

Novel breast cancer risk factors in Nigeria: the findings of Nigerian breast cancer risk factor study

Authors: Samuel O. Azubuiké^{1,*}; Dori-Michelle Beeler^{2,3}

Affiliations: ¹Department of Public Health, Faculty of Health Sciences, National Open University of Nigeria, Abuja, Nigeria; ²Department of Supportive Oncology, Levine Cancer Institute, Atrium Health, Charlotte, NC, USA; ³Sociology, Anthropology, and Public Health Department, University of Maryland Baltimore, County, USA.

ABSTRACT

INTRODUCTION: The potential roles of alcohol consumption and family history of breast cancer in breast cancer etiology have not been widely studied in Nigeria. Moreover, no African study has investigated the relationship between Light Exposure at Night (LEAN), interpregnancy gap, and breast cancer risk. This study investigated the association between LEAN alcohol consumption, family history of breast cancer, interpregnancy gap, and breast cancer risk among Nigerian women.

METHODS: A semi-structured questionnaire was used to collect relevant data from 372 cases and 403 controls in five public hospitals in Nigeria. The participants were interviewed in person between October 2016 and May 2017. Multivariable logistic regression was used to estimate odds ratios (ORs) and 95% confidence intervals (CI).

RESULTS: After adjusting for relevant confounders, frequent LEAN (OR 1.87, 95% CI: 1.09, 3.21), average interpregnancy gap (AIG) > 3 years (compared to AIG < 1.5 years) (OR 2.21, 95% CI: 1.07, 4.57), having a regular history of alcohol consumption (OR 1.67, 95% CI: 1.04, 2.69), and family history of breast cancer (OR 2.11, 95% CI: 1.14, 3.93) and were significantly associated with an increased risk of breast cancer.

CONCLUSION: We hypothesized that LEAN, longer interpregnancy gap, regular alcohol consumption, and family history of breast cancer increase the risk of breast cancer among Nigerian women.

Keywords: Light exposure at night, Alcohol consumption, family history of breast cancer, Interpregnancy gap, women, breast cancer, Nigeria

INTRODUCTION

The rising burden of breast cancer among women remains a potential threat to the social and economic well-being of many families in Africa, including Nigeria [1, 2]. Previous studies have

shown that reproductive and lifestyle variables such as low breastfeeding practice, abdominal fat accumulation, and low physical activity are implicated [3-5]. However, the potential roles of alcohol consumption and family history of breast cancer breast cancer have not been widely studied

***Corresponding author:** Samuel O. Azubuiké, Department of Public Health, Faculty of Health Sciences, National Open University of Nigeria, Abuja, Nigeria, email: samonaz2000@yahoo.com; **Potential Conflicts of Interest (CoI):** All authors: no potential conflicts of interest disclosed; **Funding:** All authors: no funding has been sought or gained for this project; **Academic Integrity.** All authors confirm that they have made substantial academic contributions to this manuscript as defined by the ICMJE; **Ethics of human subject participation:** The study was approved by the local Institutional Review Board. Informed consent was sought and gained where applicable; **Originality:** All authors: this manuscript is original has not been published elsewhere; **Review:** This manuscript was peer-reviewed by three reviewers in a double-blind review process; **Type-editor:** Emilia (USA).

Received: 30th January 2023; **Initial decision given:** 12th June 2023; **Revised manuscript received:** 30th June 2023; **Accepted:** 26th August 2023.

Copyright: © The Author(s). This is an Open Access article distributed under the terms of the Creative Commons Attribution License (CC BY-NC-ND) ([click here](#)) which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. **Publisher:** Rwanda Biomedical Centre (RBC)/Rwanda Health Communication Center, P. O. Box 4586, Kigali. ISSN: 2079-097X (print); 2410-8626 (online)

Citation for this article: Samuel O. Azubuiké; Dori-Michelle Beeler. Novel breast cancer risk factors in Nigeria: the findings of Nigerian breast cancer risk factor study. Rwanda Medical Journal, Vol. 80, no. 3, p. 24-33, 2023. <https://dx.doi.org/10.4314/rmj.v80i3.4>

in Nigeria. Moreover, while some studies in other parts of the world have investigated the potential roles of interpregnancy gap and exposure to light at night [6-10], no African study has reported such observation to the best of our knowledge. The aim of this study was to carry out an exploratory investigation of the relationship between frequency of light exposure at night (LEAN), interpregnancy gap, alcohol consumption, family history of breast cancer and the risk of breast cancer among Nigerian women based on data from the NBRIS [3, 5]. The NBRIS was instituted in 2016 to investigate traditional risk factors associated with the risk of breast cancer in Nigeria, including reproductive, adult socioeconomic status, physical activity, and anthropometric factors. The study also included data on novel/emerging breast cancer risk factors such as well as alcohol consumption, shift work duration and LEAN.

