Original Article

Pattern of breast cancer risk factors among pre and post-menopausal women at a Primary Care Clinic in Nigeria

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ABSTRACT

Context: The incidence of breast cancer is increasing worldwide. In black women, breast cancer is associated with aggressive features and poor survival.

Objective: Identification of risk factors such as early age of menarche, obesity and family history of breast cancer may permit preventive strategies.

Study Design: A cross-sectional comparative study design was used and questionnaires were administered to 400 adult women at a tertiary health centre in Nigeria. The data was analyzed with the Statistical Package for the Social Sciences version 17; the level of significance set at alpha = 0.05.

Results: There was significant association between pre-menopausal and post-menopausal women with positive family history of breast cancer with $P = 0.010$. Majority of the respondents with a positive family history of breast cancer were menopausal ($P = 0.010$). There was a statistically significant association between menopausal status and ever consuming alcohol-based herbal concoctions ($P = 0.010$) and in those whose partners smoked cigarettes ($P = 0.001$). Majority of respondents were not currently on any form of contraceptives. Parity, breastfeeding and use of hormonal contraceptives were all statistically significant ($P < 0.001$, $P < 0.001$ and $P = 0.004$, respectively). Almost all the women in our study, 97%, had never had a mammogram. There was a significant association between pre-menopausal and post-menopausal women with positive family history of breast cancer ($P = 0.010$).

Conclusion: With increasing incidence of breast cancer worldwide and late presentation in developing countries with high morbidity and mortality, effective screening for risk factors will go a long way in reducing the incidence of breast cancer.

Key words: Breast cancer; Nigeria; risk factors; women.

Introduction

Breast cancer is a non-communicable disease of huge public health importance and is the most common cancer in women in Nigeria and worldwide.[1,2] Globally, the incidence of breast cancer is increasing and even more so in societies that previously had a low incidence of the disease.[3] The highest number of deaths from breast cancer are from the United Kingdom, where approximately 42000 new cases are diagnosed annually, with a mortality rate of 15000 per

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annum.[4] In the United States of America, the incidence rate of breast cancer is 200,000 per annum, with a mortality of about 40000 per year.[4]

The prevalence of breast cancer in Nigeria was 116 per 100,000 and 27840 new cases were expected to develop in 1999.[2] In a more recent retrospective study by Agbo *et al*., reported in 2014 from the northern part of Nigeria, the prevalence rate of breast cancer was found to be 10.4 cases per 100,000.[5] The incidence rate of breast cancer in Nigeria has steadily increased from 15.3 per 100,000 in 1976 to 33.6 per 100,000 in 1992.[6] Jedy-Agba *et al*., in 2012, analyzed data from the Ibadan Population Based Cancer Registry (IBCR) and the Abuja Population Based Cancer Registry (ABCR) and reported an age standardized incidence rate (ASR) of breast cancer of 52.0 per 100,000 women in Ibadan, Nigeria and 64.6 per 100,000 women in Abuja, Nigeria.[7] Akarolo-Anthony *et al*., in 2010, reported that in Nigeria, there was a rise in the number of women at risk of breast cancer from approximately 24.5 million in 1990 to approximately 40 million in 2010 and will likely reach over 50 million by 2020.[8] Reasons adduced for the high incidence of cancer now in Nigeria could be increased reporting and improved diagnosis.[4] There is also a trend toward westernization in developing countries, with the change in demographic profile and lifestyle, and the changing socioeconomic profile of the country.

In assessing the risk of developing breast cancer, a multidisciplinary team approach should be employed. Medical and surgical history, history of exposure to possible carcinogens and a detailed family history of cancer is obtained while physical examination and radiologic imaging studies are also done.[9] The factors to be elaborated upon for pre-menopausal women include increasing age, the density of the breast, history of breast or ovarian cancer in any family member and previous procedures on the breast.[10] For post-menopausal women, areas of emphasis are age, breast density, race, ethnicity (especially Ashkenazi Jewish), family history of breast cancer, a breast procedure in the past, body mass index, menopause occurring naturally, hormone therapy, and a previous false-positive mammogram.[10]

Notable risk factors for breast cancer include age at menarche, first child birth, and menopause; parity; number of breast biopsies done in the past; histological findings of atypical hyperplasia or lobular carcinoma *in situ* in breast tissue; use of oral contraceptive pills and nulliparity.[9] There are also environmental influences important in the aetiology of breast cancer, as well as genetic factors.[3,11] Approximately 5–10% of breast cancers are familial and mutations in breast cancer susceptibility genes – BRCA 1 and BRCA 2 – are responsible for 80% of the familial cases while sporadic cases are rare.[1]

