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Body Fat Distribution and Breast Cancer Risk: Findings from the Nigerian Breast Cancer Study

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Abstract

Purpose—The relationship between overall obesity and breast cancer risk has been well recognized, but the role of central obesity in breast cancer development is uncertain.

Methods—Between 1998 and 2009, 1233 invasive breast cancer cases and 1101 community controls were recruited into the Nigerian Breast Cancer Study at Ibadan, Nigeria. Logistic regressions were used to calculate multivariate odds ratio (OR) and 95% confidence intervals (CI), adjusting for age, body mass index (BMI), and other known risk factors for breast cancer.

Results—The OR for the highest quartile group of waist circumference relative to the lowest was 2.39 (95% CI: 1.59–3.60; *P*-trend<0.001). Comparing women with waist-hip ratio (WHR) in the lowest quartile group, the OR for women in the highest quartile category was 2.15 (95% CI: 1.61–2.85; *P*-trend<0.001). An inverse association was observed between hip circumference and breast cancer, with an OR of 0.36 for the highest quartile (95% CI: 0.24–0.55; *P*-trend<0.001). The effects of these three measures existed in both pre- and post-menopausal women. Of note, we found a significant interaction between WHR and BMI (*P*-interaction=0.016): the OR comparing the highest to lowest WHR quartile was 2.81 (95% CI: 1.90–4.16) for women with BMI<25 kg/m^2 and 1.70 (95% CI: 1.11–2.61) for women with BMI ≥25 kg/m^2.

Conclusions—These results suggest that central adiposity, measured by waist circumference and waist-hip ratio, was an important risk factor for breast cancer in Nigerian women, and the effect of central adiposity was strong in normal weight women.

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Keywords

Africa; breast neoplasms; body fat distribution; waist circumference; waist-hip ratio

INTRODUCTION

Breast cancer ranks second in global cancer incidence and is among the top two cancers diagnosed among African women [1–4]. In recent years, breast cancer incidence has stabilized or decreased in some Western countries after decades of increase, but it has steadily increased in many developing countries, including Nigeria [5,6]. Reasons for the increase in breast cancer incidence in Africa are not well understood.

The relationship between overall obesity and breast cancer risk has been well recognized to be modified by menopausal status, with higher body weight or body mass index (BMI) associated with increased risk for postmenopausal women and reduced risk for premenopausal women. However, the role of central obesity in breast cancer development is not very clear. Several studies [7–11], but not all [12–17], found that larger waist circumference or waist-hip ratio was associated with increased risk of premenopausal breast cancer. Similarly, several studies [7,10–13,16,18,19], but not all [8,9,14,17,20–22], showed that waist circumference or waist-hip ratio was positively associated with increased risk of postmenopausal breast cancer. Further research is needed to evaluate this link, especially the independent effect of central obesity after controlling for overall obesity, which will give more insight into the etiology of breast cancer as well as strategies for its prevention.

Nigerian women used to have a low prevalence of obesity [23], but recent reports suggested that over-nutrition may become common in recent years [24,25]. In addition, black women tend to have less visceral fat storage than Caucasian and Asian women for a given waist circumference [26–28]. Therefore, it is important to evaluate the relationship of central obesity with breast cancer risk in indigenous African women. Using data from our pilot study [29], we previously reported a positive association of waist circumference and waist-hip ratio with breast cancer risk but the sample size was small in this pilot study. Here, we present findings from an analysis of more than 1,200 cases and 1,100 controls from the ongoing Nigerian Breast Cancer Study.

MATERIALS AND METHODS

Study population

The study protocol was approved by the institutional review boards of the University of Chicago (Illinois, USA) and the University of Ibadan (Nigeria). The Nigerian Breast Cancer Study is a case-control study of breast cancer conducted in Ibadan, Nigeria. The study setting and design have been described previously [29,30]. Briefly, all consecutive female breast cancer patients aged 18 years or older attending the surgical oncology and radiotherapy clinics of the University College Hospital, Ibadan, Nigeria, from 1998 to 2009 were approached. The majority of eligible patients provided written consent to participate in the study, with a refusal rate of only 4%. University College Hospital serves a population of

3 million people in Ibadan and is a referral center for other hospitals in the region. Based on data from the Ibadan Cancer Registry, about 60% of all breast cancer cases diagnosed in Ibadan are seen at UCH and the age distribution was similar between patients enrolled and those not enrolled.