METHODS

The details of the study setting, participants recruitment, data collection methods, important covariates, and general statistical consideration has been previously reported [3, 5].

Study variables: Participants were described as having a family history of breast cancer if they indicated that any member of their first-degree (mother or sister) or second-degree (aunt) relatives experienced breast cancer. Participants were described as having ever consumed alcohol if they indicate that they had consumed alcohol at any point in their life, irrespective of volume and duration. Participants were described as having a history of regular alcohol consumption if they indicated that they had a history of weekly consumption of alcohol, either in the past or present. The average interpregnancy gap for each participant was estimated by subtracting the age at the last full-term pregnancy from the age at first full-term pregnancy and dividing the result by the total number of pregnancies/births per participant. LEAN was described as the number of times the participants were intentionally or unintentionally exposed to light at night (including electricity and other local sources) in a typical week before breast cancer diagnoses (for cases) or interviews (for controls).

Statistical analyses: The differences in the distribution of demographic factors and explanatory variables between cases and controls

were assessed using t-tests or Mann-Whitney U (for non-normally distributed variables) for continuous variables. Categorical data were compared using chi-square (χ^2) tests.

Unconditional binary logistic regression was used to model the relationship between breast cancer and each variable of interest using Statistical Package for Social Sciences (SPSS) version 23. Unadjusted odds ratios and 95% confidence intervals were computed for each variable of interest. Multicollinearity for continuous variables was assessed and assumed not to be present if the tolerance value was >0.1 and the variance inflation factor <10 [11]. Pairwise deletion was applied to all missing values.

Selection and adjustment of relevant covariates:

All the adjusted covariates were selected based on existing literature. These were age (as a continuous variable), study sites, and ethnicity (Yoruba, Igbo, Niger Deltans, other northern tribes), reproductive variables- parity (continuous variable), age at first pregnancy/birth-AAFB (continuous variable), menopausal status (premenopausal & postmenopausal), total months of breastfeeding-TBF (continuous), age at menarche-AAM (≤ 13 yrs >13 yrs), oral contraceptive use-OCU (Yes & No) as well as family history of breast cancer and other lifestyle variables- alcohol consumption (Yes & No), body mass index, total physical activity-PA (tertiles), socioeconomic variables -educational attainment-personal and parental educational attainment (non-formal/primary, secondary, postsecondary, first degree/HND & $>$ first degree), income ($< \text{₦}18,000$; $\text{₦}18,000 - \text{₦}49,000$; $\text{₦}50,000 - \text{₦}100,000$; $> \text{₦}100,000$) and place of residence (less urbanized, more urbanized). They were adjusted in 3 models as appropriate for each association being investigated (Table 3).

RESULTS

A total of 372 cases and 403 controls participated in the study. Descriptive analyses (Table 1) show that cases did not differ significantly from controls with respect to age, ethnicity, marital status, age at first birth, age at menarche, body mass index, total months of breastfeeding, and parity. Significant differences in proportion between cases and controls were observed with respect to menopausal status, income, and education. The proportion of participants with higher levels of educational attainment, and income was higher

