

ORIGINAL ARTICLE

Factors associated with breast disorders detected by clinical breast examination during pregnancy and six months postpartum in Ibadan, South-western Nigeria

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Abstract

Background. Breast disorders (BD) during pregnancy and postpartum cause anxiety and reduce women's quality of life. The study examined BD risk factors during pregnancy and six months after delivery.

Methods. Women attending antenatal clinics at 26 weeks gestation were recruited. 1248 pregnant women were followed six months postpartum. During recruitment, a validated questionnaire was used to collect participant characteristics and risk factors. Palpable lumps, inflammation, persistent pain, and abnormal nipple discharge were classified breast disorders. Statistical analysis used multiple logistic and cox regression models at $p < 0.05$.

Results. Women with benign breast disease were more likely to develop BD (aOR = 2.63, 95% CI = 1.50–4.88). One pregnancy increases the risk of BD more than three times (aOR=0.52, 95%CI: 0.29–0.95). History of breast trauma (aHR=3.59, 95%CI: 1.40–9.17) and 3 miscarriages vs. none (aHR=2.23, 95%CI: 1.04–4.23) were also risk factors for BD. The second quartile of physical activity was associated with a lower risk of BD (aHR=0.35, 95%CI: 0.15–0.78).

Conclusion. Women with breast trauma and miscarriage are more likely to develop breast disorders during pregnancy and six months after delivery. Our findings highlight the need for additional longitudinal research to validate these findings and plans for prevention and control. **Keywords:** Breast disorders, pregnancy, postpartum, predictors, longitudinal study.

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INTRODUCTION

Breast disorders (BD) can be benign, malignant neoplastic or non-neoplastic disorders affecting the breast.¹ When diagnosed in pregnancy and during lactation, these disorders are termed pregnancy associated breast disorders.^{2,3} The prevalence of BD in pregnancy and lactation is high, largely due to hormones causing several physiological changes in the breast during pregnancy and postpartum.^{4–7} A diagnosis of benign breast disease (BBD) causes anxiety in pregnancy and can greatly influence a woman's quality of life.⁸ Moreover, BBD appears to be associated with the risk of subsequent breast cancer in future, although the magnitude of the risk is poorly defined.^{9,10} Breast cancers diagnosed during pregnancy and in the postpartum period have aggressive histological features^{11,12} with diagnoses made in early postpartum being more aggressive.¹² Unfortunately, there are yet no defined risk factors for BBD.

Identification of risk factors for non-communicable diseases (NCD) adds to knowledge for controlling these diseases and addressing them can help attainment of the United Nations goal of 25% reduction of NCDs in developing countries. Furthermore, recognizing risk factors associated with both breast cancer and BBD would aid in prediction by identifying people at high risk as well as promote prevention by controlling modifiable risk factors. It is noteworthy that some risk factors have been identified as possible modifiers facilitating BBD progression to breast cancer through unknown mechanisms. The roles of these modifying factors are yet to be clarified.^{13,14} Understanding how to decrease the incidence of BBD would greatly improve breast cancer prevention and promote its control.¹⁵

There are many well established risk factors for breast cancer, as reported by several research articles and systematic reviews conducted in both developing and developed countries. Factors include family history, genetic predisposition, alcohol consumption, physical activities and BBD.^{8,13,16–19} However, epidemiological studies on the risk factors associated with benign breast disease are few. Benign breast disease is mostly neglected and poorly investigated

with few focus on proliferative BBD in low and middle-income countries.^{8,9,20}

Inconsistent findings across studies of BBD and a dearth of systematic reviews have impeded our understanding of its etiology.^{20–22} Reasons behind the inconsistencies include different control groups used in various studies and the varied pathological classifications of BBD.^{20–22} Varying environmental exposures can also cause risk of BBD to differ across people in different geographical locations.⁸ In Nigeria, studies conducted on BD specifically occurring in pregnancy and lactation are few and the etiology of the disease is largely unexplored.^{23,24} The study therefore aimed to identify risk factors associated with BD diagnosed in pregnancy and six months postpartum, and determine whether reproductive, lifestyle, family history and anthropometric variables are potential predictors of BD in this interval.

