

Original Research Articles**AGE SPECIFIC INCIDENCE OF BREAST CANCER IN CALABAR, NIGERIA****ABSTRACT**

Aim: To determine the incidence of breast cancer in our uncharted population with a view to determining the disease burden so as to aid planning and intervention.

Study Design: A trend analysis of breast cancers in Calabar between 1st January 2004 to 31st December 2013.

Place and duration of Study: Calabar Cancer Registry, May to June 2015.

Methodology: Data obtained from record of registered cases of breast cancer seen within 2004 to 2013 from Calabar registry area, was entered and analyzed using SPSS version 21.0. The information sought for includes sex of patients, age, place domiciled in the last one year, rural or urban dwelling as well as topography and morphology of the breast cancers. The population of females domiciled in Calabar was determined using the 2006 national population census data and 3.0 % population growth as specified by the national population commission. Male patients with breast cancers as well as all cancers in males and females other than breast Cancers, were excluded.

Results: Three hundred and sixty nine cases of breast cancers, comprising 11 males and 358 females were seen during this period. Male breast cancer cases were excluded from further analysis. The mean (SD) age of female cases was 44.9 (11.9) years, ranging from 23 to 85 years. Approximately half of the cases (176 or 49.2%) were seen in the 34 to 50 years age group with commonest age group at diagnosis being 40 - 44 years age group. There was a fairly steady increase in annual frequency of cases seen within study period, with 2011 yielding the highest proportion of cases (54 or 14.5%), and about two-thirds of cases (227 or 63.4%) were seen in the latter half of the 10-year study period. Adjusted incidence rate was highest in 2010 (61.3 per 100,000), and high incidence rates was found among subjects in 65-69 year age group in 2009 (179 per 100,000), and 55-59 year age group in 2010 (192 per 100,000). The age specific incidence rate of breast cancer in Calabar is 37.4 per 100,000.

CONCLUSION: This study has shown that breast cancer is common in Calabar, and it occurs at a relatively early age.

Key words: Calabar, Breast Cancer, Incidence, Females

1. INTRODUCTION:

Breast cancer incidence is rising in Nigeria(1-3), although no national population based cancer registry is available. Data from Ibadan and Abuja registries which are population - based cancer registries operating in the cities of Ibadan and Abuja, as well as reviews from many institution based registries around the country, seem to suggest this (4-6). To date, the true incidence of breast cancer in the country is not known. Estimates from Ibadan and Abuja cancer registries with limited coverage, estimated at 2.5% of the National population, show that the age standardized incidence rates (ASR) of breast cancer in females stood at 52.0 and 64.4 per 100,000 respectively (1). This rate appears to be intermediate between the low incidence areas of the world such as Mongolia, 8.0 per 100,000 (7), Inuit population (8), Shenzhen-China (21.1 per 100,000) (9) and the high incidence areas for example, 94 per 100,000 in Aachen Germany (10), 97 per 100,000 among white American women (11) and 109.9 per 100,000 women in Manitoba Canada (12).

The Calabar cancer registry has been in operation for slightly more than three decades. It is located in Calabar the capital city of Cross River State in the Niger Delta. It covers the City of Calabar and Akpabuyo fully; this comprises three local government councils with population just above 700,000. Data from the rest of the state comprising fifteen local government councils are aggressively being refined. Previously issues of funding, lack of institutional support, lack of acceptable national population data militated against it being truly population based in the first two decades (1978-2008). With the last population census conducted in 2006, the registry quickly took advantage to become truly population based, covering the three Local government areas fully and striving to improve the remaining fifteen Local Government areas. Temporal trends from the registry, although unpublished suggest that breast cancer incidence progressively increased in the first two decades to become the dominant cancer in females over cervical cancer which used to be the commonest. The area adequately covered by the registry

includes both urban and rural settlements, however the boundary between both is not so clear cut. Consequently the incidence of breast cancer in both population groups shall be calculated as a homogeneous group. Many studies albeit, show variations in incidence rates among residents within a geopolitical areas , for example, the urbanized areas of Philippines have incidence rates three times the rates in the rural municipalities(3) .In the same vain Shenzhen China, has 5 breast cancer zones with age standardized incidence rate ranging from 20.0 per 100,000 to 54.1 per 100,00 (9).A study in Wales also highlighted this regional variations (13). A gridded incidence was also reported for Connecticut (14). Among some of the factors implicated in accounting for this variation in incidence in populations living in the same area, are life style factors (15, 16), race(11, 17), recent immigration(18, 19) , age (3, 20-22) and diet (8).