Table 1. Characteristics of study subjects

	Characteristics	Control n (%)	Case n (%)	~P-value
Age	Mean ± SD	46.8 ± 10.8	47.1 ± 10.7	0.556 ^β
Ethnicity	Yoruba	192 (47.9)	155 (41)	0.098
	Igbo	100 (24.9)	128 (33.9)	
	Hausa / Fulani	14 (3.5)	13 (3.4)	
	Niger Deltans	51 (12.7)	42 (11.1)	
	Other Northern ethnic groups	44 (11)	40 (10.6)	
Marital status	Never Married	33 (8.3)	36 (9.5)	0.545
	Widowed	32 (8.0)	26 (6.9)	
	Divorced/separated	9 (2.3)	14 (3.7)	
	Married	325 (81.5)	301 (79.8)	
Religion	Christianity	315 (78.8)	310 (82.9)	0.145
	Islam	85 (21.3)	64 (17.1)	
Body mass index-BMI (Kg/M²)	Median (IQR)	27.77 (7.29)	26.76 (7.26)	0.265 ^δ
	Parity	3.0 (2)	3.0 (2)	0.09
Median (IQR)	Total months of breast feeding (TBF)	36 (36)	36.5 (41)	0.61
Age at menarche (AAM)	≤ 13yrs	127 (33.1)	129 (35.1)	0.57
	>13yrs	257 (66.9)	239 (64.9)	
Menopausal status	Premenopausal	229 (56.8)	161 (42.5)	0.02
	Unknown/artificial*	20 (5.0)	64 (16.9)	
	Post- menopausal (Natural)	154 (38.2)	154 (40.6)	
Age at first birth (Aafb)	Mean ± SD	25.5 ± 4.8	25.3 ± 5.1	0.577 ^β
Physical activity-PA (MET-hr/wk)	< 128.20	134 (36.9)	112 (29.5)	0.082
	128.20- 184.29	118 (32.5)	131(34.5)	
	≥184.30	111 (30.6)	137 (36.1)	
Education	Non formal / Primary	37 (9.3)	63 (16.6)	<0.001
	Junior / Senior secondary	96 (24)	109 (28.8)	
	Post-secondary	73 (18.3)	71 (18.7)	
	1st degree / HND	134 (33.5)	110 (29)	
	>1st degree	60 (15)	26 (6.9)	
Respondents' income (in Naira- ₦^α)	< ₦18,000	71 (18.9)	100 (28.7)	<0.001
	₦18,000- ₦49, 000	106 (28.3)	128 (36.7)	
	₦50,000-₦100,000	123 (32.8)	77 (22.1)	
	> ₦100,000	75 (20.0)	44 (12.6)	

^βM-W=Mann-Whitney U test (p value), SD = Standard deviation, ~Differences between cases and controls based on LRT (likelihood ratio test). *Excluded (cases with contradictory answers /Participants whose menstrual flow ceased as a result of other reasons apart from the natural process). ^δBased on the t-test of independent samples. *Missing values include 'not applicable'. ^αSymbol of Naira (Nigerian currency)

for controls than cases ($p < 0.05$).

Unadjusted analysis suggests that the likelihood of breast cancer among women with history of regular alcohol consumption, women with family history of breast cancer and women with higher frequency of LEAN were significantly higher than women without regular history of alcohol consumption, family history of breast cancer, and women with lower LEAN frequency ($P < 0.05$). According to table 3, women with LEAN frequency higher than 5 times a week (compared to women without LEAN) had significantly higher risk of breast cancer after adjustments for base variables (age, study location and ethnicity). The estimate attenuated after further adjustments for educational attainments, and income. The estimate however, increased

significantly (although with a wider confidence interval and a non-significant trend) following full adjustments including reproductive factors, BMI, PA and duration of night duties (OR 1.87, 95% CI: 1.09, 3.21). Table 3 further showed that the risk of breast cancer among women with average interpregnancy gap ≥ 3 years (compared to those with average interpregnancy gap ≤ 1.5 years) had a non-significantly increased risk of breast cancer after adjustment for the base variables, educational attainment and income. The risk further increased and became significant after adjustment for parity, total months of breastfeeding, age at first full-term pregnancy, age at menarche and oral contraceptive use (OR 1.72, 95% CI: 1.03, 2.88). Every additional 1-year average increase in in interpregnancy gap

Table 2: Alcohol consumption, family history of breast cancer, average interpregnancy gap and the risk of breast cancer (unadjusted analysis).

Characteristics	Control n (%)	Case n (%)	^b OR (95% CI ^a)	^c P-value	Missing values (%)
^aLEAN frequency/week				0.026	16.8
Never	221 (67.6)	186 (57.4)	1.00 (ref)		
1-2times	22 (6.7)	28 (8.6)	1.51 (0.84, 2.73)		
3-5times	31 (9.5)	30 (9.3)	1.15 (0.67, 1.97)		
>5times	53 (16.2)	80 (24.7)	1.79 (1.20, 2.67)		
Average ^dIPG(Yrs)				0.112	15.6
≤ 1.50	102 (30.1)	86 (26.8)	1.00 (ref)		
1.51- 3.00	175 (51.6)	155 (48.3)	1.05 (0.73, 1.51)		
≥ 3.00	62 (18.3)	80 (24.9)	1.53 (0.99, 2.37)		
Ever consumed alcohol				0.894	0.5
No	235 (58.9)	225 (59.4)	1.00 (ref)		
Yes	164 (41.1)	154 (40.6)	0.98 (0.74, 1.31)		
History of regular alcohol consumption				0.003	18.8
No	235 (78.1)	225 (67.4)	1.00 (ref)		
Yes	66 (21.9)	109 (32.6)	1.73 (1.21, 2.46)		
Family History of breast cancer				0.003	0.4
No	381 (95.3)	339 (89.4)	1.00 (ref)		
Yes	19 (4.8)	40 (10.6)	2.37 (1.34, 4.17)		