Eligible controls were females aged 18 years or older, who were free of cancer, provided written consent to participate in the study, and were from a community in the city of Ibadan. Residents of this community were considered to have demographic characteristics similar to those of the patients who present to the University College Hospital. A stable, socioeconomically diverse community was randomly selected by ballot from a list of all communities in the area. Names were randomly selected from the census-derived community register. Because of the engagement of community leaders in the study, nearly 98% of individuals in the community invited for the study chose to participate. Recruitment of the cases and the controls was carried out by trained research nurses at the outpatient clinics of University College Hospital and in a designated community center, respectively. Cases were recruited at or soon after presentation following clinical and histologic confirmation of breast cancer. The same team of interviewers visited the community centre twice weekly where they gave general health talk, introduced the study and invited those who were willing and eligible to participate as controls.

Data collection and measures

Information on demographics, family history of breast cancer and history of benign breast disease, lifestyle factors, menstrual and reproductive history, and hormonal contraceptive use was elicited from participants by means of structured questionnaires administered by the research nurses. Waist and hip circumference were measured according to the guidelines in the World Health Organization MONICA Project manual [31]. Research nurses also measured weight, height, and waist and hip circumferences. BMI was calculated as weight in kilograms divided by height in meters squared. In this report, we focus on the relationship between waist circumference, hip circumference, and waist-hip ratio (WHR) and breast cancer risk. To understand the pattern of these relationships, the three anthropometric measures were grouped into categorical variables based on quartiles of controls.

The following potential confounders were categorized and were adjusted for: age at diagnosis or interview (5-year-interval categories), ethnicity (Yoruba, others), education (none, elementary, secondary, vocational, and some college or above), age at menarche, number of live births (0, 1–3, 4–6, ≥7), age at first live birth, duration of breastfeeding (0–24, 25–48, 49–72, >72 months), first-degree family history of breast cancer (yes, no), benign breast disease (yes, no), hormonal contraceptive use (ever, never), alcohol drinking (yes, no), and menopausal status (premenopausal, naturally postmenopausal, artificially postmenopausal). Alcohol intake was defined as consumption of alcoholic beverages at least once a week for 6 months or longer. Natural menopause was defined as cessation of menstrual periods for 1 year or more, and artificial menopause was considered menopause after surgery or other medical treatment. The use of postmenopausal hormone replacement therapy is rare in Nigerian women (only one woman in our sample) so we did not adjust for it in the analysis.

Statistical analysis

Age was compared between cases and controls by using *t* test. Other demographic or potential confounders were compared between cases and controls using logistic regression models adjusting for age. Pearson correlation coefficients were calculated to describe the interrelationship between anthropometric measures (waist, hip circumference, WHR and BMI). Logistic regression models were used to examine the relationship between anthropometric measures and breast cancer. Odds ratios and 95% confidence intervals were computed as measures of association from the logistic models. Three sets of multiple logistic regressions were fitted: first to adjust for age; second to adjust for age and other potential confounders listed above; third to adjust for BMI as a measure of overall obesity in order to examine whether body fat distribution has independent effect on breast cancer risk beyond overall obesity. Analyses were conducted for all women and separately for premenopausal and naturally postmenopausal women. We also examined the interaction between WHR, waist and hip circumference and BMI using logistic regression. To monitor multicollinearity problem in model building, we calculated variance inflation factor (VIF). A maximum VIF greater than 10 indicates that the model may generate instable estimates of regression coefficients. Once it occurs, we would consider necessary variable transformation (like centering) or dropping redundancy variables from the model.

About 6% of participants had a missing value for age at menarche, and <1% of them had missing values for waist or hip circumference. Data were occasionally missing for other variables as well. To use all available information and avoid bias due to listwise deletion in the multivariate analysis, we imputed missing values 20 times via the method of multiple imputation by chained equations [32]. Standard errors of regression coefficients were determined by using Rubin's general formula for combining estimates in multiple imputation [33]. Multiple imputation assumes that data are missing at random [33]. Missing menarcheal age was due to poor memory, and older women tended to forget their menarcheal age. After age was included in the multiple imputation models, it is reasonable to think that the probability of missing menarcheal age was unrelated to the missed value itself. Multiple imputation was conducted by using the *ice* module in Stata software developed by P. Royston [34]. Sensitivity analyses using data without imputation were also conducted and the results were similar except that the imputed data tended to gave narrower confidence intervals. All *P* values were 2-sided. Statistical analyses were conducted with Stata 11.0 software (StataCorp, College Station, Texas).