MATERIALS AND METHODS

Ethical considerations: The University of Ibadan/ University College Hospital Ethics Committee (Study assigned number: UI/EC/14/0098) and the Oyo State Ministry of Health Ethics Committee gave ethical approvals for the study. In addition, written informed consent was obtained from all study participants. Confidentiality was ensured, as serial numbers and barcodes were assigned to each participant for identification. Data were protected and saved on encrypted and pass-worded laptops.

Study design and population: A longitudinal study design was used. We recruited 1248 pregnant women consecutively at ≤ 26 weeks gestational age, and they were followed up in their third trimesters, six weeks postpartum and six months postpartum. The study

Supplementary information The online version of this article ([Tables/Figures](#)) contains supplementary material, which is available to authorized users.

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began recruitment of participants in June 2015 and follow up ended in September 2017. Three study centers in Ibadan, Nigeria were selected, each representing one of the three tiers of public health care system in Nigeria. They include the antenatal clinics of the University College Hospital (UCH), Adeoyo Maternity Teaching Hospital (AMTH) and the Primary Health Centre (PHC) Agbongbon.

At recruitment (baseline), participants were taught Breast Self-Examination (BSE) using the MammaCare® method, Clinical Breast Examination (CBE) using the same method was performed and a questionnaire was administered. Afterwards, CBE was performed at follow-up visits. Women found to have BD were referred for Breast Ultrasound Scan (BUS) and those classified as having Breast Imaging Reporting and Data System (BIRADS) ≥ 4 were referred for a breast ultrasound guided biopsy. A Consultant Radiologist performed the breast ultrasound scan and ultrasound-guided biopsy and the biopsy was read at the Pathology Department of the UCH Ibadan. Figure 1 shows the operational flow of the study. More information about the study design and population, the MammaCare® method of BSE and CBE can be found in our previous article.²⁵

Data collection methods: Information on socio-demographic variables, medical history, reproductive variables, anthropometric factors, lifestyle and family history of cancer was collected at recruitment using a pretested and face validated questionnaire. Prior to this study, a test-retest method was used to check for reliability of the instrument at a location different from the study centers ($\rho=0.9$). A checklist of the signs and symptoms of breast disorders was also developed prior to the study and was used to document the CBE findings. In addition, findings of the BUS and ultrasound guided biopsy investigations were also documented.

Breast disorder was defined as the detection of at least a lump or mass through palpation on the breast or axilla or around the breast, with or without the detection of other symptoms/signs such as persistent pain, skin thickening, abnormal nipple discharge, redness on the breast's skin, and recently identified nipple inversion or retraction by CBE.²⁶

Body silhouettes (Stunkard silhouettes) showing nine body sizes from very thin to very obese, were used to categorise body sizes at age 8, age at menarche, current age, and ages 20, 30, 40 if attained at time of interview. For this study, we classified body silhouettes 1-3 as low adiposity, 4-6 as medium adiposity and 7-9 as high adiposity. We estimated level of intensity of Physical Activity (PA) to be light, moderate and vigorous based on the activities around the home and at the work place (occupational activities). Metabolic Equivalents for Task (MET) values were assigned to the levels of work intensity, 1.5 MET for light intensity, 2.5 MET for moderate intensity and 6 MET for vigorous intensity.²⁷ Then, MET values were multiplied by the duration of activities at each level of intensity. Total PA was calculated as an average of the home and work related activities (MET hours/week).

Statistical analysis: The dependent variable was BD, classified as either yes or no. Independent variables included age group, health facility, education, occupation, age at menarche, menstrual irregularities, use of fertility drugs, hormonal contraceptive use, breast-feeding length, parity, number of miscarriages, age at first live birth, Body Mass Index (BMI), body silhouettes, physical activity, alcohol consumption, smoking habits and multivitamins use.

