A Matched Case-Control Study of Beans Intake And Breast Cancer Risk in Urbanized Nigerian Women.

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Abstract

Purpose. Beans intake has been associated with reduced risk of breast cancer (BRCA), however; only few studies considered molecular subtypes status and none in African women. Therefore, the purpose of this study was to examine the associations between dietary intake of beans and BRCA including its subtypes in Nigerian women.

Methods. Overall, 472 newly diagnosed patients with primary invasive BRCA were age-matched (±5 years) with 472 controls from the Nigerian Integrative Epidemiology of Breast Cancer (NIBBLE) Study from 01/2014-07/2016. We collected dietary intake of beans using a food frequency questionnaire (FFQ). Beans intake was categorized into three levels of never (never in the past year), low (≤1 portion/week) and high intake (>1 portions/week). We used conditional and unconditional logistic regression models to estimate the Odds Ratio (OR) of beans intake and the risk of overall BRCA and by its molecular subtypes.

Results. The mean (SD) age of cases was 44.4(10.0) and of controls was 43.5(9.5) years. In the case group, more than half (51.1%) has never consumed beans alone in the past year compared to 39.0% in the control group. In multivariable models, we found significant inverse associations between beans intake and overall BRCA risk (OR=0.57; 95%CI: 0.38-0.85), hormone receptor-positive BRCA (OR=0.45, 95%CI: 0.23-0.90) and triple-negative BRCA (OR=0.47 95%CI: 0.25-0.88).

Conclusion. Dietary intake of beans of more than one portions a week is associated with reduced risk of BRCA in African women and it may play a significant role in reducing the incidence of BRCA particularly of the more aggressive triple-negative subtype, which is more prevalent in SSA.

Introduction

Breast cancer is the leading cause of cancer morbidity and mortality among women worldwide. Approximately one in four (24.2%) of all new cancer cases diagnosed in women are breast cancer [1]. Although its incidence in low- and middle-income countries (LMIC) including Sub-Saharan Africa [2] is lower than that in high-income countries (HIC), the incidence in SSA is rising rapidly and it is now the commonest female cancer in Nigeria [2, 3]. From 2000 to 2015, the incidence of breast cancer in SSA increased from 21.9 (95% CI: 15.4-28.3) per 100,000 to 47.9 (95% CI: 41.2-54.6) per 100,000 [4].

The increase in the incidence of breast cancer in SSA can be explained by several risk factors including increased life expectancy, changes in obstetrics practices such as delays in commencement of childbearing, contraceptive use, reduced parity and reduced duration of breastfeeding [5, 6]. Changes in lifestyle behaviors are also occurring in SSA due to rapid urbanization and socio-economic development leading to higher alcohol intake, and higher prevalence of obesity and physical inactivity, which all contribute to the overall increased cases in breast cancer in this area [3, 7, 8].

Furthermore, SSA is undergoing nutritional transition particular among urbanized Africans. More urbanized Africans are departing from their traditional African diet rich in high fiber and plant-based proteins (e.g. beans) to consume more a ‘Western diet’ marked by high intake of meats, energy-dense and low fiber foods, as well as more intake of soft sweetened beverages [9, 10]. Previous studies suggest that there are nutrient components in the traditional African diet that are associated with reduced risks of some cancer [9, 11]. While, other components of the African diets, including certain foods and additives, the methods of foods storage and preparation may be associated with increased risk of other cancers [5]. On balance, departures from the traditional African diet as a result of the ongoing nutritional transition may contribute more to the increased incidence of breast cancer in African women but this remains largely unexplored [10].

Previous studies in other populations show that higher dietary intake of beans and legumes are associated with reduced risk of breast cancer [12–15]. In the Four-Corners Breast Cancer Case-Control Study, there was inverse association between breast cancer risk and factor-derived “Native Mexican” dietary pattern that loaded heavily with beans [13]. There have been few prospective studies examining the association between beans intake and breast cancer risk [12, 15]. Adebamowo *et. al*. found inverse association between intake of beans and lentils, and breast cancer risk in Western women [12] and Velie *et al*. found that a factor-derived “traditional southern pattern” rich in legumes was inversely associated with breast cancer [15].