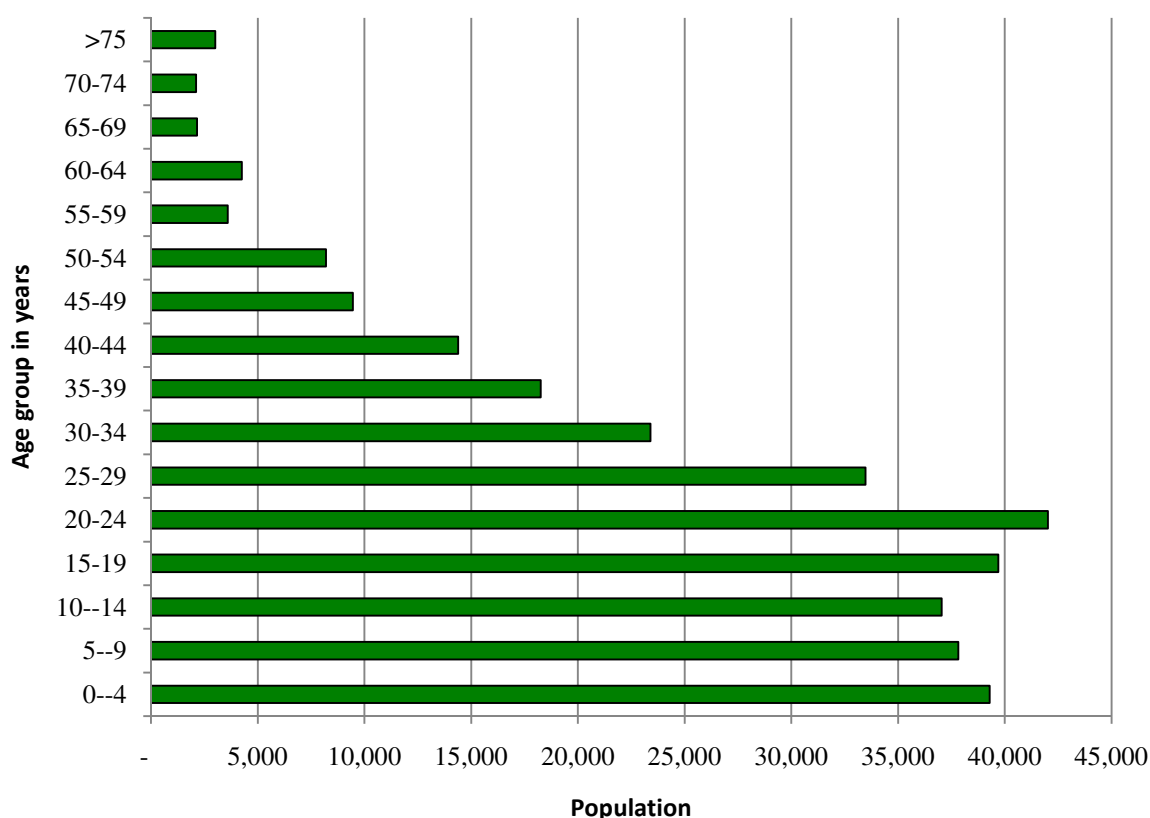
To date most breast cancer patients in Nigeria present late to hospitals(23),due to preference for alternative practitioners, quacks(24) and poor breast cancer awareness (25-27) .Other socio-demographic factors such as; being single, educational level at primary level, ignorance of illness type, belief in herbal and spiritual intervention, were found by a Lagos group to be responsible for late presentation(28).A study amongst rural dwellers in South- West Nigeria found that respondents attributed breast cancer to be caused by putting money in brassiere and attacks from enemies(29).None of this women identified early presentation as an advantage in breast cancer treatment(29).Whilst the lay communities could be accused of ignorance of breast cancer, several studies have shown unpardonable ignorance of breast cancer among medical personnel of all cadre ranging from trainees, nurses and doctors in Nigeria, as is in many third world countries(25-27, 30, 31).There is no age standardized breast cancer incidence reported for Calabar. The data analyzed involves Calabar and Akpabuyo, and involves cases resident in Calabar and Akpabuyo one year prior to the cancer incidence. The registry is fed primarily from Department of Pathology, Surgical clinics, Department of Haematology, all in the University of Calabar Teaching hospital. Additional information is obtained from General hospital Calabar, St. Joseph's Hospital Ikot Ene Akpabuyo and seven private hospitals which are visited by the Registry's team every two weeks.