Other risk factors include previous thoracic radiation therapy and the use of hormones with history of present or past use of oestrogen and progesterone. Body mass index, breast density at mammography, alcohol consumption, diet and physical activity are also implicated.[9] In a case-control study of the epidemiological risk factors for breast cancer done in the Oncology clinic of University College Hospital (UCH), Ibadan, the mean patient age of 43 years was obtained and it was also found that the incidence of breast cancer in Nigeria was increasing.[3]

The incidence of breast cancer increases with age and doubles every 10 years till menopause.[12] In the Western world, the age specific incidence of breast cancer appears to increase with age. Approximately 50% of breast cancers occur in the age group 50–65 years and 30% occur over the age of 70 years.[4] Breast cancers in Nigerian women is, however, noted to present a decade earlier than in developed countries.[4,13] The age at development of breast cancer is reducing with worse prognosis in black women, and in these group of women, breast cancer has aggressive features and poor survival.[6] The global age-standardized mortality rate for female breast cancer is shown in Figure 1, with some of the highest mortality rates found in Africa. Determining a woman's breast cancer risk will allow early detection and prompt treatment. Low technology, low-cost management options and examining the value of genetic risk factors of breast cancer in determining a population at risk are required.[3]

The incidence of breast cancer is increasing rapidly in Nigeria, therefore, there is a need for determining the pattern of breast cancer risk factors among pre- and post-menopausal women and encouraging appropriate follow-up of clients with high risk of breast cancer.

Materials and Methods

This was a cross-sectional comparative study and was conducted among 400 adult female patients above the age

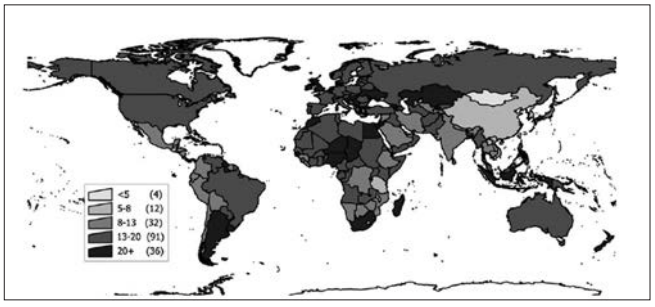

Figure 1: Estimated age-standardised mortality rates of female breast cancer by country. [GLOBOCAN 2008]. The numbers in brackets within the legend show how many countries are included in each mortality range

of 18 years attending the General Outpatients (GOP) clinic of the Department of Family Medicine, UCH, Ibadan, Oyo State, Nigeria for the first time over a period of 7 months. Ibadan is the largest city in west Africa, and has a population of 2.9 million people.[14] Women who were too ill to go through the rigours of the study and pregnant women were excluded.

The sample size was estimated by using the formula for simple proportions with an expected average prevalence of combined breast cancer risk of 33%.[15] The following assumptions were also made: Type 1 error was 0.05, the area under the normal curve was equivalent to 1.96 at 95% confidence interval and the precision was 5%.The consecutive sampling method was adopted in recruiting the participants. Validated questionnaires with sections on assessment of sociodemographic characteristics, gynaecological history, breast cancer screening, family history and lifestyle factors were administered by the interviewer after informed consent was obtained from the participants. The University of Chicago Cancer risk clinic new patient risk assessment questionnaire was adopted. Data were collected over a period of 7 months. Body mass index was used to define and classify obesity.[16]

Approval was obtained from the Head of Department of Family Medicine, UCH, Ibadan and the ethics committee of the joint University of Ibadan (UI)/UCH institutional review board. The UI/UCH EC registration number obtained was NHREC/05/01/2008a. All patients recruited were given health education and referred appropriately to general surgery and/or radiotherapy specialists within the health facility for further evaluation and management, if indicated.

The data collected from the participants were coded serially, cleaned and entered into a computer using the software programme; Statistical Package for Social Sciences for data analysis (SPSS® version 17) was used for data analysis. Discrete variables were summarized using proportions and Chi-square test were used to explore statistical relationships.