^aLight exposure at night. ^bOdds ratio. ^cConfidence interval. ^dAverage interpregnancy gap. IPG: Interpregnancy gap. LEAN: Light Exposure at Night

per birth was associated with a 20% (95% CI: 3%, 36%) increase risk of breast cancer following full adjustment.

Tables 4 and 5 suggest that the increased risk of breast cancer associated with every additional 1-year increase in the interpregnancy gap was more pronounced and significant among postmenopausal women (OR 1.29, 95% CI: 1.07, 1.57), women >40 years (OR 1.25, 95% CI: 1.05, 1.44), women with age at first full-term pregnancy <25 years (OR 1.27, 95% CI: 1.05, 1.54) and women with 1-3 children (OR 1.23, 95% CI: 1.06, 1.44)

compared to premenopausal women, women < 40 years, women with age at first full-term pregnancy > 25 years and women who had more than 3 children respectively.

Moreover, as shown in Table 3, the risk of breast cancer between women who had ever consumed alcohol and women who had never consumed alcohol was not significantly different following full adjustments. However, in an analysis restricted to women with a history of regular alcohol consumption (compared to women without a regular history of alcohol

Table 3: Novel breast cancer risk factors (Multivariable analysis)

Main effects	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)
^bLEAN			
Never	1.00 (ref) ^a	1.00 (ref) ^b	1.00 (ref) ^c
1-2times	1.43 (0.78, 2.63)	1.59 (0.82, 3.07)	1.32 (0.52, 3.37)
3-5times	1.21 (0.70, 2.11)	1.21 (0.66, 2.19)	1.41 (0.64, 3.10)
>5times	1.86 (1.24, 2.79)	1.73 (1.12, 2.66)	1.87 (1.09, 3.21)
P for trend	0.023	0.067	0.153
Average IPG(Yrs)			
≤1.50	1.00 (ref) ^a	1.00 (ref) ^b	1.00 (ref) ^d
1.51- 3.00	0.98 (0.66, 1.44)	0.93 (0.63, 1.39)	0.94 (0.61, 1.45)
>3.00	0.69 (0.45, 1.05)	1.48 (0.91, 2.39)	1.72 (1.03, 2.88)
Per 1-year average increase	1.16 (1.04, 1.30)	1.15 (1.02, 1.29)	1.20 (1.06, 1.36)
P for trend	0.006	0.015	0.004
Ever consumed alcohol			
No	1.00 (ref) ^a	1.00 (ref) ^e	1.00 (ref) ^f
Yes	0.99 (0.67, 1.22)	0.88 (0.64, 1.21)	0.98 (0.66, 1.45)
History of regular alcohol consumption			
No	1.00 (ref) ^a	1.00 (ref) ^e	1.00 (ref) ^f
Yes	1.62 (1.12, 2.34)	1.51 (1.02, 2.24)	1.66 (1.03, 2.67)
Family History of breast cancer			
No	1.00 (ref) ^g	1.00 (ref) ^h	1.00 (ref) ⁱ
Yes	2.52 (1.42, 4.47)	2.51 (1.41, 4.48)	2.11 (1.13, 3.92)

^aAdjusted for age, study locations/study sites, and ethnicity. ^bAdditionally adjusted for educational attainment and income. ^cAdditionally adjusted parity, TBF, AAFP, menopausal status, duration of night duties, BMI, and total PA. ^dAdditionally adjusted for parity, AAFP, TBF, AAM, OCU. ^eAdjusted further for family history of breast cancer, income, educational attainment. ^fAdjusted further for parity, menopausal status, age at first birth, and BMI. ^gAdjusted for age and study location. ^hAdditionally adjusted for ethnicity. ⁱAdditionally adjusted for maternal and paternal education, and Height.

consumption), the increased risk of breast cancer attenuated but remained significant following adjustment for age, study sites, and ethnicity (OR 1.62, 95% CI: 1.12, 2.34). The estimate remained elevated and significant following adjustments for family history of breast cancer, SES, reproductive and anthropometric variables (OR 1.67, 95% CI: 1.04, 2.69). Table 4 suggests that the estimate was significantly stronger among younger/premenopausal women than older/postmenopausal women.