With the rising incidence of breast cancer in SSA along with the ongoing nutritional transitions, there is a unique opportunity to examine whether there is a link between these two changes. Therefore, the primary study aim was to examine the association between dietary intake of beans and breast cancer in Nigerian women. The secondary aim was to examine the association between dietary intake of beans and breast cancer subtypes (e.g., hormone receptor-positive, triple-negative) in Nigerian women, in particular the more aggressive subtype, triple-negative, which is more prevalent in SSA. Our hypothesis is that there will be a significant inverse association between high intake of dietary beans and lower risks of breast cancer including its subtypes in Nigerian women.

Methods

Study design and setting

We studied women enrolled in the Nigerian Integrative Epidemiology of Breast Cancer (NIBBLE) Study, a case-control study of female breast cancer that recruited participants at six government hospitals in Nigeria, five of whom are located in Abuja (National Hospital, University of Abuja Teaching Hospital Gwagwalada, Asokoro District Hospital, Garki Hospital and Wuse General Hospital) and the sixth hospital, the University of Nigeria Teaching Hospital, in Enugu, between January 2014 and July 2016. The details about the study design and setting have been previously published [16].

Participants

Overall, 508 newly diagnosed patients with primary invasive breast cancer aged 18 years or older were identified at their first visit to the clinical sites. Research nurses informed potential participants about the study and obtained their informed consent. Age-matched hospital-based controls (892) were women who did not have cancer or endocrine diseases and were within 5 years of the age of specific breast cancer patients enrolled within one month in the same hospital. Most (94.0%) of the women approached consented to participate. Research nurses conducted face-to-face interviews in English language (70.6%) or local Nigerian language (29.4%) according to the patient's preference.

Primary exposure

Beans intake was calculated from the dietary intake data that were collected during face-to-face interview using a Semi-quantitative Food Frequency Questionnaire (FFQ) constructed from a list of 200 food items typically eaten in Nigeria. Participants indicated each food and beverage item they had eaten within the preceding year and the frequency with which they consumed the food (e.g. never, less than once a month, and up to several times a day) and the portion sizes they usually consumed (i.e. 1-serving spoon, 2-serving spoons, 3-serving spoons). The FFQ asked about consumption of single items such as beans alone or common beans dishes such as porridge beans (Ewa Oloyin), stewed beans (Ewa Riro), beans soups (Adalu), beans pudding (Moin Moin), beans cakes (Akara). For the purposes of this study, we calculated intake of beans alone per week by multiplying the frequency of intake per week with reported portion size to create a continuous variable. Then, we categorized beans alone intake into three categories of never (never consumed beans in the past year), low (≤1 portion per week) and high intake (>1 portions per week).

Breast cancer and breast cancer subtypes

Needle core biopsies were performed using Bard Magnum Biopsy Gun®. Breast specimens were fixed in 10% neutral buffered formalin and processed within 48 hours of fixation with a minimum fixation time of 8 hours in Leica® automatic tissue processors at the African Collaborative Center for Microbiome and Genomics Research (ACCME) Laboratory at the Institute of Human Virology, Nigeria.

Histology

Sections of Paraffin-embedded blocks were cut at 3-4 μm and stained with hematoxylin and eosin stains. Histological features were classified according to the 2003 WHO classification of breast diseases and graded using the Nottingham modification of the Bloom-Richardson grading [17]. Only participants with final histologic confirmation of breast cancer were included in the analysis.

Immunohistochemistry (IHC)