RESULTS

There were 1233 women diagnosed with invasive breast cancer and 1101 community controls in the study. Table 1 shows selected characteristics of study participants. Women with breast cancer were older than the controls and about 60% of cases were younger than 50 years, and 16% were 60 years and older. Since age was a potential confounder and results from univariate analysis may be misleading, we present age-adjusted p values in Table 1. The majority of study participants were Yoruba (other ethnicities included Hausa and Ibo), which reflects the ethnic distribution of the population in southwestern Nigeria. Cases and controls were different in ethnicity and education levels. Compared with controls, cases were more likely to have a family history of breast cancer, a history of benign breast disease, and to have consumed alcohol. Cases and controls were similar in marital status and use of hormonal contraceptives. The distributions of some reproductive factors and height were different between cases and controls but detailed analysis results can be found in our previous papers [30,35]. All these variables were considered to be potential confounders and were adjusted for in subsequent analyses.

Waist circumference was strongly correlated with hip circumference (r=0.78) and moderately correlated with waist-hip ratio (r=0.61, p<0.001). There was no correlation between hip circumference and waist-hip ratio (r=0.001, p=0.98). Although waist circumference and hip circumference were strongly correlated with BMI (both r=0.80, p<0.001), waist-hip ratio was only weakly correlated with BMI (r=0.28, p<0.001). As shown in Table 2, waist circumference was on average 3.5-cm larger in cases than in controls. After adjusting for multiple potential confounders, a non-significant positive association was observed between waist circumference and breast cancer risk. However, the positive association was stronger and statistically significant after further adjusting for BMI and hip circumference (p<0.001). This effect was similar in pre- and post-menopausal women, with an odds ratio of 1.40 and 1.37 per 10 cm increment for pre- and post-menopausal women, respectively. The interpretation of this result is that for two women with the same BMI and hip circumference values, the woman with larger waist circumference has increased risk for breast cancer. However, we need to be cautious that the difference in waist circumference between the two women is likely to be small, given that they have the same BMI and hip circumference values.

Although hip circumference was positively correlated with waist circumference, it was negatively associated with breast cancer risk. As shown in Table 3, women with hip circumference greater than 92 cm had about one third reduced risk of breast cancer comparing to women with hip circumference smaller than 93 cm, after adjusting for multiple potential confounders. Further adjustment of BMI and waist circumference made the association stronger (p<0.001). This inverse relationship existed in both pre- and post-menopausal women, with about 28% risk reduction for every 10 cm increment in hip circumference.

Table 4 presents the relation between waist-hip ratio and breast cancer in all women and stratified by menopausal status. A positive dose-response relationship was observed between WHR and breast cancer risk after adjusting for multiple potential confounders including BMI (p<0.001). Compared to women in the lowest quartile of WHR (< 0.77), the odds ratio for the second, third and highest quartiles of WHR was 1.00, 1.77, and 2.15, respectively, suggesting that median WHR (0.81) was a good risk cutoff point in this population. Very similar relationships between WHR and breast cancer risk was observed in pre- and post-menopausal women (p for interaction = 0.98).

We examined whether the relationship between WHR and breast cancer risk varied according to BMI (Table 5). Interestingly, we found that WHR was strongly positively associated with breast cancer risk in women with normal weight (BMI < 25kg/m^2), but only moderately associated with breast cancer risk in overweight and obese women (p for interaction = 0.016). The multivariable-adjusted odds ratio per 0.1 unit increase in WHR was 1.72 for normal weight women and 1.21 for overweight or obese women. We also examined whether there was interaction between waist circumference and BMI (Table 6) and found that the effect of waist circumference on breast cancer risk mainly confined to women with normal weight (p for interaction = 0.042). No significant interaction was observed between hip circumference and BMI (data not shown).

DISCUSSION

The present study, conducted in indigenous African population with low breast cancer incidence, found that elevated waist circumference and waist-hip ratio were associated with increased risk of breast cancer in both premenopausal and postmenopausal women, even after accounting for BMI, an indicator of overall obesity. The study also found that waist-hip ratio had stronger positive association with breast cancer risk in normal weight women than in overweight or obese women. On the other hand, the present study found hip circumference was inversely associated with breast cancer risk.