In the bivariate analysis of factors related to BD detected at recruitment, Chi-square test or Fisher's exact test was used for categorical variables and Student's t-test was used for continuous variables. Significant variables with p-value of <0.05 from bivariate analysis were included in the multiple logistic regression model. Wald statistics and backward selection method were used to fit the final model.

Women found not to have BD at recruitment were followed up to determine factors associated with time to BD detection in pregnancy and six months postpartum. Cox proportional hazard regression model was used to investigate variables related to incident BD outcome. Variables were selected into the model if the log rank test had a p-value of <0.05 for categorical independent variables and were selected if univariate Cox proportional hazard regression model had a p-value of <0.05 for continuous independent variables. Hazard ratios (HR) and their

95% confidence intervals (95%CI) were reported. Proportional hazard assumption was checked by including the interaction term of time and its covariates in the model. Data were analyzed using Stata version 14 (TX, USA).

RESULTS

The age range of the 1248 study participants was 16 to 46 years, 540 (43.3%) had a secondary education or less, 1154 (92.5%) were predominately Yoruba, a major ethnic group in south-western Nigeria, and about half (51.1%) were artisans, small-scale entrepreneurs, or laborers. The majority (62.9%) were registered at the AMTH's antenatal clinic. At recruitment, 149 (11.9%) women were identified as having BD through CBE, and 17 (1.4%) of these women reported a history of BBD when interviewed. The frequency distribution of selected participant characteristics and their BD status at recruitment is shown in Table 1.

Factors found to be significantly associated with high BD detection at recruitment were age >25 years ($p=0.002$), PHC facility ($p=0.014$), secondary and below level of education ($p=0.003$), full-time housewife or unemployment ($p=0.003$), history of BBD ($p=0.002$), menarche at 14-16 years ($p=0.014$), no infertility history ($p=0.032$), two pregnancies ($p=0.030$), 2 miscarriages ($p=0.043$), and BMI 18 kg/m². These variables were included in multiple logistic regression model (Table 2). Women with a history of BBD had a greater likelihood of developing BD than women with no such history (aOR = 2.63, 95% CI: 1.50–4.88). Multigravida with 3 pregnancies were less likely to have BD in pregnancy at recruitment compared to primigravida (aOR=0.52, 95% CI: 0.29–0.94), as were those who reported an early age (14 years) at first menstrual period compared to those who reported ages 14–16 years (aOR=0.56, 95% CI: 0.34–0.94).

We followed 1,099 women with no detectable BD at recruitment for six months after delivery. The maximum duration of follow-up was 596 days, during which 74 (6.7%) participants were identified as incident cases with breast disorders.

Probability of developing BD varied significantly between the three centers ($p=0.001$) It was discovered that participants with no or only primary education had a higher probability than others ($p=0.001$). The probability of BD was lower among participants with a professional occupation ($p=0.001$) than among those with other occupations. Breast trauma history was a significant predictor ($p=0.001$) Those who had used oral contraceptives had a lower probability than those who had never used them ($p=0.025$). Those with a history of one to two miscarriages had a lower probability compared to those with none or three or more miscarriages ($p=0.037$). Moderate physical activity was significantly advantageous ($p=0.014$). Participants in the lowest quartile of total PA (the least amount of exercise) had a greater likelihood of BD than those in the other quartiles ($p=0.028$).

There was no significant association between time to first BD detection and variables such as age group, religion, ethnicity, family history of cancer, family history of BBD, infertility history, age at menarche, menstrual irregularities, number of pregnancies, average breastfeeding length, alcohol status, BMI, silhouettes at age 8, frequent use of multivitamins before pregnancy, light or vigorous physical activity ($p>0.05$).

Table 3 presents the Cox regression analysis of time to first detection of BD. History of breast trauma (HR = 3.59, 95% CI: 1.40 – 9.17) and 3 miscarriages (HR = 2.23, 95% CI: 1.04 – 4.83) were significantly associated with a higher risk of BD compared to no history of these events. Lower risk of BD was associated with having a secondary level of education (aHR = 0.35, 95% CI: 0.17 – 0.76) and tertiary level of education (aHR = 0.39, 95% CI: 0.16 – 0.95) as compared to having none/primary level of education; also with being in the second quartile of total PA as compared to the first quartile (aHR = 0.35, 95% CI: 0.15 – 0.79). The risk of BD decreases with each 10 kg increase in body weight (aHR = 0.77, 95% CI: 0.62 – 0.95).