The risk of breast cancer among women with a family history of breast cancer (compared to women without a family history of breast cancer) increased after adjustments for age and study location (OR 2.52, 95% CI: 1.42, 4.47). The risk attenuated progressively but remained significant following adjustments for ethnicity, maternal education, paternal education, and height (OR 2.11, 95% CI: 1.14, 3.93).

DISCUSSION

The findings suggest that higher LEAN frequency, average interpregnancy gap ≥ 3 -year, history of regular alcohol consumption, and family history of

breast cancer were significantly associated with an increased risk of breast cancer. While the increased risk of breast cancer associated with regular consumption of alcohol was more pronounced among premenopausal and younger women, the increased risk of breast cancer associated with average interpregnancy gap was more pronounced among postmenopausal women, women above 40 years old, women with age at first full-term pregnancy < 25 years and women who had 1-3 children.

There were no existing African studies on the relationship between LEAN frequency and breast cancer risk. However, our finding was consistent with observations in other parts of the world [9, 12-14]. With the increasing family and work responsibilities among women, especially those residing in the urban environment of Nigeria, it will be expected that many may have a course to stay awake at night to meet family and societal expectations. However, we did not consider whether this habitual light exposure occurred while sleeping or while they were awake. We recommend that the study be confirmed in the future based on a hypothesis-driven investigation capable of assessing subgroup effects. According

Table 4: The relationship between regular alcohol consumption, interpregnancy gap, and the risk of breast cancer stratified by menopausal status

	Stratification					
	Premenopausal			Post-menopausal		
	^a OR (95% CI)			^a OR (95% CI)		
History of regular alcohol consumption						
No	93 (66.4)	134 (80.7)	1.00 (ref)	90 (65.7)	90 (73.2)	1.00 (ref)
Yes	47 (33.6)	32 (19.3)	2.67 (1.24, 5.79)	47 (34.3)	33 (26.8)	1.23 (0.63, 2.40)
Average interpregnancy gap-AIPG (Yrs)						
≤ 1.50	48 (39)	64 (34.2)	1.00 (ref)	25 (17.9)	34 (24.3)	1.00 (ref)
1.51- 3.00	52 (42.3)	95 (50.8)	0.71 (0.37, 1.37)	69 (49.3)	74 (52.9)	1.08 (0.51, 2.31)
≥ 3.01	23 (18.7)	28 (15.0)	1.28 (0.54, 3.07)	46 (32.9)	32 (22.9)	2.38 (1.06, 5.33)
Per additional 1 year average			1.11 (0.90, 1.37)			1.29 (1.07, 1.57)
P for trend			0.335			0.008

AIPG: Average interpregnancy gap. CI: Confidence interval

Table 5: The relationship between regular alcohol consumption, interpregnancy gap, and the risk of breast cancer stratified by age

		Age stratification				
		Age < 40yrs			Age ≥ 40yrs	
		ªOR (95% CI)			ªOR (95% CI)	
History of regular alcohol consumption						
No						
Yes	135(68.2)	143(78.6)	1.00(ref)	90(66.2)	92(77.3)	1.00(ref)
	63(31.8)	39(21.4)	2.18(1.04, 4.59)	46(33.8)	27(22.7)	1.43(0.69,2.96)
AIPG (Yrs)						
≤1.50	64(35.4)	69(35.0)	1.00 (ref)	22(15.7)	33(23.2)	1.00 (ref)
1.51- 3.00	87(48.1)	100(50.8)	0.69 (0.29, 1.64)	68(48.6)	75(52.8)	1.35 (0.80, 2.29)
≥3.01	30(16.6)	28(14.2)	0.53 (0.12, 2.28)	50(35.7)	34(23.9)	2.23 (1.22, 4.08)
Per additional 1 year average			0.91 (0.62, 1.35)		1.25 (1.05, 1.44)	
P for trend			0.647		0.002	
Age at first full-term pregnancy						
AAFP <25 YEARS			AAFP>25 YEARS			
AIPG (Yrs)						
≤1.50	19(13.3)	24(17.4)	1.00(ref)	65(36.9)	78(38.8)	1.00(ref)
1.51- 3.00	72(50.3)	80(58.0)	0.89 (0.40, 1.99)	83(47.2)	95(47.3)	1.04 (0.61, 1.77)
≥3.01	52(36.4)	34(24.6)	2.09(0.89, 4.88)	28(15.9)	28(13.9)	1.27 (0.63, 2.57)
Per additional 1 year average			1.27(1.05,1.54)		1.15(0.96, 1.38)	
P for trend			0.011		0.113	
Parity						
1-3 births			≥4births			
AIPG (Yrs)						
≤1.50	57(36.3)	76(39.4)	1.00(ref)	26(16.1)	25(17.2)	1.00(ref)
1.51- 3.00	59(37.6)	82(42.5)	0.98 (0.54, 1.77)	96(59.6)	93(64.1)	0.95 (0.48, 1.91)
≥3.01	41(26.1)	35(18.1)	1.90 (0.94, 3.83)	39(24.2)	27(18.6)	1.60 (0.67, 3.82)
Per additional 1 year average			1.23 (1.06, 1.44)		1.18 (0.89, 1.57)	
P for trend			0.006		0.249	