These study findings confirmed our pilot data and another study in Nigerian population that WHR was associated with both pre- and post-menopausal breast cancer, although the two previous studies did not control for overall obesity [29,36]. A study conducted in North Carolina found that the positive association between WHR and breast cancer existed in African Americans [37], whereas a recent report from California showed no association between WHR and breast cancer in African Americans [38]. A prospective study in African Americans did not found association between waist circumference or WHR and breast cancer risk [17]. African Americans in all these three studies had high obesity prevalence [37,38]. A study conducted in African-Barbadian women showed that WHR had dual effect: reduced risk in women younger than age 50 and increased risk in women 50 years or older [16]. Data from other populations are not always consistent either, but two summaries might be made from review of the literature and this study. First, most studies showed that waist circumference or WHR was either positively associated with increased risk of breast cancer or there was no association [7–15,17–21,29,36,37]. while few studies found inverse association [22,39], suggesting that central obesity is more likely to be a risk factor and chance variability may be a reason for null association, especially when sample size is small. Second, the positive association between central obesity and breast cancer risk apparently existed for both premenopausal and postmenopausal women. This is in contrast to the relationship between overall obesity and breast cancer, which is a positively correlation in postmenopausal women but an inverse correlation in premenopausal women, suggesting that the mechanisms by which total body mass and fat distribution affect breast cancer risk may not be exactly the same.

Our finding of significant interaction between waist-hip ratio and BMI is worthy of note. In women with normal weight defined by BMI $< 25\text{kg/m}^2$, the risk of breast cancer increased by 181% comparing the highest quartile of WHR to the lowest quartile. In contrast, the risk of breast cancer increased by 70% comparing the highest quartile of WHR to the lowest quartile in overweight/obese women (BMI $\geq 25\text{kg/m}^2$). A study conducted in Italy showed that the positive WHR effect is confined to thinner women (BMI < 24 kg/m^2) [8], and a study in China found that the WHR was positively associated with premenopausal breast cancer risk in thinner women but not in overweight/obese women [40].

As waist circumference is a good surrogate measure for visceral fat and WHR is a good indicator for fat distribution, our study findings suggest that central adiposity, especially abdominal visceral fat, may play role in breast cancer development. The proportion of visceral adipose tissue in women with normal BMI and high WHR is much higher than that in women with normal BMI and low WHR. In obese women, there is less contrast between high WHR and low WHR regarding the proportion of visceral adipose tissue. There are several plausible biological mechanisms why body fat distribution might be a predictor of breast cancer risk. The first mechanism is that central obesity is associated with hyperinsulinaemia and insulin resistance [41,42]. A meta-analysis showed that type II diabetes is associated with increased risk of breast cancer [43], supporting this theory. Another proposed mechnasim is that body fat distribution is related to hormone levels. Visceral adiposity is associated with decreased sex hormone binding globulin (SHBG) and thus unbound, bioavailable oestrogen and testosterone levels may be increased in women with central obesity [41,44–46]. The third proposed mechanism is that obesity affects breast cancer risk through inflammation and aromatase axis. An animal study showed that obesity, either diet-induced or genetically-engineered, is associated with inflammation and elevated aromatase activity in both mammary gland and visceral fat [47].

There are few studies reporting the relationship between hip circumference and breast cancer, possibly because hip circumference is not considered an optimal indicator for central obesity. Our finding of a negative association between hip circumference and breast cancer risk is consistent with some studies [7,22], but not others [19,20,40]. The reason for the inverse association between hip circumference and breast cancer risk is unclear, but possibly because larger hip circumference indicates greater lean mass and subcutaneous fat mass in the lower body, which has been linked with reduced insulin resistance [48].

To our knowledge, this is the largest case-control study of central obesity measures and breast cancer from an indigenous African population, which provided adequate power to explore these associations. Another strength is the high participation rate, which minimizes selection bias. Several limitations should be considered when interpreting our study findings. Cases were significantly older than controls because controls were randomly selected from the community and were not matched on age. We found age to be the single most important confounder in the analysis, but it was adjusted for in the multivariate logistic models. Nevertheless, there could still be residual biases and confounding from variables that we did not collect. Our study may be subject to inherent limitations of case-control design, including inaccurate recall, which could lead to misclassification of exposure variables and confounders. Since the Nigerian population has not been well studied, the misclassifications are more likely to be non-differential between cases and controls. Another limitation is that waist and hip circumferences and WHR are indirect measures of abdominal visceral fat or fat distribution, so caution should be taken on the inference to visceral fat. Lastly, although incident cases were enrolled at the presentation to the hospital, delayed diagnosis is not uncommon in Ibadan, Nigeria, as many patients had locally advanced or distant metastatic disease [30]. Changes in body size and fat distribution due to disease progression might affect our study findings.