Histologically confirmed invasive breast tumors were stained by immunohistochemical techniques using the Thermo Scientific Lab Vision primary antibodies (clones ER-SP1; PR-SP2; Her2-SP3) and Thermo Scientific™ Ultra Vision™ Quanto HRP DAB detection kit according to manufacturer’s recommended protocol. In brief, formalin-fixed paraffin-embedded (FFPE) tissues were sectioned serially into 4 μm, placed in histogrip coated microscope slides, incubated overnight at 60 C, deparaffinized in series of xylene (three changes), graded alcohol (2 changes 100%, 90%, and 70% ethanol) and rehydrated in distilled water. Antigen retrieval was performed, sections were washed with Phosphate Buffered Saline (PBS) and blocked with hydrogen peroxide for 10 minutes. Then Ultra V was applied to block nonspecific background staining for 5 minutes. Sections were washed with PBS and primary antibodies (ER-SP1; PR-SP2; Her2-SP3) were applied on the sections and incubated at room temperature for 1 hour followed by application of primary antibody enhancer and HRP polymer. Staining was visualized using Diaminobenzidine (DAB) and counterstained with haematoxylin. Sections were dehydrated and cover slipped. We planned to perform immunohistochemistry (IHC) for all participants recruited into the NIBBLE study but in a few cases the core tissue biopsies were too small so IHC was not feasible.

IHC interpretation

We considered ER and PR were positive if ≥ 1% nuclei of the tumor cells were stained per the American Society College Oncology/College American Pathology (ASCO/CAP) guidelines [18]. HER2 staining was scored as 0, 1+, 2+, or 3+ and we considered a staining of 3+ (uniform, intense membrane staining of > 30% of invasive tumor cells) a positive HER2 result [19].

Breast cancer subtypes

Overall, 57% of the cases (292/508) had estrogen, progesterone and human epidermal growth factor 2 test results (Figure 1). We classified breast cancer subtypes using combinations of the IHC markers as follows (a) hormone receptor positive (HP) were tumors that had positive estrogen and progesterone tests but negative HER2 test and (b) triple-negative breast cancer (TNBC) were tumors that lacked all 3 markers [20]. Overall, 32.2% (n=94/292) were classified as HP, and 42.1% (n=123/292) as TNBC (Figure 2).

Covariates

We collected information on age in years, years of education completed (elementary, completed high school, post-high school with no university degree, completed university), marital status (married, single, separated/divorced/widowed), occupation (self employed, unskilled manual, skilled manual, professional executive), smoking experience (yes vs. no), alcohol use (yes vs. no), age at menarche, number of pregnancies which was categorized into 0, 1-2, 3-5, >5), ever used oral contraceptive (yes vs. no), menopausal status (premenopausal vs. postmenopausal), and breastfeeding experience of more than one month (yes vs. no). The research nurses measured participants' height, weight, waist, and hip circumferences, and we derived body mass index (BMI kg/m^2) and waist-hip ratio (WHR) from these measurements. Participants with extreme values of WHR of less than 0.7 or higher than 1.6 or with a BMI less than 10 kg/m^2 or greater than 50 kg/m^2 were excluded from the analyses. BMI was categorized into < 25, 25 - 29.9, ≥30) and WHR was categorized to ≤0.85 and > 0.85. To derive socio-economic status, we calculated the 'wealth index' using the following variables - house ownership and type of house owned (e.g. home, apartment, house or duplex); source of drinking water (e.g. from outside, well, borehole, piped or bottled); type of cooking fuel; use of separate room for cooking; type of toilet; and ownership of household goods including car and refrigerator. We used Principal Component Analysis (PCA) with varimax rotation to compute factor scores based on the sum of responses to these variables weighted by their factor loading. We used the first component in the PCA that explained (35%) of the variations in the data, to generate a wealth index. The wealth index variable was used to classify participants to low socio-economic status (lowest 40% of the score distribution), middle (middle 30%) and high (highest 30%) socio-economic class.

Statistical Analysis

Overall breast cancer

From the initial study sample (n=1,400), we matched 472 cases with 472 controls based on age (±5 year) using propensity score with the optimal matching procedure. Therefore, from the initial 508 cases, 36 were not matched due to age difference of 5 years or more and additional 420 unmatched controls were excluded making a final matched sample of 1:1 ratio with 944 participants (Figure 1). Compared to the final sample, excluded participants were significantly younger (37.8±9.7 vs. 44.0 ±9.7) (p-value<0.001), and there were no significant differences in LTPA between excluded and included participants (data are not shown).