AIPG: Average interpregnancy gap. CI: Confidence interval

to existing literature, the hypothesized mechanism by which LEAN could increase breast cancer risk

is mediated by the suppressive effect of LEAN on melatonin levels [12, 14, 15]. Melatonin, which

reaches its secretion peak at night, has been postulated to have anticarcinogenic properties mediated by its direct oncostatic properties (including antiproliferative and antioxidant effects) and its indirect antiestrogenic effects [16].

The relationship between an average interpregnancy gap and breast cancer risk has been reported only in a few analytical studies globally. However, our findings among all women were consistent with the increased risk of breast cancer associated with a longer interpregnancy gap compared with a shorter interpregnancy gap in the available studies [6-8]. A Finnish study has observed that the increased risk of breast cancer associated with a longer average interpregnancy gap may be more applicable to lobular breast cancer (than ductal breast cancer), especially among older women [7]. While this observation was consistent with our stratified analysis by age and menopausal status, our cases were not segregated into ductal and lobular breast cancer subtypes. Moreover, while the increased risk of breast cancer associated with an average longer interpregnancy gap among women with age at first full-term birth <25 years in our study may be consistent with the observation of Kauppilla and colleagues with respect to ductal breast cancer among women with age at first birth < 30 years, the observation in that study unlike our study was restricted to the interpregnancy gap between 1st and 2nd pregnancy among women aged < 50 years [17]. There is, therefore, need for a larger study within Africa with specific data on specific birth intervals between the first and subsequent pregnancies. Although our findings seem to indicate that a shorter interpregnancy gap < 3 years may be beneficial, especially among women with fewer children, this needs to be confirmed in a more robustly designed hypothesis-driven study. Our findings with respect to alcohol consumption were consistent with other previous sub-Saharan African studies although these studies have small sample sizes and adjusted for a fewer number of confounders [18, 19]. Nevertheless, our finding corroborated the increased risk of breast cancer among women with weekly history of alcohol consumption reported in the African Breast Cancer Study (ABCS) comprising participants from Nigeria, Uganda and Cameroon [20]. However, other studies did not observe a significant association between alcohol consumption and breast cancer risk [21, 22]. This may be attributed to the type

of questions asked. For example, we only observed a significant finding when the case definition was restricted to weekly (regular) consumption of alcohol. When compared to the distribution of regular alcohol consumption reported in previous Nigerian studies [19, 22], our findings may reflect a rising trend of alcohol usage among Nigerian women, especially the younger generation. Incidentally, alcohol usage is not an acceptable practice among Nigerian women, and given that its usage among them may be underestimated, most educational and intervention programmes towards its adverse effects have targeted mostly male folks. Our study suggests the need to widen the scope of such awareness programmes to include women, given the need to prevent the rising trend of breast cancer among them. The potential carcinogenic effect of alcohol has been linked to the carcinogenic effect of ethanol metabolite- acetyl aldehyde, and the capacity of alcohol to alter blood estrogen levels [23].