2. MATERIALS AND METHODS:

79 Database of breast cancer cases between 1st January 2004 and 31st December 2013 , stored as Can
80 Reg. 4 format, in the Calabar Cancer registry was accessed. Data obtained from record of registered
81 cases of breast cancer seen within 2004 to 2013 from Calabar registry area, was entered and analyzed
82 using SPSS version 21.0. The patients age, sex, date of incidence, area domiciled in the last one year,
83 whether rural or urban and histological diagnosis were the important research questions.

84 2.1. POPULATION:

85 Age distribution of the population of female residents in the study area was obtained from database of
86 population census conducted in 2006, with intercensal estimations made in collaboration with the National
87 Population Commission, Calabar, Nigeria, using constant annual growth rate of 3.0% (Fig. 1). World
88 standard population was used to calculate the age-standardized or adjusted rates.

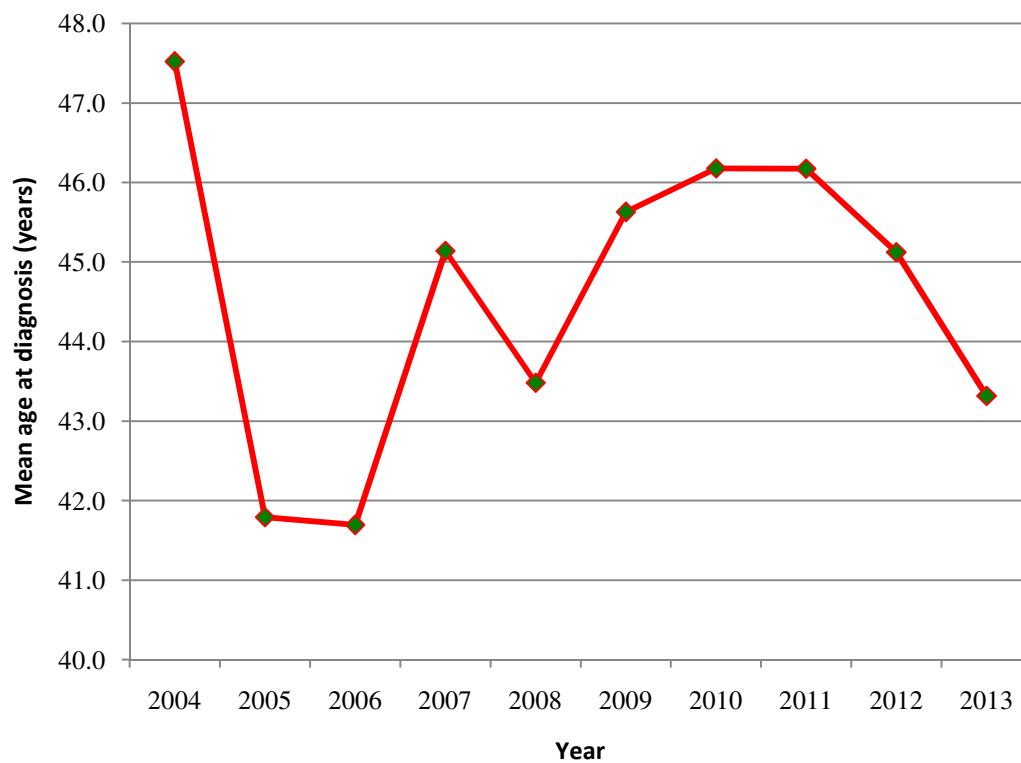


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90 **Figure 1:** Female population of Calabar Registry Area (Calabar Municipality, Calabar-South and
91 Akpabuyo), by age group, census of 2006.