DISCUSSION

This study is distinctive due to its focus on BD during pregnancy and six months postpartum. During the study period, risk factors for BD were identified through CBE in order to improve the planning of interventions for the prevention and control of pregnancy-associated breast disorders, particularly among Nigerian women. The prevalence of BBD was statistically associated with an increased likelihood of BD at recruitment. Compared to primigravidae, women with three or more pregnancies had lower odds of developing BD. Women who reported a menarche age of less than 14 years were less likely to develop BD than those who reported a menarche age of 14 to 16 years. History of breast trauma and history of three or more miscarriages were found to be associated with a greater risk of BD during pregnancy and six months postpartum compared to no history. Women with a secondary or tertiary education, moderate physical activity, a history of oral contraceptive use, and a 10 kg increase in body weight were found to be at lower risk for breast disorders than those with no education or a primary education.

The multiple recurrence and incidence of fibrocystic diseases and other types of BBD in women is a well-established and well-known theory based on epidemiological studies.^{28–30} According to Freire de Oliveira,³⁰ the increased likelihood of cystic disease recurrence in premenopausal women is likely related to the increased likelihood of ovarian cancer during the premenopausal stage of BBD. This study, which was conducted on pregnant women, confirms this recurrence, as both a history of BBD and breast trauma were found to be associated with developing BD. This study did not histologically classify BD, but, consistent with a study conducted in China,²⁸ would have likely found a relatively common recurrence effect among women with proliferative BBD.³¹

We examined the relationship between reproductive variables and the detection of BD and found that women with three or more pregnancies were less likely to have BD than those with one pregnancy. Similarly, a study in Japan and a systematic review of all women reported that having fewer children was associated with an increased risk of

Proliferative-Benign Breast Diseases (P-BBD). In the same study, lower parity was linked to fibrocystic diseases, but there was no association between parity and fibroadenoma.^{21,29} In a Nigerian study, pregnant women had a lower breast cancer risk than nonpregnant women, and a long-term protective effect of pregnancy was observed.^{18,32}

This study found that participants with more than two miscarriages had a greater risk for BD. However, Silvera and Rohan³³ found no association between miscarriages and benign proliferative epithelial disease in their systematic review. In a follow-up study of women with fibroadenoma in Shanghai, miscarriage was also not found to be associated with fibroadenoma.³¹ It is possible that our findings reflect a set of characteristics unique to the study population of pregnant and lactating women.

Insufficient physical activity is a crucial modifiable risk factor. Independent of body fat, physical activity was found to be negatively associated with all types of BBD. It is significantly associated with a reduced risk of breast cancer in premenopausal and postmenopausal Brazilian and Nigerian women.^{8,7} According to a Nigerian study, occupational or work-related activities are the most significant contributor to total PA.²⁷ Women with middle and upper quartile levels of occupational light PA had decreased odds of BD during pregnancy and six months postpartum, according to our study. In addition, women in the middle and upper quartiles of total PA had a lower risk.

In this study, there was an inverse relationship between body weight measured in the second trimester or earlier and BD. Previous research conducted on women as a whole revealed a strong, consistent protective effect of obesity against both fibroadenoma and fibrocystic diseases.²⁹ In contrast, some studies found inverse associations between BBD and both weight and BMI. Other studies failed to find a correlation between BMI and benign proliferative epithelial diseases, most likely because they did not account for menopausal status.^{9,33} Premature death is known to be inversely related to body mass index, positively associated with postmenopausal breast cancer but not with menopausal breast cancer.^{20,33,34}

In a systematic review, a higher level of education was found to be positively associated with fibrocystic disease, although socioeconomic factors were not matched between study control groups. However, there was no correlation between education and fibroadenoma.²⁹ According to Goehring and Morabia, the possible protective effect of a higher level of education may be due to selection bias.²⁹ Similarly, our study discovered a decreased likelihood of BD with increasing levels of education.

