, southern and eastern India) at the time of enrolment. Eligible study participants were enrolled simultaneously during the study period. Forty percent of the controls enrolled in the study were first degree relatives (mother, sister or daughter) from various disease management groups (DMGs). The remaining were other relatives, friends and neighbours of different cancer site patients. The detail of questionnaire and methodology study has been mentioned in Supplementary Document.

#### 2.3. Quality control

Data were checked at three levels (one by interviewer, study co-ordinator and data entry operator) and entered twice onto the software. We obtained over 90% correlation on all the variables collected on an abbreviated reproducibility questionnaire.

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