In summary, we found central adiposity, measured by waist circumference and waist-hip ratio, was positively associated with breast cancer risk in Nigerian women. This finding along with previous literature suggests that obesity measurements should include both body mass index and waist circumference or waist-hip ratio when used to quantify breast cancer risk in African population. Our study finding that waist-hip ratio had stronger association with breast cancer risk in normal weight women emphasizes that women with overall normal weight should also watch their body fat distribution. The effect of exercise and diet in controlling body fat distribution could represent low cost interventions to reduce breast cancer risk in rapidly changing African populations.

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Table 1

Selected Characteristics of Cases with Invasive Breast Cancer and Community Controls, Nigeria, 1998–2009

Characteristic	Cases (n=1233)	Controls (n=1101)	p-value*
Age in years, mean (SD)	47.0 (11.5)	40.8 (12.8)	<0.001
Ethnicity, n (%)			<0.001
Yoruba	903 (73.2)	1045 (94.9)	
Ibo	157 (12.7)	25 (2.3)	
Hausa	19 (1.5)	1 (0.1)	
Others	154 (12.5)	30 (2.7)	
Education, n (%)			0.001
No formal	271 (22.0)	170 (15.5)	
Elementary	293 (23.8)	172 (15.6)	
Secondary	221 (17.9)	264 (24.0)	
Vocational	170 (13.8)	137 (12.5)	
Some college or above	277 (22.5)	357 (32.5)	
Marital status, n (%)			0.15
Married	1056 (85.7)	921 (83.7)	
Single	29 (2.4)	111 (10.1)	
Divorced/separated	25 (2.0)	10 (0.9)	
Widowed	122 (9.9)	59 (5.4)	
Family history of breast cancer, n (%)	99 (8.0)	51 (4.6)	<0.001
Benign breast disease, n (%)	107 (8.7)	45 (4.1)	<0.001
Age at menarche, mean (SD)	15.2 (2.1)	15.3 (2.2)	0.018
Menopausal status, n (%)			0.09
Premenopausal	707 (57.4)	820 (74.6)	
Postmenopausal, natural	498 (40.4)	266 (24.2)	
Postmenopausal, artificial	27 (2.2)	13 (1.2)	
Age at natural menopause, mean (SD)	48.5 (5.4)	49.6 (5.2)	0.064
Number of live birth, mean (SD)	4.1 (2.4)	3.3 (2.4)	0.22
Age at first live birth†, mean (SD)	23.0 (4.7)	23.8 (4.1)	0.001
Months of lactation†, mean (SD)	65.4 (42.9)	57.1 (38.9)	0.96
Hormone contraceptive use, n (%)	305 (24.8)	232 (21.1)	0.25
Alcohol drink, n (%)	137 (11.4)	65 (5.9)	0.001
Height in cm, mean (SD)	160.2 ± 6.8	158.8 ± 6.4	<0.001
< 155, n (%)	221 (18.6)	262 (23.9)	
155–159	323 (27.1)	352 (32.1)	
160–164	347 (29.2)	287 (26.1)	
≥165	299 (25.1)	197 (17.9)	
Weight in kg, mean (SD)	65.8 ± 14.8	63.2 ± 13.5	0.20
< 55, n (%)	286 (24.1)	321 (29.3)	
55–64	341 (28.7)	330 (30.1)	

Characteristic	Cases (n=1233)	Controls (n=1101)	p-value*
65–74	262 (22.1)	228 (20.8)	
≥ 75	299 (25.2)	218 (19.9)	
Body mass index in kg/m^2, mean (SD)	25.7 ± 5.6	25.1 ± 5.4	0.25
< 25, n (%)	609 (51.3)	603 (55.0)	
25–29.9	326 (27.5)	309 (28.2)	
≥ 30	252 (21.2)	185 (16.9)	

Abbreviation: SD, standard deviation

*P values were age adjusted in logistic regressions.