Due to the large sample size and follow-ups, there is a higher likelihood of a causal association and temporality in this study. The possibility of misclassification bias is a limitation because the findings were based on CBE detection of BD. BD is also heterogeneous by nature. If additional risk factors were identified based on the histological classification of BD, the results of this study would have been more convincing. In addition, had information on genetic breast cancer predispositions been collected, the study could have investigated genetic risk factors. Other study limitations were discussed in our previous article.²⁵

CONCLUSION

A better understanding of risk factors will increase the clinical and policy relevance of this field of research by allowing the identification of high-risk groups for prevention and control. The effectiveness of this strategy cannot be overstated. This study has significantly advanced our understanding of the risk factors associated with breast disorders during pregnancy and after delivery in Nigeria. Modifiable factors, such as physical activity, breast trauma, and the incidence of miscarriage, play a role in the protection against breast disorders during pregnancy and six months after delivery. More longitudinal studies are required to confirm these findings and inform the development of appropriate control measures.

INFORMATION

Acknowledgement and funding. The study acknowledges the cooperation of all the pregnant women who participated in the study and the NIH-D43 University of Chicago-University of Ibadan International Partnership for Interdisciplinary Research Training team for the financial assistance and mentoring.

Funding. University of Chicago NIH D43 TW009112; American Cancer Society (O.I.O), and Susan G. Komen for the Cure (SAC110026 to O.I.O.).

Authors' contributions. SOO was involved with the study design, data collection, analysis, interpretation, and drafting of the manuscript; IOA supervised data collection and participated in the study conception and design; IOM supervised data collection and participated in the study conception and design; BA supervised data analysis and participated in the study conception and design; DH supervised data analysis and participated in the study conception and design; DH supervised data analysis and participated in the study conception and design; OIO participated in the study conception and design, and supervised the implementation. All authors participated in the critical revision of the manuscript, and all authors approved its final form.

Disclosures about potential conflict of interest. Authors declare no conflict of interest, except Olu-funmilayo I. Olopade who is an equity stock holder of CancerIQ.

Further information. Abstract presented in part at the International Cancer Screening Network Conference (ICSN) June 2019 conference in Rotterdam, Netherlands.