92 3. RESULTS:

93 Data obtained from record of registered cases of breast cancer seen within 2004 to 2013 from Calabar
94 registry area, was entered and analyzed using SPSS version 21.0. Within the study period, three hundred
95 and sixty nine cases of breast cancer were seen, comprising of eleven (11) cases among males (3.0%),
96 and three hundred and fifty eight (358) cases among females (97%). Only female breast cancer cases
97 were further analyzed.

98 **3.1. FEMALE BREAST CANCER:** The mean (SD) age of female cases was 44.9 (11.9) years, ranging
99 from 23 to 85 years. There appears to be a fairly steady decrease in the mean age at diagnosis,
100 especially in the later years (Figure 2), but there was no significant difference in mean age comparing the
101 years ($F=0.80$, $p=0.62$). Approximately half of cases seen (176 or 49.2%) were between 34 and 50 years
102 old at time of diagnosis, with the commonest age group being 40-44 years (Table 1). There was a fairly
103 steady increase in annual frequency of cases seen within study period, with 2011 yielding the highest
104 proportion of cases (54 or 14.5%), and about two-thirds of cases (227 or 63.4%) seen in the latter half of
105 the 10-year study period (Table 2).



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107 **Figure 2:** Mean age at diagnosis of female breast cancer in Calabar, by year (2004-2013)

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Table 1: Age-group distribution of breast cancer subjects (N=358)

Age group (years)	Frequency	Percentage
20-24	2	0.6
25-29	20	5.6
30-34	49	13.7
35-39	58	16.2
40-44	63	17.6
45-49	55	15.4
50-54	32	8.9
55-59	30	8.4
60-64	21	5.9
65-69	15	4.2
70-74	7	2.0
≥ 75	6	1.7
Total	358	100.0

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Table 2: Annual distribution of female breast cancer cases seen in Calabar (N=358)

Year	Frequency	Percentage
2004	27	7.5
2005	24	6.7
2006	26	7.3
2007	29	8.1
2008	25	7.0
2009	43	12.0
2010	45	12.6
2011	52	14.5
2012	49	13.7
2013	38	10.6
Total	358	100.0

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114 Most types of breast cancers (303 or 84.6%) were not otherwise specified (NOS), with about one-tenth
 115 (34 or 9.5%) occurring at upper-outer quadrant, and the remaining (21) constituting about 5.9% of cases
 116 (Table 3).

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Table 3: Frequency distribution of type of female breast cancer in Calabar (N=358)

Site	ICD Coding	Frequency	Percentage
Breast - NOS(Mammary gland)	C 50.9	303	84.6
Upper-outer quadrant of breast	C 50.4	34	9.5
Overlapping lesion of breast	C 50.8	8	2.2
Upper -inner quadrant of breast	C 50.2	4	1.1
Lower-outer quadrant of breast	C 50.5	4	1.1
Lower-inner quadrant of breast	C 50.3	3	0.8
Central portion of breast	C 50.1	1	0.3
Nipple	C 50.0	1	0.3
Total	-	358	100

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119 Adjusted incidence rate was highest in 2010 (61.3 per 100,000), and high incidence rates were found
 120 among subjects in 65-69 year age group in 2009 (179 per 100,000), and 55-59 year age group in 2010
 121 (192 per 100,000) (Table 4). Incidence rates appear to be decreasing, following a peak incidence of 61.3
 122 per 100,000 in 2010 (Table 4, Figure 3).

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Table 4: Annual crude, adjusted and age-specific incidence rates of female breast cancer in Calabar (2004-2013)