To examine bivariate associations between the independent variables by cases and controls, we implemented conditional logistic regressions for each independent variable separately. To construct our multivariable models, we selected independent variables with p-value < 0.20 in the bivariate analysis for inclusion. Multiple imputations technique was performed to impute missing values of the independent variables after conducting missing completely at random test (MCAT) (p-value=0.63). For multivariable analyses, we conducted conditional logistic regression models and used Wald tests to identify covariates with significant associations (p-value < 0.05) with risk of overall and molecular subtypes of breast cancer.

Breast cancer subtypes

We used unconditional logistic regression models to identify age-adjusted variables with p-value < 0.20 in bivariate analyses. These variables were included in multivariable unconditional logistic regression models for each breast cancer subtype, separately.

We present the adjusted odds ratios (ORs) and their 95% confidence intervals for breast cancer overall and by subtypes. Test of trend was conducted by treating the tertiles as ordered three-category variable. All analyses were performed using Stata SE version 15.1 (College Station, Texas) and R-Studio Version 1.1.447 – © 2009-2018 RStudio, Inc.

Ethical approval

Ethical approval was obtained from the National Health Research Ethics Committee of Nigeria, Health Research Ethics Committees in each participating hospital and the institutional ethics committee at the University of Maryland School of Medicine, Baltimore (US). The study was carried out in compliance with the Nigerian National Code for Health Research Ethics. All participants gave written informed consent in accordance with the Declaration of Helsinki and the Nigerian National Code for Health Research Ethics.

Results

The characteristics of study sample are described in Table 1. The mean (SD) age between cases (44.4 (10.0)) was similar to controls (43.5 (9.5)) years after age matching. Cases and controls were similar in their level of socio-economic status, marital status, number of pregnancies, and breastfeeding experience. Women with breast cancer were older, had higher WHR and lower educational attainment, and were more likely to be post-menopausal and have non-professional jobs compared to women in the control group. Higher prevalence of obesity measured by BMI ≥30 was observed in controls vs. cases (31.2 vs. 39.2%, p-value=0.01) while higher abdominal fat measured by WHR was observed in cases compared to controls (69.9 vs. 64.8%, p-value=0.07). More than half of the cases (51.1%) have never consumed beans alone in the past year compared to 39.0% in the controls. High intake of beans of more than one portion a week was higher in the controls (21.4%) compared to cases (16.3%).

Table 2 shows the final results from the multivariable conditional logistic regression models. After adjusting for associated covariates, there was a significant association between higher beans intake and lower odds of having breast cancer. Women who reported high level of beans intake had a significant reduction in their odds of having breast cancer compared to women who reported never consuming beans in the past year (OR=0.57, 95% CI: 0.38-0.85, p-value=0.005) after adjusting for associated covariates.

Table 3 shows the final results of the multivariable logistic regression models examining beans intake and the risk of having breast cancer by its molecular subtypes. The adjusted model shows that women who had intake of more than one portion of beans in a week had significantly lower odds of having hormone receptor-positive breast cancer (OR=0.45, 95% CI: 0.23-0.90, *p*-trend=0.002) compared with those who reported never consuming beans in the past year. Similar results were observed in women with triple-negative breast cancer. Reduced odds of having triple-negative breast cancer was observed among those with high intake of beans compared with never (OR=0.47, 95% CI: 0.25-0.88, *p*-trend=0.001).

Discussion

Our study hypothesis was confirmed where we showed for the first time that dietary intake of beans is associated with reduced odds of overall, hormone receptor-positive and triple-negative breast cancer in African women after adjusting for well-established covariates including obesity, leisure time physical activity, menopausal status, marital status, number of pregnancies, breastfeeding experience, demographic variables, and type of occupation.

Our findings are similar to studies conducted in other populations [12-15]. For example, in prospective study of dietary beans intake, *Adebamowo et. al.* studied 90,630 nurses from the United States who participate in the Nurses' Health Study II, aged 26-46 years at baseline and followed for 8 years to examine their dietary intake and the association with breast cancer risk. The authors found that high cumulative average intake of beans or lentils, two or more times a week, compared with intake of less than once a month is associated with reduced risk of breast cancer (Relative Risk (RR)=0.76, 95% CI: 0.57-1.00; *p*-trend=0.03) [12]. Also, in experimental animal studies suggest inverse associations between consumption of a 60% bean diet with chemically induced breast cancer in rat models [23].

