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Waist–hip ratio and breast cancer risk in urbanized Nigerian women

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Abstract

Background: The aim of the study was to examine the relationship between waist–hip ratio and the risk of breast cancer in an urban Nigerian population.

Methods: Between March 1998 and August 2000, we conducted a case–control study of hospital-based breast cancer patients (n=234) and population-based controls (n=273) using nurse interviewers in urban Southwestern Nigeria.

Results: Multivariable logistic regression showed a significant association between the highest tertile of waist–hip ratio and the risk of breast cancer (odds ratio=2.67, 95% confidence interval=1.05–6.80) among postmenopausal women. No association was found in premenopausal women.

Conclusion: The present study, the first in an indigenous African population, supports other studies that have shown a positive association between obesity and breast cancer risk among postmenopausal women.

Keywords: breast cancer, Nigeria, obesity, waist–hip ratio, women

Introduction

Breast cancer is the leading female malignancy in the world and is now the most common cancer in Nigeria [1–3]. Despite this, there is a sixfold variation in incidence when Western countries are compared with the developing countries of Africa and Asia, and immigrants from low incidence countries tend to acquire the rate of their new environments [2,4]. Some of this variation may be due to demographic factors such as longer life expectancy, better reporting of disease and improved access to clinical care. There is increasing interest, however, in the relative importance of environmental and genetic factors as explanations for this difference.

In general, African breast cancer patients tend to present at a young age, with large tumors and multiple nodal involvements, and have poorer clinical and pathological prognostic factors compared with Caucasian patients. These characteristics are somewhat similar to that of African-Americans but are in contrast with those of non-Hispanic Whites in the USA, thus heightening the interest in the role of genetic factors in the etiology of breast cancer in general, and in people of African origin in particular [3,5].

One of the often cited reasons for the difference in breast cancer incidence in Africa compared with Western countries is the difference in environmental risk factors such as

BMI = body mass index; LRT = likelihood ratio test; SHBG = sex hormone binding globulin; WHR = waist–hip ratio.

diet and physical activity (both contributing to obesity), use of hormones/other medications, and obstetric/gynecological practices [6]. In the current paper, we present the results of the first study of the association between waist–hip ratio (WHR) and breast cancer in an indigenous African population.

The WHR has emerged as an important metameter of the association between central adiposity and many obesity-related diseases. Positive correlations have been seen with coronary heart disease, adult-onset diabetes mellitus and stroke [7]. However, the result with breast cancer has been inconsistent [8]. Abdominal obesity may be related to breast cancer through aberrant insulin signaling leading to increased endogenous androgen and estrogen levels [9].

Methods

Case ascertainment

All consecutive cases of breast cancer, regardless of previous history, seen at presentation and later confirmed histologically in the Departments of Surgery and Radiotherapy of the University College Hospital, Ibadan, Nigeria, from March 1998 to August 2000 were recruited at their first clinic presentation, after obtaining informed consent. Nurse interviewers asked them which risk factors did apply at the time when they were last well. The interviewer then measured the height, weight, and hip circumference at its widest diameter. Waist circumference was measured according to the guidelines in the World Health Organization MONICA Project manual [10].

There were 312 cases, of which 73 indicated that they had lived predominantly in a rural area and were excluded. There were five refusals and no further information was available from these, leaving 234 cases.

Control ascertainment

During the period of case recruitment, a community adjoining the hospital was randomly selected by ballot based on comparability with the hypothetical catchment area of the hospital. Community consent was sought from the Chief-in-Council and approval for the study was communicated to members of the community through heads of households. The census register of the people living in the community was obtained and community consent sought for the study. Names were then randomly selected from the community register and the people were invited to visit a clinic set up in the community for the study.

Inclusion criteria for the controls were females aged older than 18 years, absence of any type of cancer at recruitment, predominant urban residence for most of their lives and the ability to give informed consent. No matching of controls to cases was performed. After explaining the project to the potential participant, a complete physical examination was carried out. A trained nurse then interviewed the participants, measured their height, their weight, their hip circumference at its widest diameter and their waist circumference 1 inch below the navel, and completed the questionnaires. A total of 278 subjects were interviewed, of which 273 were recruited; there were three refusals, and two people were not recruited on account of a diagnosis of cancer (head of the pancreas cancer in one and colorectal cancer in the other).

Data collection and analysis

The information obtained from the cases and controls include age, self-reported social status based on family income and other baseline demographic information. Obstetric and gynecological history such as age of onset of menarche, menstrual cycle history, whether periods had usually been regular, age at onset of menopause (natural or otherwise) and history of previous breast disease, as well as smoking, drug and alcohol use history, were obtained from the subjects. Other information obtained included first-degree family history of breast cancer, history of ever using estrogen-containing contraceptives and where they had lived most of their lives (whether in a rural or urban setting). No information about post-menopausal hormonal use was obtained as this is an uncommon practice in Nigeria.