†Among parous women

Table 2

Waist circumference and breast cancer risk in Nigerian women, 1998–2009

	Cases	Controls	Age-adjusted OR (95% CI)	Adjusted OR (95% CI)†	Adjusted OR (95% CI)‡
Total					
45–73 cm	223	304	1.0 (ref.)	1.0 (ref.)	1.0 (ref.)
74–81 cm	265	278	0.95 (0.73–1.22)	0.87 (0.66–1.15)	1.08 (0.80–1.44)
82–89 cm	309	254	1.12 (0.87–1.45)	1.06 (0.80–1.40)	1.61 (1.16–2.23)
90–138 cm	425	261	1.33 (1.03–1.71)	1.19 (0.90–1.56)	2.39 (1.59–3.60)
P for trend			0.006	0.08	<0.001
Mean ± SD	85.2 ± 12.7	81.7 ± 12.0			
Per 10 cm			1.09 (1.01–1.17)	1.05 (0.97–1.14)	1.39 (1.20–1.60)
Premenopausal					
45–73 cm	138	263	1.0 (ref.)	1.0 (ref.)	1.0 (ref.)
74–81 cm	179	207	1.18 (0.87–1.60)	1.03 (0.74–1.44)	1.29 (0.92–1.82)
82–89 cm	175	186	1.19 (0.87–1.62)	1.11 (0.79–1.55)	1.71 (1.17–2.50)
90–138 cm	210	163	1.47 (1.08–2.01)	1.20 (0.85–1.69)	2.40 (1.52–3.78)
P for trend			0.017	0.26	<0.001
Mean ± SD	84.0 ± 12.3	80.1 ± 11.4			
Per 10 cm			1.13 (1.03–1.24)	1.06 (0.96–1.18)	1.40 (1.20–1.64)
Postmenopausal					
45–73 cm	85	41	1.0 (ref.)	1.0 (ref.)	1.0 (ref.)
74–81 cm	86	71	0.55 (0.34–0.90)	0.57 (0.34–0.96)	0.70 (0.42–1.19)
82–89 cm	134	68	0.90 (0.56–1.46)	0.93 (0.56–1.54)	1.38 (0.81–2.36)
90–138 cm	215	98	1.02 (0.65–1.59)	1.07 (0.66–1.71)	2.21 (1.25–3.91)
P for trend			0.17	0.14	<0.001
Mean ± SD	86.9 ± 13.0	86.4 ± 12.6			
Per 10 cm			1.03 (0.91–1.15)	1.04 (0.92–1.18)	1.37 (1.15–1.62)
P for interaction*			0.74	0.69	0.98

Abbreviations: OR, odds ratio; CI, confidence interval; SD, standard deviation

*Interaction between waist circumference and menopausal status

†Adjusted for age at diagnosis or interview (categorical), ethnicity, education (categorical), age at menarche (continuous), number of live birth (categorical), age at first live birth (continuous), duration of breastfeeding (categorical), menopausal status, family history of breast cancer, benign breast disease, hormonal contraceptive use, alcohol drinking, and height (continuous).

‡Adjusted for body mass index (continuous) and hip circumference (continuous) in addition to the above variables.

Categories of waist circumferences are based on quartiles in controls.