Other studies examined intake of beans while using factor analyses to derive dietary patterns. In a US-wide prospective cohort study of 40,559 women by *Velie et. al.,* three major dietary patterns were derived after using principal components factor analysis: vegetable-fish/poultry-fruit, beef/pork-starch, and traditional southern dietary patterns. The traditional southern pattern which is characterized by high intake of traditional rural southern US foods, including cooked greens, cooked beans and legumes, sweet potatoes, cornbread, cabbage, fried fish, chicken, and rice but low intake of cheese, mayonnaise–salad dressing, wine, liquor, and salty snacks was inversely associated with invasive breast cancer (Relative Hazard (RH)=0.78, 95% CI: 0.65-0.95; *p*-trend = 0.003) [15].

In a case–control study of 2,135 breast cancer cases and 2,571 controls, the researchers showed that high intake of total beans was associated with reduced risk for breast cancer (OR=0.81, 95%CI: 0.66–1.01, *p*-trend= 0.03). There was an inverse association between estrogen and progesterone breast cancer and high intake of beans (OR=0.72, 95% CI: 0.50–1.05, *p*-trend= 0.04)[14]. In another case-control study of breast cancer in the United States, the Four-Corners Breast Cancer Study, Murtagh *et. al.* found an inverse association between breast cancer risk and factor-derived “Native Mexican” dietary pattern that heavily loaded with Mexican cheeses, soups, meat dishes, legumes and tomato-based sauces in Hispanic and non-Hispanic white women (OR=0.68, 95%CI: 0.55-0.85; *p*-trend < 0.01) [13].

Beans is one of the commonest food items eaten in SSA and Latin America even though the amount consumed per capita is falling. In Nigeria, it is most commonly consumed alone or as porridge beans, stewed, soups, pudding or cakes. In this study, we examined intake of beans only because approximately half of our study participants consumed it in this form daily whereas consumption in other forms was less common. Other survey showed that approximately two third of Nigerians consume bean in different types of dishes daily [2]. Beans is an excellent source of plant proteins (23%), complex carbohydrates, dietary fiber, flavonoids, some vitamins and minerals [24].

There are several mechanisms that might explain our study findings. The first one is the high fiber content in beans. Animal studies have shown that soluble fiber reduced mammary tumor growth, angiogenesis and metastasis in mice [25]. Fiber has been associated with slowing glucose absorption, reducing insulin secretion, and regulation of the bioavailability of insulin-like growth factors, which are important pathways in breast carcinogenesis [25,26]. Epidemiological studies have shown inconsistent association between dietary fiber intake and serum estrogen. Conjugated estrogens in the liver are excreted into the bile and reabsorbed in the intestine and fiber may bind estrogens in the colon during the enterohepatic circulation and increase the fecal excretion of estrogens [25-26]. Fiber may also act by reducing β-glucuronidase activity in the feces leading to a decrease in the reabsortion of estrogen in the colon [27]. Furthermore, high intake of dietary fiber may reduce breast cancer risk by reducing the risk of overweight and obesity.

The second explanation is that beans contain a wide range of flavonoids and is the source of the greatest amount of flavonoids intake in the Nigerian diet. The Mexican diet is also rich in flavonoids, including flavones and lignans from beans, corn and green vegetables [28]. A hospital-based case–control study conducted in Mexico City found that in postmenopausal women, high dietary intake of flavonols and flavones was associated with a significant reduction of breast cancer risk [28]. Flavonoids may reduce carcinogenesis by preventing oxidative stress, inhibiting cell proliferation, inducing cell-cycle arrest, and maintaining DNA methylation [12, 29-31].

Lastly, women who have high beans' intake may also have retained other components of the traditional African diets, which are rich in anti-cancer agents. Whereas, women who reported never eating beans may have replaced it with other food items that are associated with increased risk for breast cancer such as charred red/organ meats, fat and calories[33]. However, more studies are needed to test these hypotheses because we did not examine them in the current study.