The body mass index (BMI) (weight [kg]/height [m^2]; obesity = BMI $\geq$ 30) and WHR were computed (waist circumference [cm]/hip circumference [cm]), and four subjects with WHR > 1.2 and WHR < 0.6 were excluded. The rest were divided into tertiles and treated as categories. Statistical analysis of the data was carried out with SAS version 8.0 (SAS Institute, Inc., Cary, NC, USA) separately for premenopausal and postmenopausal women. Univariate analysis was used to identify variables to be included in multivariable analysis using $P \leq 0.10$. Purposeful stepwise multivariable logistic regression models were built to identify statistically significant variables at $P = 0.05$, and a 10% or greater change in the β-coefficient was used to identify confounders. In addition, automated stepwise multivariate logistic regression models were run as an adjunct to the aforementioned method.

Continuous variables were examined for assumption of linearity; age and age at onset of regular menstrual periods were found to be nonlinear. Age was subsequently divided into 5-year categories while age at onset of regular menstrual periods was left as it was because the range of values was narrow, but it was subsequently modeled as a categorical variable.

Results

The WHR in this study was measured at presentation in cases and, since most patients presented in an advanced stage of disease, there may have been significant weight loss among the cases prior to recruitment. However, there

Table 1

Continuous predictors of breast cancer among premenopausal women in Nigeria, 1998–2000

Predictor	Cases	Controls	Odds ratio	95% confidence interval	*P* value
Age (years)	38.34 (6.55)	34.23 (8.80)	1.07	1.04–1.10	<0.01
Total number of pregnancies	4.41 (2.29)	3.82 (2.69)	0.90	0.79–1.03	0.13
Age at menarche (years)	15.01 (1.88)	15.51 (2.30)	0.86	0.77–0.97	0.01
Age at first full-term pregnancy (years)	23.80 (4.30)	22.54 (3.70)	1.09	1.02–1.16	0.01
Height (cm)	160.50 (8.62)	159.38 (7.17)	1.03	1.00–1.07	0.07
Weight (kg)	64.25 (14.51)	65.52 (15.28)	1.01	0.99–1.03	0.19
Body mass index (weight/height^2)	24.76 (5.55)	23.65 (4.85)	1.02	0.97–1.07	0.54
Waist circumference (cm)	80.60 (11.84)	77.56 (10.73)	1.01	0.99–1.04	0.28
Hip circumference (cm)	99.03 (14.89)	97.07 (11.07)	1.01	0.99–1.02	0.61

Data presented as mean (standard deviation), age-adjusted odds ratio, 95% confidence interval, and *P* value for cases and controls.

was no significant difference in the frequency of the stage of disease (based on size of tumor at presentation) by obesity (BMI > 30) among premenopausal (P [chi-squared test] = 0.18) and postmenopausal women ($P = 0.20$) on the one hand, and in WHR among premenopausal women ($P = 0.26$) and postmenopausal women ($P = 0.63$) on the other.

Premenopausal women

Tables 1 and 2 present the results of age-adjusted analysis. Increasing age and age at first full-term pregnancy were positively associated with risk of breast cancer, while increasing age at onset of menarche was protective. Overall, categories of WHR were not significantly associated with the risk of breast cancer but there was a marginally significant test of trend for a positive association between increasing WHR and breast cancer risk. There was no association with total number of pregnancies, height, obesity (BMI ≥ 30) weight, BMI, waist and hip circumferences, family history of breast cancer, having ever breastfed and use of oral contraceptives. In multivariable logistic regression analysis, adjusted for age, age at menarche, age at first pregnancy and height, there was no significant association between the WHR and breast cancer risk (Table 3).

Postmenopausal women

On the other hand, in age-adjusted logistic regression models among postmenopausal women (Tables 4 and 5), increasing age was associated with a reduced breast cancer risk, while increasing height, waist circumference and obesity (BMI ≥ 30) were positively associated with breast cancer risk. There was a significant association with the highest tertile of WHR but the likelihood ratio test (LRT) for trend ($P = 0.07$) was not significant. The association with having ever breastfed could not be ascertained because of an inadequate sample size. In multivariable logistic regression analysis, adjusted for age and height, there was a significant association between the highest tertile of WHR and breast cancer risk (LRT $P = 0.10$; Table 6).