Table 3

Hip circumference and breast cancer risk in Nigerian women, 1998–2009

	Cases	Controls	Age-adjusted OR (95% CI)	Adjusted OR (95% CI)†	Adjusted OR (95% CI)‡
Total					
54–92 cm	312	282	1.0 (ref.)	1.0 (ref.)	1.0 (ref.)
93–99 cm	266	286	0.67 (0.52–0.86)	0.64 (0.49–0.83)	0.53 (0.40–0.70)
100–107 cm	283	251	0.73 (0.57–0.94)	0.62 (0.47–0.82)	0.44 (0.32–0.62)
108–157 cm	361	279	0.76 (0.59–0.97)	0.62 (0.48–0.82)	0.36 (0.24–0.55)
P for trend			0.10	0.003	<0.001
Mean ± SD	101.3±13.0	100.2±11.6			
Per 10 cm			0.95 (0.88–1.02)	0.90 (0.83–0.97)	0.72 (0.63–0.83)
Premenopausal					
54–92 cm	185	224	1.0 (ref.)	1.0 (ref.)	1.0 (ref.)
93–99 cm	153	231	0.60 (0.44–0.81)	0.53 (0.38–0.74)	0.44 (0.31–0.63)
100–107 cm	161	185	0.70 (0.52–0.96)	0.57 (0.41–0.81)	0.41 (0.28–0.60)
108–157 cm	205	180	0.83 (0.61–1.13)	0.61 (0.43–0.85)	0.35 (0.22–0.56)
P for trend			0.61	0.02	<0.001
Mean ± SD	101.0±12.8	99.0 ± 11.2			
Per 10 cm			0.99 (0.91–1.09)	0.91 (0.82–1.00)	0.73 (0.63–0.85)
Postmenopausal					
54–92 cm	127	58	1.0 (ref.)	1.0 (ref.)	1.0 (ref.)
93–99 cm	113	55	0.88 (0.56–1.38)	0.93 (0.58–1.49)	0.76 (0.47–1.23)
100–107 cm	122	66	0.79 (0.51–1.23)	0.74 (0.47–1.18)	0.52 (0.31–0.85)
108–157 cm	156	99	0.68 (0.45–1.01)	0.69 (0.44–1.06)	0.38 (0.22–0.66)
P for trend			0.05	0.06	<0.001
Mean ± SD	101.7±13.2	103.6±12.1			
Per 10 cm			0.88 (0.78–0.98)	0.88 (0.78–0.99)	0.71 (0.59–0.84)
P for interaction*			0.20	0.98	0.92

Abbreviations: OR, odds ratio; CI, confidence interval; SD, standard deviation

[*] Interaction between hip circumference and menopausal status

[†] Adjusted for age at diagnosis or interview (categorical), ethnicity, education (categorical), age at menarche (continuous), number of live birth (categorical), age at first live birth (continuous), duration of breastfeeding (categorical), menopausal status, family history of breast cancer, benign breast disease, hormonal contraceptive use, alcohol drinking, and height (continuous).

[‡] Adjusted for body mass index (continuous) and waist circumference (continuous) in addition to the above variables.

Categories of hip circumferences are based on quartiles in controls.

Table 4

Waist-hip ratio and breast cancer risk in Nigerian women, 1998–2009

	Cases	Controls	Age-adjusted OR (95% CI)	Adjusted OR (95% CI)†	Adjusted OR (95% CI)‡
Total					
< 0.77	211	298	1.0 (ref.)	1.0 (ref.)	1.0 (ref.)
0.77 to <0.81	204	266	0.96 (0.74–1.26)	0.98 (0.73–1.31)	1.00 (0.74–1.34)
0.81 to <0.87	398	303	1.54 (1.21–1.97)	1.70 (1.30–2.22)	1.77 (1.35–2.31)
≥ 0.87	407	230	1.90 (1.47–2.44)	2.01 (1.52–2.65)	2.15 (1.61–2.85)
P for trend			<0.001	<0.001	<0.001
Mean ± SD	0.843±0.088	0.816±0.074			
Per 0.1 unit			1.38 (1.23–1.54)	1.42 (1.25–1.60)	1.45 (1.28–1.65)
Premenopausal					
< 0.77	146	246	1.0 (ref.)	1.0 (ref.)	1.0 (ref.)
0.77 to <0.81	130	214	0.89 (0.65–1.22)	0.93 (0.66–1.32)	0.95 (0.67–1.35)
0.81 to <0.87	222	216	1.47 (1.10–1.97)	1.64 (1.19–2.27)	1.71 (1.24–2.36)
≥ 0.87	204	143	1.88 (1.38–2.56)	1.99 (1.41–2.80)	2.12 (1.49–2.99)
P for trend			<0.001	<0.001	<0.001
Mean ± SD	0.834±0.086	0.809±0.071			
Per 0.1 unit			1.36 (1.18–1.56)	1.40 (1.20–1.65)	1.44 (1.22–1.69)
Postmenopausal					
< 0.77	65	52	1.0 (ref.)	1.0 (ref.)	1.0 (ref.)
0.77 to <0.81	74	52	1.19 (0.71–1.99)	1.11 (0.64–1.92)	1.11 (0.64–1.94)
0.81 to <0.87	176	87	1.70 (1.08–2.68)	1.84 (1.13–2.97)	1.91 (1.17–3.09)
≥ 0.87	203	87	2.02 (1.28–3.17)	2.10 (1.30–3.39)	2.26 (1.39–3.68)
P for trend			0.001	0.001	<0.001
Mean ± SD	0.856±0.088	0.835±0.078			
Per 0.1 unit			1.40 (1.16–1.69)	1.43 (1.18–1.74)	1.47 (1.21–1.80)
P for interaction*			0.95	0.96	0.98

Abbreviations: OR, odds ratio; CI, confidence interval; SD, standard deviation

* Interaction between waist-hip ratio and menopausal status

† Adjusted for age at diagnosis or interview (categorical), ethnicity, education (categorical), age at menarche (continuous), number of live birth (categorical), age at first live birth (continuous), duration of breastfeeding (categorical), menopausal status, family history of breast cancer, benign breast disease, hormonal contraceptive use, alcohol drinking, and height (continuous).