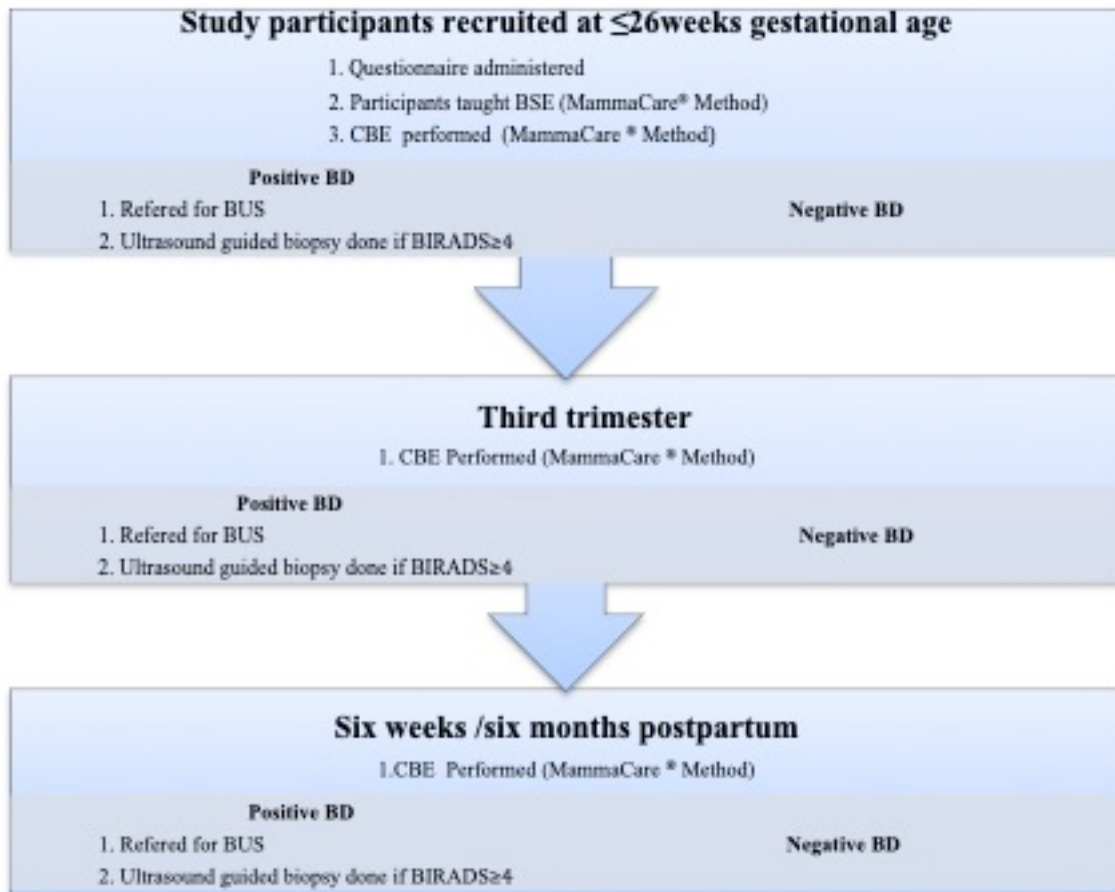


FIGURE 1: Operational flow chart of the study at the antenatal clinics. BD-Breast Disorder, BUS-Breast Ultrasound Scan, CBE-Clinical Breast Examination, BSE-Breast Self-Examination, BIRADS- Breast Imaging Reporting and Data System.

BREAST DISORDERS IN NIGERIAN PREGNANCIES

Table 1: Frequency distribution of selected characteristics of study participants (N=1248).