The limitations of our study include recall bias, and potential impact of breast cancer on dietary intake in general and specifically of bean intake. We did not adjust for family history of breast cancer, but previous studies showed low prevalence of this risk factor in Nigerian breast cancer patients. We also did not adjust for intake of other foods and nutrients. However, we adjusted for alcohol intake, the dietary factor that is most consistently associated with breast cancer risk as well as obesity measured by BMI and WHR. We used a modified FFQ, which has not been extensively validated in African populations. Despite these limitations, the strengths of our study include histological and immunohistochemical confirmation of breast cancer and its molecular subtypes, a large sample size with sufficient power to detect significant results, inclusion of a broad range of well-established covariates and confounders such as BMI, menopausal status, demographic variables, types of occupation, as well as relative homogeneity of the study population.

Conclusion

We found a significant association between high intake of beans and reduced risks of total, hormone receptor-positive and triple-negative breast cancer in urbanized Nigerian women. In LMICs where the incidence of breast cancer is rising, increased dietary intake of bean can significantly reduce the incidence of breast cancer, particularly of the more aggressive subtype as triple-negative breast cancer, which is more prevalent in women in Sub-Saharan Africa. Future studies are needed to evaluate the causality of these relationships and the specific component of beans that might be attributed to preventing breast cancer in African women.

Declarations

Ethical approval and consent to participate

Ethical approval was obtained from the National Health Research Ethics Committee of Nigeria, Health Research Ethics Committees in each participating hospital and the institutional ethics committees at the University of Maryland School of Medicine, Baltimore (US). All participants gave written informed consent in accordance with the Declaration of Helsinki and the Nigerian National Code for Health Research Ethics.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of Interest information

The authors declare that they have no Conflict of Interest information

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Authors' Contributions

CAA had the idea for the NIBBLE study, designed it, obtained funding, supervised implementation, and data management. SA contributed to the study design, data management, data analysis. GB conducted the statistical analysis and generated the first draft of the manuscript which was revised by the co-authors. TY, MY, OO, OB, EE, IS, EM, IA, and BA enrolled participants, conducted biopsies, data collection and ensured data quality. AF and BA conducted the laboratory diagnosis All authors contributed to drafting the manuscript, provided critical revisions and approved the final draft.

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Tables

Table 1 Descriptive characteristics of the study sample, the Nigerian Integrative Epidemiology of Breast Cancer Study (NIBBLE), year 2014-2016.

N=944		Cases [a] N=472 N(%) / Mean±SD	Control [a] N=472 N(%) / Mean±SD	*p-value* [a]
Age, years		44.4 ± 10.0	43.5 ± 9.5	0.18+
Age at first menstrual period, years		14.4 ± 1.7	14.5 ± 1.9	0.23
BMI kg/m^2				0.01
	<25	147 (31.1)	116 (24.6)	
	25-29.99	162 (34.3)	161 (34.1)	
	≥30	147 (31.2)	185 (39.2)	
	Missing	16 (3.4)	10 (2.1)	
WHR				0.07
	High, >0.85	330 (69.9)	306 (64.8)	
	Missing	16 (3.4)	14 (3.0)	
Education				0.01
	Elementary≤	135 (28.6)	94 (19.9)	
	Complete HS	101 (21.4)	120 (25.4)	
	Post HS no university	118 (25.0)	111 (23.6)	
	Completed University	112 (23.7)	145 (30.7)	
	Missing	6 (1.3)	2 (0.4)	
Marital status				0.93
	Married	341 (72.3)	344 (72.9)	
	Single	53 (11.2)	54 (11.4)	
	Separated/Divorced/Widowed	72 (15.3)	73 (15.5)	
	Missing	6 (1.3)	1 (0.2)	
Occupation				<0.01
	Self-employed	124 (26.3)	49 (10.4)	
	Unskilled manual	197 (41.7)	258 (54.7)	
	Skilled manual	112 (23.7)	76 (16.1)	
	Professional/executive	22 (4.7)	71 (15.0)	