Results

The frequency distribution of sociodemographic characteristics of the 400 respondents is shown in Table 1. Over two-thirds of the women were pre-menopausal with the highest proportion of women being between 25 and 34 years old. The greatest proportion of women who were post-menopausal was those above 55 years of age. All the single respondents were pre-menopausal. Majority of the married respondents were pre-menopausal (69.5%), whereas many of the widowed respondents were post-menopausal (79.5%).

Table 1: Frequency distribution of socio-demographic characteristics of the respondents

Characteristics	Pre-menopausal *n* (%)	Post-menopausal *n* (%)	Total *N* (%)
Age group (years)			
≤24	38 (97.4)	1 (2.6)	39 (100.0)
25-34	101 (100.0)	0 (0.0)	101 (100.0)
35-44	94 (87.9)	13 (12.1)	107 (100.0)
45-54	43 (43.0)	57 (57.0)	100 (100.0)
55 above	4 (7.5)	49 (92.5)	53 (100.0)
Marital status			
Single	75 (100.0)	0 (0.0)	75 (100.0)
Married	194 (69.5)	85 (30.5)	279 (100.0)
Separated/Divorced	3 (42.9)	4 (57.1)	7 (100.0)
Widowed	8 (20.5)	31 (79.5)	39 (100.0)
Level of education			
Non-formal education	9 (23.7)	29 (76.3)	38 (100.0)
Primary	21 (39.6)	32 (60.4)	51 (100.0)
Secondary	82 (79.6)	21 (20.4)	103 (100.0)
Tertiary	168 (81.6)	38 (18.4)	206 (100.0)
Occupation			
Trader	121 (61.7)	75 (38.3)	196 (100.0)
Civil servant	76 (74.5)	26 (25.5)	102 (100.0)
Student	47 (94.0)	3 (6.0)	50 (100.0)
Others	36 (69.2)	16 (30.8)	52 (100.0)
Religion			
Christianity	200 (71.4)	80 (28.6)	280 (100.0)
Islam	80 (66.7)	40 (33.3)	120 (100.0)
Ethnic group			
Yoruba	246 (70.3)	104 (29.7)	350 (100.0)
Igbo	22 (66.7)	11 (33.3)	33 (100.0)
Others	12 (70.6)	5 (29.4)	17 (100.0)

*Significant at $P<0.05$

Among the pre-menopausal group of respondents, the highest level of education of the respondents was tertiary education (81.6%) followed by secondary education (79.6%). However, among the post-menopausal group of respondents, non-formal education (76.3%) was the most common followed by primary education (60.4%). Most of the pre-menopausal respondents were students (94%), whereas majority of the post-menopausal respondents were traders (38.3%). Many (71.4%) of the premenopausal women were Christians whereas the highest proportion among the post-menopausal women were Muslims (33.3%). The Igbo tribe was the most predominant among the post-menopausal respondents (33.3%), whereas it was the least among the pre-menopausal group of respondents (66.7%).

The distribution of lifestyle and risks factors of the respondents is depicted in Table 2. Out of the 400 respondents in this study, 280 (70%) were pre-menopausal whereas 120 (30%) were post-menopausal. Only a small proportion 15 (3.8%) of the respondents had a positive family history of breast cancer with the majority 9 (60.0%) being post-menopausal.

Table 2: Lifestyle and risk factors of the respondents

Characteristics	Pre-menopausal *n* (%)	Post-menopausal *n* (%)	*P*
Has any family member ever been diagnosed with cancer?			
Yes	6 (40.0)	9 (60.0)	0.010*
No	274 (71.2)	111 (28.8)	
Ever had any surgical procedure (hysterectomy, oophorectomy)?			
Yes	2 (66.7)	1 (33.3)	0.658
No	278 (70.0)	119 (53.4)	
Ever consumed any alcohol once a week for 6months?			
Yes	11 (68.8)	5 (31.2)	0.911
No	269 (46.4)	115 (29.9)	
Currently consuming alcohol at least once a week?			
Yes	9 (69.2)	4 (30.8)	0.951
No	271 (70.0)	116 (30.0)	
Do you take herbal concoction with alcohol base?			
Yes	10 (45.5)	12 (54.5)	0.010*
No	270 (71.4)	108 (28.6)	
Ever smoked at least 1 cigarette daily for 3 months?			
Yes	0 (0.0)	2 (100.0)	0.089
No	280 (70.4)	118 (29.6)	
Do you chew tobacco?			
Yes	1 (100.0)	0 (0.0)	0.700
No	279 (69.9)	120 (30.1)	
Does your partner smoke?			
Yes	4 (28.6)	10 (71.4)	0.001*
No	276 (71.5)	110 (28.5)	
Body mass index			
Underweight	26 (83.9)	5 (16.1)	0.118
Normal weight	118 (74.7)	40 (25.3)	
Overweight	72 (64.3)	40 (35.7)	
Obesity class 1	39 (65.0)	21 (35.0)	
Obesity class 2	15 (57.7)	11 (42.3)	
Obesity class 3	5 (71.4)	2 (28.6)	