			20-	25-	30-	35-	40-	45-	50-	55-	60-	65-	70-	
Year	Crude	Adj.	24yr	29yr	34yr	39 yr	44yr	49yr	54yr	59yr	64yr	69yr	74yr	≥75yr
2004	31.7	42.8	0.0	3.0	12.9	16.5	35.0	74.5	0.0	83.9	23.6	46.6	94.9	66.7
2005	27.1	30.0	0.0	3.0	38.6	11.0	20.9	42.4	12.2	0.0	70.7	0.0	47.3	0.0
2006	29.3	32.0	0.0	6.0	21.4	27.4	27.8	52.9	24.4	24.4	23.5	46.3	0.0	0.0
2007	32.5	37.0	0.0	0.0	21.3	43.7	20.8	52.7	0.0	116.2	0.0	46.2	0.0	33.1
2008	28.0	28.7	2.4	3.0	12.7	49.0	13.8	31.5	12.1	82.8	70.1	0.0	0.0	0.0
2009	47.9	56.4	0.0	5.9	8.5	38.0	68.9	104.8	36.3	55.1	23.3	178.6	0.0	32.9
2010	50.0	61.3	0.0	14.8	16.9	21.7	61.8	31.4	72.4	192.2	23.2	91.5	46.2	65.5
2011	57.7	60.1	0.0	11.8	25.3	32.4	41.1	114.6	60.1	27.4	115.8	136.9	46.4	32.7
2012	54.2	56.1	2.3	11.7	29.4	37.7	68.3	31.2	47.9	136.4	92.3	45.5	92.6	0.0
2013	41.9	40.1	0.0	11.7	16.7	32.2	61.3	31.1	95.6	54.4	23.0	45.4	0.0	0.0

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125 Within the 5-year period from 2004 to 2008, there was an average annual decrease in incidence rate of
 126 3.5% (95% CI: 1.1%-4.9%). However, within the 5-year period from 2009 to 2013, there was an average
 127 annual increase in incidence rate of 1.9%% (95%CI: -0.85% to 2.2%).

128 4. DISCUSSION:

129 The mean age of breast cancer patients in Calabar is 44.9(11.9) years;this is similar to several Nigerian
 130 institution based studies , Adisa reported 47years (32),Adebamowo 43years(33),Ekanem 45.7years ,
 131 42,7(12.2) years by Ikpatt , Ndoma and Collan(34)and 46 years .The age is similar to some African
 132 reports , for example, Boder et al Libya 46years,(35) .The Calabar mean age is a decade less than
 133 reports in some western countries,for example a comparative African and Caucasian study by Ikpatt et al
 134 in their series,compared the age in a Nigerian breast cancer cohort,42.7(12.2)years to a Finish Cohort a
 135 58.7(12.)years. In the same vain Jack et al in south east England reported that black African and
 136 Caribbean breast cancer patients were on the average younger than their Caucasian counterparts

(36).What appears to be the emerging difference between countries in the low risk breast cancer belts and the high risk areas is that in the low risk areas, the breast cancer increased incidence is accompanied by a drop in the average age the cancer occurs and many are in the premenopausal age group compared to post menopausal dominance in the high risk areas(15, 21, 23, 35). There appears to be a fairly steady decrease in the mean age at diagnosis of breast cancer in Calabar , especially in the later years, whether increasing urbanization and change in life style or other factors are at play, needs to be investigated.

The crude and adjusted incidence rates of breast cancer in Calabar witnessed progressive increases from 2009 to 2011.While the crude rate peaked at 57.7 per 100,000 in 2011, the adjusted rate peaked at 61.3 per 100,000 in 2010.Both rates progressively declined to 41.9 per 100,00 and 40.1 per 100,000 respectively. Even with the seeming decrease in the last two years,the rates are still higher than that recorded for both values in the first five years from 2004 to 2008, except for 42.8 per 100,000 adjusted incidence rate recorded in 2004.Our analysis did not discriminate between the incidence rate in the largely rural parts of Akpabuyo and the largely urban parts of Calabar like a China cancer registry study did.By analysing the rural and urban cancer registries separately, the Chinese discovered that breast cancer incidence rates were three times as high in the urban than in rural areas(37).Several other studies reported disparities between rural and urban dwellers(3, 7, 9, 14) .Future reports should strive to further categorize the population better so as to aid analysis and bring out the inherent differences in breast cancer subsets in our cancer registration process. The difficulty in classification also stems from the fact that Akpabuyo has witnessed a massive injection of a middle class population with the construction of housing estates for civil servants in the last 10 years. It is doubtful if the new middle class population injection may be rightly classified as living a rural life. What constitutes rural has to be rigorously defined with regards to Akpabuyo to facilitate thorough analysis.