	Missing	17 (3.6)	18 (3.8)	
Wealth index				0.43
	Low	183 (38.8)	188 (39.8)	
	Middle	152 (32.2)	123 (26.1)	
	High	126 (26.7)	154 (32.6)	
	Missing	11 (2.3)	7 (1.5)	
Ever used oral contraceptives				0.25
	Yes	141 (29.9)	160 (33.9)	
	Missing	11 (2.3)	6 (1.3)	
Number of pregnancies				0.97
	0	49 (10.4)	45 (9.5)	
	1-2	86 (18.2)	95 (20.1)	
	3-5	227 (48.1)	231 (48.9)	
	≥6	99 (21.0)	98 (20.9)	
	Missing	11 (2.3)	3 (0.6)	
Menopausal status				0.05
	Postmenopausal	167 (35.4)	146 (30.9)	
	Missing	6 (1.3)	2 (0.4)	
Ever breastfed more than one month				0.21
	Yes	364 (77.1)	377 (79.9)	
	Missing	14 (3.0)	14 (3.0)	
Smoke				NA
	Yes	2 (0.4)	3 (0.6)	
	Missing	7 (1.5)	2 (0.4)	
Alcohol use				0.06
	Yes	100 (21.2)	79 (16.7)	
	Missing	9 (1.9)	4 (0.9)	
Leisure-time physical activity (meet the WHO recommendations)				<0.01

	Physical active	83 (17.6)	135 (28.6)	
	Physical inactive	356 (75.4)	322 (68.2)	
	Missing	33 (7.0)	15 (3.2)	
Beans intake				<0.01
	Never (in the past year)	241 (51.1)	185 (39.2)	
	Low (≤1 portion/week)	154 (32.6)	186 (39.4)	
	High (>1 portion/week)	77 (16.3)	101 (21.4)	

[a] Cases and controls are matched by age (±5 years)

[+]t-test

BMI, Body Mass Index; WHR, Waist-Hip Ratio; HS, High School; WHO, World Health Organization

Table 2. Age-adjusted and multivariable models of total beans intakes per week and risk of breast cancer in the Nigerian Integrative Epidemiology of Breast Cancer Study (NIBBLE), the year 2014-2016

	Age-adjusted model [a]		Multivariable model [a] [b]	
	OR (95% CI)	P-value	[b] OR (95% CI)	P-value
Beans intake		<0.01[c]		<0.01[c]
Never (in the past year)	1		1	1
Low (≤1 portion/week)	0.63 (0.47-0.84)	<0.01	0.60 (0.43-0.84)	<0.01
High (>1 portion/week)	0.59 (0.41-0.84)	<0.01	0.57 (0.38-0.85)	<0.01

[a] Cases and controls were matched by age (±5 years) analyses were done using a conditional logistic regression model.

[b] The models were adjusted for age, WHR, BMI, occupation, menopause status, alcohol use, and physical activity.

[c] P-value for trend

OR, Odds Ratio; CI, Confidence Interval;

Table 3 Age-adjusted and multivariable models of total beans intakes per week and risk of breast cancer subtypes in the Nigerian Integrative Epidemiology of Breast Cancer Study (NIBBLE), the year 2014-2016.

	HR (ER+/PR+)/her2-		TNBC	
	Age-Adjusted model [a] OR (95% CI)	Multivariable Model [a b] OR (95% CI)	Age-Adjusted model [a] OR (95% CI)	Multivariable Model [a b] OR (95% CI)
Beans intake				
Never (in the past year)	1.00	1.00	1.00	1.00
Low (≤1 portion/week)	0.73 (0.45-1.18)	0.79 (0.47-1.33)	0.67 (0.44-1.02)	0.70 (0.43-1.12)
High (>1 portion/week)	0.45 (0.24-0.86)	0.45 (0.23-0.90)	0.41 (0.23-0.73)	0.47 (0.25-0.88)
P-value for trend	0.01	0.02	<0.01	0.01

[a] Unconditional logistic regression models with complete study sample

[b] The models were adjusted for age, WHR, BMI, occupation, menopause status, alcohol use, and physical activity.