*Significant at $P<0.05$

There was significant association between pre-menopausal and post-menopausal women with positive family history of breast cancer with $P = 0.010$.

Only 2 (66.7%) of the pre-menopausal women and 1 (33.3%) post-menopausal women had ever undergone surgical procedures such as hysterectomy and oophorectomy. There was no significant association between pre and post-menopausal women and ever having any surgical procedures ($P = 0.899$). Majority of the respondents, 9 (69.2%) and 11 (68.8%), respectively, were currently consuming alcohol at least once a week and had ever consumed alcohol once a week for six months or longer were pre-menopausal.

Twenty-two (5.5%) of the respondents had taken alcohol-based herbal concoction, out of which 12 (54.5%) of the respondents were post-menopausal. There was a statistically significant association between ever consuming alcohol-based herbal concoctions ($P = 0.010$). Only one (0.3%) of the respondents had ever chewed tobacco and was pre-menopausal. Fourteen (3.5%) of the respondents had their spouses smoking cigarettes. There was a statistically significant association between pre-menopausal and post-menopausal women whose partners smoked cigarettes ($P = 0.001$).

The highest proportion 158 (40.1%) of the respondents were of normal weight. This was followed by overweight 112 (28.4%) and obese respondents were 93 (23.6%) with class 1 being predominant 60 (64.5%). There was no statistically significant association between pre-menopausal and post-menopausal women who were obese using the body mass index category ($P = 0.118$).

The gynaecological history of the respondents is shown in Table 3. The mean age at menarche was 14.76 and 15.2 years for the pre-menopausal and post-menopausal group of women, respectively (standard deviation: ±2.3 years). Seventy-seven (19.3%) women were nulliparous and mainly pre-menopausal (96.1%). Approximately one-third of the women in the study were parous [323 (80.8%)]. The majority 161 (55.1%) were in the para 2–4 category. The pre-menopausal set constituted approximately 70% of women in the 2–4 parous categories. The post-menopausal women contributed only 30%.

Most 285 (75.8%) out of 376 women in our study breastfed their children. Those in the pre-menopausal category were predominant among those who breastfed or did not breastfeed 175 (61.4%) and 82 (90.1%), respectively (OR = 0.18: CI = 0.08–0.36). Majority of women 184 (66.9%) breastfed for more than 1 year with the pre-menopausal fraction being the most predominant 116 (68.6%). Most women 289 (72.3%) had never used any method of hormonal family planning. One hundred and eleven women (27.8%) out of 400 women evaluated had ever used a hormonal family planning method. Sixty percent (66) were pre-menopausal whereas 41% (45) were post-menopausal. The pre-menopausal women 214 (74.0%)

Table 3: Gynaecological history of the respondents

Characteristics	Menopausal status (Pre) *n* (%)	Menopausal status (Post) *n* (%)	*P*
Age at First Menstrual Period	14.76±2.3 years	15.5±2.3 years	
Parity			
None			
One	37 (86.0)	6 (14.0)	0.000*
2-4	112 (69.6)	49 (30.4)	
>5	29 (33.0)	59 (67.0)	
Did you breast feed			
Yes	175 (61.4)	110 (38.6)	0.000*
No	82 (90.1)	9 (9.9)	
Duration of breast feeding			
0-6 months	8 (53.3)	7 (46.7)	0.679
7-12months	45 (59.2)	31 (40.8)	
More than 1 year	116 (63.0)	68 (37.0)	
Ever used any method of Hormonal family planning			
Yes	66 (59.5)	45 (40.5)	0.004*
No	214 (74.0)	75 (26.0)	
Type of hormonal family planning used			
Oral contraceptives	10 (76.9)	3 (23.1)	0.030
Injectable hormonals	21 (77.8)	6 (22.2)	
Hormonal implants	4 (50.0)	4 (50.0)	
Intra Uterine device	24 (47.1)	27 (52.9)	
Currently using any family planning			
Yes	21 (70.0)	9 (30.0)	0.997
No	243 (70.0)	104 (30.0)	
Ever Had Mammogram			
Yes	7 (58.3)	5 (41.7)	0.371
No	273 (70.4)	115 (29.6)	
Do you examine your breast for lumps			
Yes	164 (70.4)	69 (29.6)	0.842
No	116 (69.5)	51 (30.5)	
Have you ever detected a lump			
Yes	34 (73.9)	12 (26.1)	0.538
No	246 (69.5)	108 (30.5)	