The increased risk of breast cancer associated with family history of cancer in our study corroborated the observation in previous indigenous studies and other international studies [18, 22, 24, 25, 26]. The estimate could reflect the prevalence of inherited breast cancer genes (BRCA1 and BRCA2) in Nigeria, which have been reported to have an overall mutation rate of 11% [27]. It is, however, notable that most breast cancer cases in this study (89%) had no family history of breast cancer. This suggests that the high prevalence of inheritable breast cancer genes may not to a large extent, account for the current incidence rate of breast cancer in Nigeria. Therefore, the role of changes in reproductive and other lifestyle variables should not be underestimated.

The interpretation of our findings should consider the fact that the findings were not based on prior specific hypothesis with respect to these putative risk factors. For example, we lacked data on the quantity and duration of alcohol consumed. Hence, it was not certain if the findings could have been different had these been taken into consideration. There was also the potential to underreport alcohol consumption, given that it is not desirable among Nigerian women for cultural and religious reasons. Moreover, the study sample size was not large enough to explore detailed subgroup analyses observed in previous studies. However, post hoc computation suggests that it was sufficient to produce the main findings. All the

same, the findings showed consistency with similar previous studies within and outside Africa. Notably, this study is the first African study to investigate the association between the interpregnancy gap, LEAN, and the risk of breast cancer. Hence it has generated an important hypothesis that should be further investigated in future studies. If LEAN is confirmed as an emerging breast cancer risk factor in sub-Saharan Africa, then our observation provides a good opportunity for breast cancer prevention since LEAN is a factor that could be modified.

CONCLUSION

The findings suggest that habitual LEAN, longer interpregnancy gap, consumption of alcohol, and family history of breast cancer were associated with an increased risk of breast cancer among Nigerian women. The study also hypothesizes that frequent exposure to light at night and longer interpregnancy gaps increase breast cancer risk in Nigeria. Further investigation is therefore recommended. Furthermore, the study suggests the need to strengthen the campaign and advocacy towards reduced alcohol consumption among women and prioritize breast cancer risk reduction intervention among women with a family history of breast cancer.

REFERENCES

1. Azubuike, S. O.; Muirhead, C.; Hayes, L; and McNally, R. Rising global burden of breast cancer: the case of sub-Saharan Africa (with emphasis on Nigeria) and implications for regional development: a review. *World journal of surgical oncology* 2018, 16, 63.
2. Iddrisu, M.; Aziato, L.; Ohene, L. A. Socio-economic impact of breast cancer on young women in Ghana: A qualitative study. *Nursing Open* 2021, 8, 29-38.
3. Azubuike, S. O.; Hayes, L.; Sharp, L.; Alabi, A.; Oyeseun, R.; McNally, R. Socio-economic status and the risk of breast cancer among Nigerian women: a case control study. *The Pan African Medical Journal* 2022, 41.
4. Ogundiran, T. O.; Huo, D.; Adenipekun, A.; Campbell, O.; Oyeseun, R.; Akang, E.; Adebamowo, C; Olopade, O. I. Body fat distribution and breast cancer risk: findings from the Nigerian breast cancer study. *Cancer Causes & Control* 2012, 23, 565-74.
5. Azubuike, S. O.; Hayes, L.; Sharp, L.; Alabi, A.; Oyeseun, R; McNally, R.. Physical activity and the risk of breast cancer among Nigerian women. *Cancer Epidemiology* 2022, 78, 102163.
6. Albrektsen, G.; Heuch, I.; Hansen, S.; Kvåle, G. Breast cancer risk by age at birth, time since birth and time intervals between births: exploring interaction effects. *British journal of cancer* 2005, 92, 167-75.
7. Katuwal, S.; Tapanainen, J. S.; Pukkala, E.; Kauppila, A. The effect of length of birth interval on the risk of breast cancer by subtype in grand multiparous women. *BMC cancer* 2019, 19, 1-7.
8. Pasdar, Z.; Scott, N. W.; Iversen, L.; Hannaford, P. C.; Myint, P. K; Bhattacharya, S. Reproductive pattern of parous women and the risk of cancer in later life. *Cancers* 2021, 13, 3731.
9. Urbano, T.; Vinceti, M.; Wise, L. A; and Filippini, T. Light at night and risk of breast cancer: a systematic review and dose-response meta-analysis. *Int J Health Geogr* 2021, 20, 44.
10. Johns, L. E.; Jones, M. E.; Schoemaker, M. J.; McFadden, E.; Ashworth, A.; Swerdlow, A. J. Domestic light at night and breast cancer risk: a prospective analysis of 105000 UK women in the Generations Study. *Br J Cancer* 2018, 118, 600-6.
11. Field, A. *Discovering statistics using SPSS*. 4th ed. London: Sage publications; 2009.
12. Davis, S.; Mirick, D. K.; and Stevens, R. G. Night shift work, light at night, and risk of breast cancer. *Journal of the national cancer institute* 2001, 93, 1557-62.
13. Lai, K. Y.; Sarkar, C.; Ni, M. Y.; Cheung, L. W. T.; Gallacher, J.; Webster, C. Exposure to light at night (LAN) and risk of breast cancer: A systematic review and meta-analysis. *Science of The Total Environment* 2021, 762, 143159.
14. Hurley, S.; Goldberg, D.; Nelson, D.; Hertz, A.; Horn-Ross, P. L.; Bernstein, L; and Reynolds, P.. Light at Night and Breast Cancer Risk Among California Teachers. *Epidemiology* 2014, 25, 697-706.
15. Spivey, A. Light at night and breast cancer risk worldwide. *Environ Health Perspect* 2010, 118, 525.
16. Garcia, E.; Hurley, S.; Nelson, D. O.; Gunier, R. B.; Hertz, A.; Reynolds, P. 'Evaluation o. Evaluation of the agreement between modeled and monitored ambient hazardous air pollutants in California. *International journal of environmental health research* 2014, 24, 363-77.
17. Kauppila, A.; Kyrrönen, P.; Lehtinen, M.; Pukkala, E. Dual effect of short interval between