Characteristics	Breast Disorders		Total (N=1248) n (%)	X ²	p-value						
	Yes (N=149) n (%)	No (N=1099) n (%)				No of miscarriages					
Age group (years)						0	102 (68.5)	730 (66.4)	832 (66.7)		
<25	40 (26.8)	164 (14.9)	204 (16.4)			1-2	45 (30.2)	304 (27.7)	349 (27.9)		
25-29	49 (32.9)	363 (33.0)	412 (33.0)			>2	2 (1.3)	65 (5.9)	67 (5.4)	5.49	0.043**
30-34	38 (25.5)	345 (31.4)	383 (30.7)			Mean ± SD age at first live birth* N=680	24.0 ± 4.2	25.4 ± (4.2)	25.2 ± 4.2		0.014**
>34	22 (14.8)	227 (20.7)	249 (19.9)	15.18	0.002 **	Average breastfeeding length (months)					
Mean ± SD	28.2 ± 5.4	29.9 ± 5.2	29.7 ± 5.2		<0.001**	0	81 (54.4)	493 (44.9)	574 (45.9)		
Health facility type						<7	6 (4.0)	34 (3.1)	40 (3.2)		
PHC	15 (10.1)	87 (7.9)	102 (8.2)			7-12	9 (6.0)	107 (9.7)	116 (9.3)	6.29	0.098
UCH	28 (18.8)	333 (30.3)	361 (28.9)			>12	53 (35.6)	465 (42.3)	518 (41.5)		
AMTH	106 (71.1)	679 (61.8)	785 (62.9)	8.58	0.014 **	Oral contraceptive use	11 (7.4)	83 (7.6)	94 (7.5)	0.01	0.941
Education						BMI (kg) * N=1202					
None/Primary	12 (8.0)	72 (6.6)	84 (6.7)			>18.5	6 (4.2)	29 (2.7)	35 (2.9)		
Secondary	73 (48.9)	383 (34.9)	456 (36.5)			18.5-25	72 (50.7)	443 (41.8)	515 (42.9)		
Polytechnic	30 (20.1)	232 (21.1)	262 (20.9)			25-30	35 (24.7)	343 (32.7)	378 (31.5)		
B.Sc./HND	28 (18.8)	317 (28.8)	345 (27.6)			>30	29 (20.4)	245 (23.1)	274 (22.8)	6.79	0.110
Postgraduate	6 (4.0)	95 (8.6)	101 (8.1)	15.94	0.003 **	Mean ± SD bodyweight N=1209	63.9 ± 12.3	67.2 ± 13.0	66.8 ± 12.9		0.003**
Ethnicity						Ever consumed alcohol	12 (8.1)	108 (9.8)	120 (9.6)	0.47	0.491
Yoruba	138 (92.6)	1016 (92.5)	1154 (92.5)			Workplace light PA (MET hrs/wk)					
Ibo	5 (3.4)	43 (3.9)	48 (3.9)			Quartile 1 (0-1.3)	76 (51.0)	443 (40.3)	519 (41.6)		
Hausa	3 (2.0)	9 (0.8)	12 (0.9)			Quartile 2 (1.3-10.4)	8 (5.4)	98 (8.9)	106 (8.5)		
Others	3 (2.0)	31 (2.8)	34 (2.7)	2.37	0.489	Quartile 3 (5.0-9.3)	29 (19.5)	288 (26.2)	317 (25.4)		
Occupation*						Quartile 4 (9.4-140.0)	36 (24.2)	270 (24.6)	306 (24.5)	7.91	0.048**
Professionals	5 (3.3)	91 (8.3)	96 (7.7)			Home related vigorous PA (MET hrs/wk)					
Civil servants	33 (22.2)	356 (32.4)	389 (31.2)			Quartile 1 (0-0.2)	34 (22.8)	344 (31.3)	378 (30.3)		
Full time housewife/unemployed	19 (12.8)	106 (9.7)	125 (10.0)			Quartile 2 (1.3-10.4)	40 (26.9)	234 (21.2)	374 (21.9)		
Artisan, small scale entrepreneur, labourers	92 (61.7)	545 (49.6)	637 (51.1)	15.01	0.003 **	Quartile 3 (10.5-47.9)	30 (20.1)	269 (24.5)	299 (23.9)		
Family history of cancer	8 (5.4)	50 (4.6)	58 (4.6)	0.19	0.656	Quartile 4 (7.5-126.0)	45 (30.2)	252 (22.9)	297 (23.8)	8.91	0.031**
Family history of benign breast diseases	5 (3.4)	39 (3.6)	44 (3.5)	0.01	0.905	PHC, Primary Health Center Agbongbon; AMTH, Adeoyo Maternity Teaching Hospital; UCH, University College Hospital; HND, Higher National Diploma; BMI, Body Mass Index; Q, Quartile; MET, Metabolic Equivalents of Task; *missing N= 1248, **significant at p<0.05.					
Ever had benign breast diseases	17 (11.4)	55(5.0)	72 (5.8)	1.90	0.002 **						
Age at menarche (years) *N=1239											
<14	25 (16.9)	308 (28.2)	333 (26.9)								
14-16	79 (53.4)	506 (46.4)	585 (47.2)								
>16	44 (29.7)	277 (25.4)	321 (25.9)		0.014**						
Infertility history	8 (5.4)	122 (11.1)	130 (10.4)	8.53	0.032**						
No of pregnancies											
1	48 (32.2)	297 (27.0)	345 (27.6)								
2-3	45 (30.2)	263 (23.9)	308 (24.7)								
>3	56 (37.6)	539 (49.0)	595 (47.7)	6.98	0.030**						

[CONTINUED]

Table 2: Predictors of breast disorders in pregnancy at baseline.