*Significant at $P<0.05$

predominated in this set. Intrauterine contraceptive device (IUCD), injectables and oral contraceptives were the three most frequently used forms of hormonal contraceptive by pre-menopausal women, i.e. 24 (47.1%), 21 (77.8%), 10 (76.9%), respectively; whereas, IUCD was the single most common form of hormonal contraceptive used by post-menopausal women. Majority of women in our study were not on any form of contraceptive. Parity, breastfeeding and use of hormonal contraceptives were statistically significant ($P < 0.001$, $P < 0.001$ and $P = 0.004$, respectively), however, the duration of breastfeeding was not statistically significant.

Most women in our study 97% never had a mammogram and two-thirds 273 were pre-menopausal (70.4%). Two-hundred and thirty-three women (58.3%) had examined their own breasts for lumps whereas 167 (41.8%) did not examine their breasts. In both groups, the pre-menopausal fraction constituted approximately two-third of the women (70.4% and 69.5%, respectively).

The proportion of women who examined their breasts for lumps and those who did not examine their breast were 58.3% and 41.8%, respectively. The proportion of women in both groups were alike 70.4% and 69.5% in the pre-menopausal category and 29.6% and 30.5% in the post-menopausal category, respectively.

The majority of women in our study 88.5% (354) had never detected a breast lump. Most of the women in this group were also pre-menopausal, 69.5% (246), with only 30.5% (106) in the post-menopausal group. Approximately 12% (46) of the 400 women evaluated had detected a lump. In this category, the pre-menopausal women also predominated 73.9% (34).

Mammography, breast examination and lump detection were not statistically significant ($P = 0.371$, $P = 0.842$ and $P = 0.538$, respectively).

Discussion

The highest proportion of women (26.8%) in this study were those between age 25–34 years for pre-menopausal respondents and greater than 55 years for the post-menopausal respondents. This is comparable to a study in Nigeria in which the women were found to be in a similar age group bracket.[17] In another Nigerian study, the highest prevalence of breast cancer was in those whose age group was 26 to 45 years,[18] whereas majority of cases in another study were in the age group 40 to 49 years.[19]

Most of the married women in the study were pre-menopausal, whereas many of the widowed women were post-menopausal. This was comparable to a study in southwestern Nigeria.[2] The highest level of education of the pre-menopausal respondents in this study was tertiary education, whereas in the post-menopausal women it was non-formal education. This was in line with the study by Meshram *et al*. in 2009.[19]

Studies have linked the risk of developing breast cancer with positive family history in first degree relatives (FDR).[20] This finding was in agreement with our study, which revealed

family history as a strong risk factor to developing breast cancer ($P = 0.01$). Cancer in FDR was considered more important in post-menopausal women.[21]

Ovarian cancer risk is lowered more than 90% in women with BRCA1 or BRCA2 mutations who decided to have risk-reducing salpingo-oophorectomy. In this same population, prophylactic removal of the ovaries was found to be associated with approximately 50% reduction in the risk of breast cancer.[22] Our study, however, did not show any relationship between breast cancer and salpingo-oophorectomy or hysterectomy.

The risk of breast cancer is said to increase by approximately 10% for each 10 g of daily alcohol consumption.[23] Prior studies of BRCA1/BRCA2 mutation carriers, however, did not find any increased risk with alcohol intake.[24,25] Our study found no significant interaction between alcohol, duration of consumption and the period of onset of breast cancer in either pre-menopausal or post-menopausal women. This was also buttressed by the Tecumseh Community Health Study (TCHS).[26] There was, however, a strong association between consumption of alcohol-based native medication and risk of developing breast cancer noted in our study, with ($P = 0.01$).