first and second birth on ductal breast cancer risk in Finland. *Cancer Causes and Control* 2012, 23, 187-93.

18. Balekouzou, A.; Yin, P.; Afewerky, H. K.; Bekolo, C.; Pamatika, C. M.; Nambei, S. W.; Djeintote, M.; Doui Doumga, A.; Mossoro-Kpinde, C. D. et al. Behavioral risk factors of breast cancer in Bangui of Central African Republic: A retrospective case-control study. *PLoS One* 2017, 12, e0171154.

19. Adebamowo, C; Adekunle, O. Case-controlled study of the epidemiological risk factors for breast cancer in Nigeria. *British Journal of Surgery* 1999, 86, 665-8.

20. Qian, F; Ogundiran, T.; Hou, N.; Ndom, P.; Gakwaya, A.; Jombwe, J.; Morhason-Bello, I.; Adebamowo, C.; Ademola, A; Ojengbede, O. Alcohol consumption and breast cancer risk among women in three sub-Saharan African countries. *PLoS On* 2014, 9, e106908.

21. Galukande, M.; Wabinga, H.; Mirembe, F.; Karamagi, C; Asea, A. Breast Cancer Risk Factors among Ugandan Women at a Tertiary Hospital: A Case-Control Study. *Oncology* 2016, 90, 356-62.

22. Okobia, M.; Bunker, C.; Zmuda, J.; Kammerer, C.; Vogel, V.; Uche, E.; Anyanwu, S.; Ezeome, E.; Ferrell, R; Kuller, L. et al. Case-control study of

risk factors for breast cancer in Nigerian women. *International Journal of Cancer* 2006, 119, 2179-85.

23. Seitz, HK; Becker, P. Alcohol metabolism and cancer risk. *Alcohol Research & Health* 2007, 30, 38.

24. Brinton, L. A.; Awuah, B.; Nat Clegg-Lamprey, J.; Wiafe-Addai, B.; Ansong, D.; Nyarko, K. M.; Wiafe, S.; Yarney, J.; Biritwum, R.; Brotzman, M. et al. Design considerations for identifying breast cancer risk factors in a population-based study in Africa. *Int J Cancer* 2017, 140, 2667-77.

25. Brewer, H. R.; Jones, M. E.; Schoemaker, M. J.; Ashworth, A.; Swerdlow, A. J. Family history and risk of breast cancer: an analysis accounting for family structure. *Breast cancer research and treatment* 2017, 165, 193-200.

26. Colditz, G. A.; Kaphingst, K. A.; Hankinson, S. E.; Rosner, B. Family history and risk of breast cancer: nurses' health study. *Breast cancer research and treatment* 2012, 133, 1097-104.

27. Zheng, Y.; Walsh, T.; Gulsuner, S.; Casadei, S.; Lee, M. K.; Ogundiran, T. O.; Ademola, A.; Falusi, A. G.; Adebamowo, C. A; Oluwasola, A. O. et al. Inherited breast cancer in Nigerian women. *Journal of Clinical Oncology* 2018, 36, 2820.