Significant variables	OR	95% CI	aOR	95% CI
Age group (years)				
<25	1(ref)		1(ref)	
25–29	0.55	0.35–0.87	0.84	0.49–1.42
30–34	0.45	0.28–0.73	0.86	0.47–1.60
>34	0.39	0.23–0.69	0.86	0.41–1.79
p-value for trend	0.002		0.934	
Health facility type				
UCH	1(ref)		1(ref)	
AMTH	1.86	1.19–2.87	0.99	0.55–1.78
PHC	2.05	1.04–4.00	0.76	0.33–1.75
Education				
None/Primary	1(ref)		1(ref)	
Secondary	1.14	0.59–2.21	1.06	0.52–2.16
Tertiary	0.59	0.3–1.16	0.77	0.34–1.74
p-value for trend	0.002		0.498	
Occupation				
Professionals	0.33	0.13–0.82	0.46	0.16–1.31
Civil servants	0.55	0.36–0.84	0.74	0.41–1.09
Artisan, small scale entrepreneur, labourers	1(ref)		1(ref)	
Full time housewife/ unemployed	1.06	0.62–1.81	0.92	0.48–1.77
Home related vigorous PA (MET hrs/wk)				
Quartile 1 (0–0.2)	1(ref)		1(ref)	
Quartile 2 (0.2–3.4)	1.73	1.06–2.81	1.24	0.72–2.13
Quartile 3 (3.5–7.4)	1.13	0.67–1.89	0.89	0.49–1.54
Quartile 4 (7.5–126.0)	1.81	1.12–2.90	1.24	0.72–2.11
p-value for trend	0.033		0.493	
Workplace light PA (MET hrs/wk)				
Quartile 1 (0–1.3)	1(ref)		1(ref)	
Quartile 2 (1.3–10.4)	0.48	0.22–1.02	0.62	0.28–1.37
Quartile 3 (10.5–47.9)	0.59	0.37–0.92	0.66	0.41–1.09
Quartile 4 (48.0–136.5)	0.78	0.50–1.19	0.72	0.45–1.15
p-value for trend	0.051		0.258	
Clomiphene citrate use				
No	1(ref)		1(ref)	
Yes	0.25	0.06–1.03	0.54	0.10–2.88
Mean age at first live-birth (years)*				
	0.94	0.89–0.98	0.97	0.90–1.04
<i>[CONTINUED]</i>				
No. of pregnancies				
1	1(ref)		1(ref)	
2–3	1.06	0.68–1.64	0.92	0.56–1.53
>3	0.64	0.43–0.97	0.52	0.29–0.94
p-value for trend	0.032		0.045	
Age at menarche (years)				
<14	0.52	0.32–0.83	0.56	0.34–0.92
14–16	1(ref)		1(ref)	
>16	1.02	0.68–1.51	0.98	0.64–1.49
p-value for trend	0.016		0.069	
No. of miscarriages				
0	1(ref)		1(ref)	
1–2	1.06	0.73–1.54	1.29	0.82–2.04
>2	0.22	0.05–0.91	0.19	0.03–1.47
p-value for trend	0.102		0.120	
Ever had infertility				
No	1(ref)		1(ref)	
Yes	0.45	0.22–0.95	0.57	0.23–1.39
Ever had benign breast disease				
No	1(ref)		1(ref)	
Yes	2.44	1.38–4.34	2.63	1.43–4.84

aOR, Adjusted Odds Ratio. OR adjusted for age group, health facility, education, occupation, vigorous PA, light PA in workplace, clomiphene citrate use, mean age at first live-birth, number of pregnancies, age at menarche, number of miscarriages, infertility and history of benign breast disease. CI, Confidence Interval; PHC, Primary Health Center Agbongbon; AMTH, Adeoyo Maternity Teaching Hospital; UCH, University College Hospital; BMI, Body Mass Index; Q, Quartile; PA, Physical Activity; MET, Metabolic Equivalents of Task; *Mean age at first live birth of 25.2 years was used in place of missing values

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How to cite this article: Odedina S.O., Ajayi I.O., Morhason-Bello I.O., Adedokun B., Huo D., Olopade O.I., Ojengbede O.A. Factors associated with breast disorders detected by clinical breast examination during pregnancy and six months postpartum in Ibadan, South-western Nigeria. *Journal of Public Health in Africa*. 2022;13:1812. <https://doi.org/10.4081/jphia.2022.1812>