‡ Adjusted for body mass index (continuous) in addition to the above variables.

Categories of waist-hip ratio are based on quartiles in controls.

Table 5

Waist-hip ratio and breast cancer risk by body mass index in Nigerian women, 1998–2009

WHR	Cases	Controls	Age-adjusted OR (95% CI)	Adjusted OR (95% CI)†
BMI < 25kg/m²				
< 0.77	132	205	1.0 (ref.)	1.0 (ref.)
0.77 to <0.81	112	168	0.86 (0.61–1.21)	0.85 (0.58–1.24)
0.81 to <0.87	196	148	1.71 (1.23–2.36)	1.86 (1.31–2.65)
≥ 0.87	165	82	2.52 (1.75–3.61)	2.81 (1.90–4.16)
P for trend			<0.001	<0.001
Mean ± SD	0.832±0.093	0.799±0.069		
Per 0.1 unit			1.60 (1.35–1.89)	1.72 (1.43–2.07)
BMI ≥ 25kg/m²				
< 0.77	76	93	1.0 (ref.)	1.0 (ref.)
0.77 to <0.81	87	98	1.14 (0.74–1.75)	1.23 (0.76–1.99)
0.81 to <0.87	195	194	1.44 (0.98–2.10)	1.63 (1.06–2.50)
≥ 0.87	219	148	1.64 (1.12–2.40)	1.70 (1.11–2.61)
P for trend			0.005	0.01
Mean ± SD	0.850±0.079	0.836±0.075		
Per 0.1 unit			1.23 (1.04–1.44)	1.21 (1.01–1.45)
P for interaction*			0.031	0.016

Abbreviations: BMI, body mass index; WHR, waist-hip ratio; OR, odds ratio; CI, confidence interval; SD, standard deviation

*Interaction between waist to hip ratio and body mass index

†Adjusted for age at diagnosis or interview (categorical), ethnicity, education (categorical), age at menarche (continuous), number of live birth (categorical), age at first live birth (continuous), duration of breastfeeding (categorical), menopausal status, family history of breast cancer, benign breast disease, hormonal contraceptive use, alcohol drinking, and height (continuous).

Categories of waist-hip ratio are based on quartiles in controls.

Table 6

Waist circumference and breast cancer risk by body mass index in Nigerian women, 1998–2009

Waist circumference	Cases	Controls	Age-adjusted OR (95% CI)	Adjusted OR (95% CI)†
BMI < 25kg/m²				
45–81 cm	412	507	1.0 (ref.)	1.0 (ref.)
82–138 cm	194	96	2.03 (1.52–2.71)	1.91 (1.39–2.61)
P value			<0.001	<0.001
Mean ± SD	77.6±9.3	74.3±7.9		
Per10 cm			1.31 (1.14–1.51)	1.26 (1.07–1.47)
BMI ≥ 25kg/m²				
45–81 cm	65	74	1.0 (ref.)	1.0 (ref.)
82–138 cm	512	419	1.15 (0.79–1.68)	1.11 (0.73–1.68)
P value			0.46	0.62
Mean ± SD	92.9±10.7	90.8±9.8		
Per10 cm			1.13 (1.00–1.27)	1.08 (0.95–1.23)
P for interaction*			0.021	0.042

Abbreviations: BMI, body mass index; WHR, waist-hip ratio; OR, odds ratio; CI, confidence interval; SD, standard deviation

*Interaction between waist circumference and body mass index

†Adjusted for age at diagnosis or interview (categorical), ethnicity, education (categorical), age at menarche (continuous), number of live birth (categorical), age at first live birth (continuous), duration of breastfeeding (categorical), menopausal status, family history of breast cancer, benign breast disease, hormonal contraceptive use, alcohol drinking, and height (continuous).

Categories of waist circumference are based on median in controls.