Weight gain and being overweight are well-known risk factors for breast cancer. In general, overweight women are most commonly observed to be at a greater risk of post-menopausal breast cancer and at lower risk of pre-menopausal breast cancer. Sedentary lifestyle may also be a risk factor.[27] In our study, there was no statistically significant association between obesity using body mass index and being pre and post-menopausal. One study[28] found a reduced risk of breast cancer among BRCA1/BRCA2 mutation carriers who smoked, however, an expanded follow-up study failed to find an association.[29] Our study however revealed strong association between women whose spouses smoked cigarettes ($P = 0.001$).

In the woman's contraceptive and Reproductive Experiences Study, women who reported having at least one full-term pregnancy before the age of 25 years were at 36% reduced risk of breast cancer compared to nulligravida. Parous women in the study with a late age at first birth had an increased risk of both ERPR-positive and ERPR-negative tumors with each additional birth although neither result was statistically significant.[30] Low parity and late age at first birth were confirmed as significant and independent determinants of breast-cancer risk.[31] Nulliparity was also associated with a 30% increase in risk compared with parous women, and for every two births, the risk was reduced by approximately 16%.[31]

A woman's risk of developing breast cancer has been shown in various studies to be related to her exposure to hormones produced by her ovaries. Reproductive factors that increase the duration and/or levels of exposure to ovarian hormones, which stimulate cell growth, have been associated with an increase in breast cancer risk. These factors include early onset of menses, late onset of menopause, later age at first pregnancy and nulliparity. Pregnancy and breastfeeding are considered as protective against breast cancer as both reduce a woman's lifetime number of menstrual cycles, and therefore her cumulative exposure to endogenous hormones.[32] In addition, pregnancy and breastfeeding have direct effects on breast cells, causing them to differentiate, or mature, so that they can produce milk. Some researchers hypothesize that these differentiated cells are more resistant to becoming transformed into cancer cells than cells that have not undergone differentiation.[33,34] Breastfeeding for an extended period (at least 1 year) is associated with a decreased risk of both hormone receptor-positive and hormone receptor-negative breast cancer.[35,36] International Agency for Research on Cancer (IARC) has classified the current or recent use of combined oestrogen-progestogen oral contraceptives (OCs) as a cause of breast cancer.[37] OCs contain synthetic sex hormones, which may explain the link between OC use and breast cancer risk. An estimated 1% of female breast cancers in the UK are linked to OCs because breast cancer risk is generally low in the OC-using population (typically younger women).[38] A meta-analysis showed that current users of OCs have approximately 24% higher breast cancer risk compared to never users and that breast cancers in OC users tend to be less advanced compared with those in OC never-users.[39] The relative risk of breast cancer declines after OC cessation such that 10 years after cessation no excess risk remains.[39,40] Breast cancer risk does not appear to increase with longer duration of OC use. Young age at first OC use is associated with a larger increase in breast cancer risk.[39] The risks associated with OC use appears to be similar across OC formulations.[39,40]

Some types of benign breast disease are linked with increased breast cancer risk. Among women with benign breast disease, cancer is more common in the breast with the benign disease than in the opposite breast.[41] Breast cancer risk is generally not increased in women in non-proliferative disease (NP). Proliferative disease without atypia (PDWA) has a breast cancer risk of 44% higher in women compared with women with NP.[42] However, breast cancer risk does appear to be increased in women with NP or PDWA and a FDR with breast cancer.[42] Atypical hyperplasia (AH) has close to a threefold higher risk for breast cancer in women compared with women with NP. Lobular AH is associated with higher breast cancer

risk than is ductal AH. Having a FDR with breast cancer does not appear to further increase breast cancer risk in women with AH.[42]

Breast cancer is a significant problem among women worldwide with associated high morbidity and mortality. The incidence of breast cancer is increasing worldwide with late presentation most especially in developing countries. Effective screening will go a long way in reducing the incidence of breast cancer. Effective screening through detailed family and gynaecological history with regular breast examination and radiological screening (sonomammogram and conventional mammogram) will allow for early diagnosis and prompt treatment of breast cancer, hence reducing morbidity and mortality associated with breast cancer. Mammograms should be encouraged as it has been reported in a Nigerian study that the level of awareness of mammograms is very low in Nigeria.[43] There was strong association between breast cancer and family history of breast and ovarian cancer among women attending the primary care clinic. This underscores the need for provision of screening services at the clinic and effective health education to promote preventive practices and inculcate a screening culture among women.

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Conflicts of interest

There are no conflicts of interest.

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