HP, Hormone Receptor Positive; ER, estrogen; PR, progesterone; her2, human epidermal growth factor-2; TNBC, Triple-Negative Breast Cancer; OR, Odds Ratio; CI, Confidence Interval

Figures

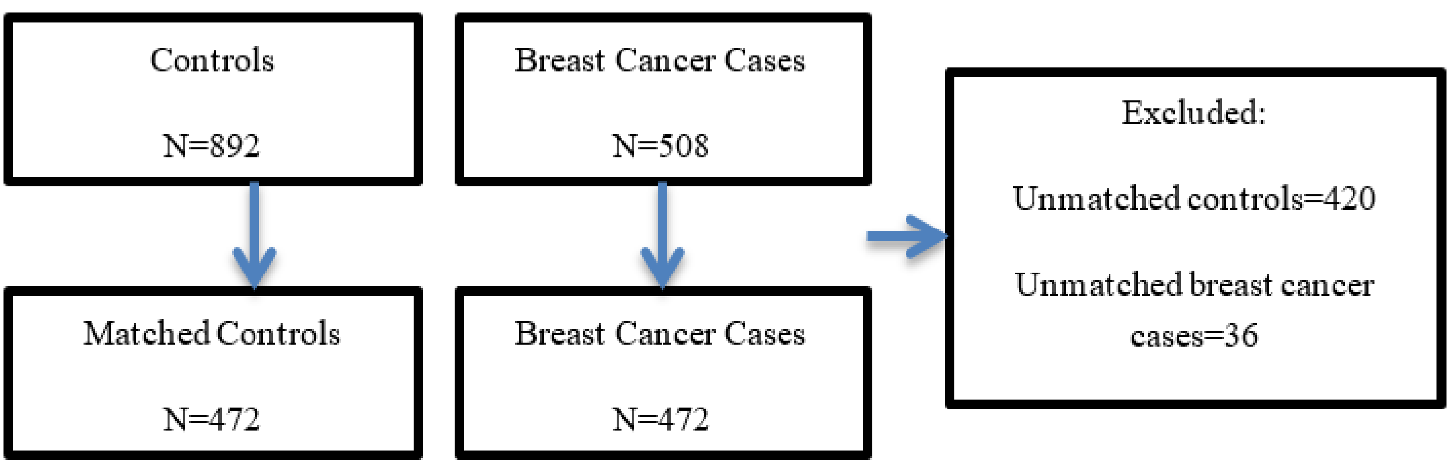

Figure 1

<p>Flowchart describing the final matched case control sample for the overall breast cancer analysis </p><p> </p><p> </p>

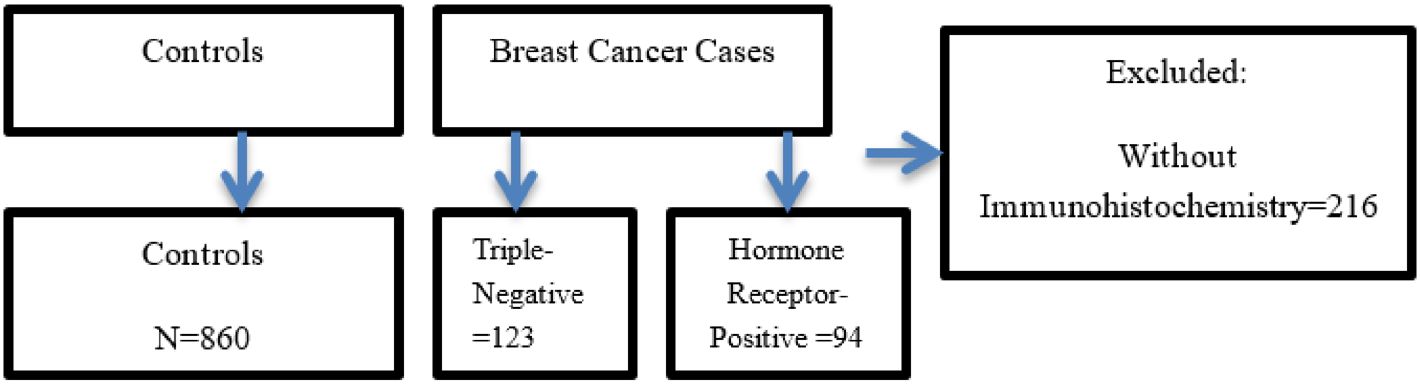

Figure 2

<p>Flowchart describing the final subsamples for the breast cancer subtype analyses </p>