Discussion

The earliest reports of the positive association between energy balance and breast cancer date back to 1942 [11]. Numerous case–control and cohort studies have subsequently supported this association. However, the strength of the association and the category of patients in whom the association was seen varied from study to study. In addition, there are methodological concerns about the most appropriate measure of obesity, and which component or type of obesity is etiologically significant.

The WHR, a measure of central adiposity, is gaining increased use as a measure of etiologically significant obesity and is thought to be more closely related to pathology, especially coronary heart disease, diabetes mellitus and stroke [7]. The metabolic changes that accompany obesity include peripheral hyperinsulinemia, hyperglycemia and glucose intolerance, hypertriglyceridemia, decreased serum low-density lipoprotein, increased serum very low-density lipoprotein, increased serum leptin, dyslipidemia, increased serum cortisol clearance, increased serum C-peptide level, downregulation of insulin receptors and an exaggerated insulin response to an oral glucose load [12–15]. These changes, especially when they occur in early adulthood, may be of fundamental importance in the development of breast cancer [9,16].

Obesity is also associated with significant hormonal changes such as decreased serum estradiol and sex hormone binding globulin (SHBG) levels, increased

Table 2

Categorical predictors of breast cancer among premenopausal women in Nigeria, 1998–2000

Predictor	Cases	Controls	Odds ratio	95% confidence interval	*P* value
Waist–hip ratio					
≤0.77	37 (30.8)	64 (35.6)	1.00		
>0.77 to ≤0.85	45 (37.5)	78 (43.3)	0.88	0.50–1.55	0.65
>0.85	38 (31.67)	38 (21.2)	1.41	0.80–2.78	0.22
Family history of breast cancer					
Yes	11 (9.17)	14 (7.78)	1.37	0.58–3.22	0.48
No	109 (90.83)	166 (92.22)			
Obesity (body mass index ≥30)					
Yes	29 (24.17)	25 (13.89)	1.52	0.82–2.82	0.18
No	91 (75.83)	155 (86.11)			
Having ever breastfed					
Yes	102 (85.71)	133 (73.89)	1.04	0.50–2.18	0.91
No	17 (14.29)	47 (26.11)			
Use of contraceptive pill					
Yes	53 (45.30)	62 (34.44)	0.84	0.51–1.39	0.50
No	64 (54.70)	118 (65.56)			
Social status					
Low	54 (46.15)	98 (54. 75)	1.00		0.15
Middle	60 (51.28)	80 (44.69)	1.36	0.85–2.18	
High	3 (2.56)	1 (0.56)	5.44	0.55–53.62	

Data presented as number (%), age-adjusted odds ratio, 95% confidence interval, and *P* value for cases and controls.

Table 3

Multivariable odds ratio, 95% confidence interval and *P* value, adjusted for age in categories, age at first pregnancy, height and age at menarche in premenopausal women in Nigeria, 1998–2000

Predictor	Adjusted odds ratio	95% confidence interval	*P* value
Waist–hip ratio			
≤0.77	1.00		
>0.77 to ≤0.85	0.80	0.40–1.60	0.53
>0.85	1.80	0.85–3.81	0.13

peripheral fat conversion of estrogens to progesterone and increased serum testosterone levels that may be associated with an increased risk of breast cancer [17]. Estrogens are necessary for normal breast development, and they induce and promote mammary tumor growth in animal studies [18]. In addition, the close association between increased risk of breast cancer and certain reproductive factors such as early menarche and late menopause [19], as well as the fall off in the rate of increase in the incidence of disease at menopause [20] and the lowered risk of breast cancer in oophorectomized women and those taking antiestrogens [21,22], all support the role of estrogen in breast carcinogenesis.

The results from cohort studies about the association between WHR and the risk of breast cancer are inconsistent. In the Nurses' Health Study, the adjusted risk for the highest quintile compared with the lowest quintile of WHR among postmenopausal women who had never used hormone replacement therapy was 1.85 (95% confidence interval = 1.25–2.74) [23]. Kaaks *et al*. reported a risk ratio of 2.63 (95% confidence interval = 1.09–6.35) comparing the highest quintile with the lowest quintile of WHR [24]. These are similar to the results obtained in the present study. In contrast, the Iowa Women's Health Study showed no association with WHR, and an earlier report of interaction with family history appeared to have attenuated with time [25,26]. In the New York University Women's

Table 4

Continuous predictors of breast cancer among postmenopausal women in Nigeria, 1998–2000