Approximately half(49.2%) of the breast cancer occurring in females in Calabar was between the ages of 30 and 50 years. This pattern conforms with reports in many African and Afro Caribbean studies(1, 17, 23, 34-36).Even though the peak incidence periods were in the 40 to 44 years age bracket, the average age specific incidence rate was highest in the 55 to 59 years (77.3 per 100,000), followed by 57.0 per 100,000 for 45 to 49 years group. There was generally a progressive annual increase in average

age specific incidence rate from age 30 to 34 years at 20.4 per 100,000 to its peak at 77.3 per 100,000 at 55-59 years, before a gradual decline from age 65 to 69 years .An unexplainable drop was witnessed in the 50 to 54 years group with an average age specific incidence rate of 36.1 per 100,000. Annual age specific incidence rate also witnessed a progressive increase from age 30 to 43 years, with the highest rates seen in 2009 and 2010, as follows 65 to 69 years (178.6 per 100,00) and peak of 192.2 per 100,000 in the 55 to 59 years group respectively. This is similar to a study in Manila- where the rate started to rise in the 30 to 34 years group and peaked at a higher age of 70 to 74 years(3) .The age specific incidence rate is reported to have doubled in Japan in the 35 to 44 years age group since 1960(38).Our observation that the highest yearly age specific incidence of 192.2 per 100,000 occurred in age 55 to 59 years may signal an early change in demographics as was observed in a Singaporean study. The study found that in 30 years the peak age of diagnosis of breast cancer changed from 45 to 49 years to late 50's(16), perhaps coinciding with a change in their economic fortunes and adoption of a western lifestyle. Whether such a change may occur in Calabar in future, time and an anticipated change in our economic fortunes will tell. Worldwide it has been recorded that breast cancer incidence rose by 30 to 40 % between 1970's and 1990's (11).In Calabar even though our records date back to the late 1970's, records in the first two decades were not refined enough to be reliably extrapolated on the population.

At an average age specific incidence rate of breast cancer at 37 per 100,000, Calabar boasts an incidence rate like many Eastern European countries(39).Quite worryingly, the frequency of diagnosis in young women is alarming. In a region still grappling with infectious diseases, a rise in cancer burden as is now experienced will further put a strain on our already low health budget (1), and low sectorial allocation to cancer care .The belief that breast cancer incidence is low in this part of the world may soon be vigorously challenged. If one considers that our population is young and life expectancy is low, were our women to be living as long as their western counterparts the breast cancer picture in Nigeria might be different from what we know today. Time is now to invest on unravelling aetiological factors of breast Cancer in Nigerian women and other women of African ancestry which appear different from their Caucasian breast cancer counterparts(17, 20, 32, 33, 40-44).

192 Within the 5-year period from 2004 to 2008, there was an average annual decrease in incidence rate of
 193 3.5% (95% CI: 1.1%-4.9%). However, within the 5-year period from 2009 to 2013, there was an average
 194 annual increase in incidence rate of 1.9%% (95%CI: -0.85% to 2.2%). What might reasonably explain the
 195 initial decreased incidence is still farfetched. In the last five years however fine needle aspiration cytology,
 196 screening mammography and expansion of surgical services in Calabar may have contributed to the later
 197 increases. We do not have credible data on the extent of use of combined oestrogen and progesterone
 198 oral contraceptives in Calabar, which are known to increase the relative risk of breast cancer(45).There
 199 no records on the extent of use of postmenopausal hormone replacement therapy, the reduction of which
 200 is reported to cause a decrease in annual incidence in the United states up to 8.6%(46).

201 **5. CONCLUSION:**

202 Breast cancer is proving to be an extremely common disease in Calabar -Nigeria. Little work has been
 203 done on its aetiology and epidemiology. More attention should be paid on relieving human suffering and
 204 especially early and painful death which many breast cancer patients experience here. To reduce the
 205 high incidence of advanced breast cancer, a well coordinated government sponsored intensive breast
 206 awareness and mammographic screening programme for high risk groups at designated centres in the
 207 six geopolitical zones is recommended. This would contribute to early detection and effective control of
 208 breast Cancer in Nigeria.

209 **ETHICAL APPROVAL:** Ethical permission for this study was granted to the Calabar Breast Study
 210 Group by the University of Calabar Teaching Hospital Ethical review board.

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