Predictor	Cases	Controls	Odds ratio	95% confidence interval	*P* value
Age (years)	53.62 (9.55)	58.42 (7.92)	0.939	0.09–0.97	0.01
Total number of pregnancies	5.99 (2.21)	6.75 (2.24)	0.89	0.71–1.02	0.10
Age at menarche (years)	15.58 (2.11)	16.35 (2.72)	0.89	0.78–1.02	0.08
Age at first full-term pregnancy (years)	23.34 (4.23)	22.99 (4.20)	0.98	0.92–1.06	0.65
Age at onset of natural menopause (years)	47.37 (6.49)	50.02 (5.59)	0.97	0.91–1.03	0.35
Height (cm)	159.37 (6.66)	155.99 (9.33)	1.07	1.02–1.13	0.01
Weight (kg)	65.52 (15.28)	62.32 (13.66)	1.02	1.00–1.04	0.07
Body mass index (weight/height^2)	25.71 (5.86)	25.39 (5.63)	1.02	0.97–1.08	0.48
Waist (cm)	86.11 (14.18)	83.28 (10.36)	1.01	1.00–1.05	0.03
Hip (cm)	102.31 (17.05)	102.88 (16.93)	1.00	0.98–1.02	0.93

Data presented as mean (standard deviation), age-adjusted odds ratio, 95% confidence interval, and *P* value for cases and controls.

Table 5

Comparison of categorical predictors of breast cancer among postmenopausal women in Nigeria, 1998–2000

Predictor	Cases	Controls	Odds ratio	95% confidence interval	*P* value
Waist–hip ratio					
≤0.77	16 (15.4)	21 (23.6)	1.00		
>0.77 to ≤ 0.85	40 (38.5)	40 (44.9)	1.52	0.67–3.42	0.31
>0.85	48 (46.15)	28 (31.5)	2.79	1.21–6.45	0.02
Family history of breast cancer					
Yes	7 (6.73)	8 (8.99)	0.70	0.23–2.09	0.52
No	97 (93.27)	81 (91.01)			
Obesity					
Yes	31 (29.81)	16 (17.98)	2.01	0.99–4.09	0.05
No	73 (70.19)	73 (82.02)			
Having ever breastfed					
Yes	101 (97.12)	89 (100)	[a]	[a]	[a]
No	3 (2.88)	0 (0)			
Use of contraceptive pill					
Yes	34 (34)	25 (28.09)	0.96	0.50–1.84	0.90
No	66 (66)	64 (71.91)			
Social status					
Low	49 (47.12)	57 (64.77)	1.00	0.97–3.19	0.06
Middle	47 (45.19)	31 (35.23)	1.79		
High	8 (7.69)	0	[a]	[a]	

Data presented as number (%), age-adjusted odds ratio, 95% confidence interval, and *P* value for cases and controls.
[a] Values could not be computed because of zero-cell.

Table 6

Multivariable odds ratio, 95% confidence interval and *P* value, adjusted for age in categories and height in postmenopausal women in Nigeria, 1998–2000

Predictor	Adjusted odds ratio	95% confidence interval	*P* value
Waist–hip ratio			
≤0.77	1.00		
>0.77 to ≤0.85	1.68	0.68–4.19	0.26
>0.85	2.67	1.05–6.80	0.04

Health Study, the multivariable analysis showed an association between the lowest quintile and the highest quintile of WHR and breast cancer of 1.72 (95% confidence interval=1.0–3.1) among premenopausal women, but there was no association among postmenopausal women [27].

Most case–control studies have found an association between WHR and the risk of postmenopausal breast cancer [28–37], and most report either null or weakly positive association with premenopausal breast cancer. In the present study, there was no statistically significant association between breast cancer and WHR for premenopausal women.

Studies of WHR and the risk of breast cancer are limited by systematic bias in the measurement of WHR across studies [36], which may have been controlled somewhat in this study by using nurse interviewers and adhering to the World Health Organization MONICA guidelines [10]. In case–control studies like the present one, selection and recall bias can be problematic. While we restricted our analysis to urban dwellers, finer adjustment based on the community of residence or the restriction of cases to only those from the community from which controls were selected would have increased the validity of the result. The finding of two cases of cancer among the controls may be due to chance.

The prevalence of obesity in the cases and controls also appears higher than expected but this may be consistent with the increasing rate of obesity in developing countries, especially in the urban areas [38]. Preclinical weight loss is not usually a problem in breast cancer [39], and subanalysis of our data confirmed this. Inclusion of obesity in the multivariate analysis did not change the result, and obesity was not a significant predictor of outcome in multivariate regression analysis. Other limitations of this study include the absence of information about breastfeeding and the features of a 'Western lifestyle' such as physical activity, diet and use of postmenopausal hormones and other medications.

In conclusion, the present study is consistent with findings in other environments that central adiposity is a risk factor for breast cancer in postmenopausal women.

Competing interests

None declared.

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