SOME ENVIRONMENTAL AND NON-HORMONAL RISK FACTORS AND BREAST CANCER AMONG WOMEN IN PORT HARCOURT: A CASE-CONTROL STUDY

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Breast cancer, Heavy Metals, Radiation, Other Non-Hormonal Risk factors.

Abstract

Context: The relationship between heavy metal pollutants and human cancer induction has long been established, as well as a close association between heavy metal (such as Lead and Cadmium) and breast cancer especially in the environment of crude exploration, production and distribution.
Aims: The aim of this study therefore was to find out the association between these risk factors and breast cancer, among women in Port Harcourt, Rivers State Nigeria.
Settings and Design: Out-patient clinics of public tertiary health care facilities in Port Harcourt. This was a case control study.
Methods and Material: Cases were patients with clinically and histologically confirmed breast cancer and controls were matched and selected from the out-patient clinics of the same facilities.
Statistical analysis used: SPSS vs 21 was used to analyse data, descriptive statistics, chi square and Mantel-Haenszel Chi Square tests were done, P- value was set at ≤ 0.05.
Results: The mean age for the cases and controls was 44.67±13.41 and 46.11±13.76 years respectively. Exposure to crude oil spillage does not appear to be a risk factor for developing breast cancer (OR=0.84, 95% CI=0.54-1.31).
Conclusions: This study showed no significant risk association between some of these environmental factors and breast cancer.

Introduction

Breast Cancer remains the commonest malignancy worldwide; between 2008 and 2012, 1.7 million new cases of breast cancers were diagnosed[1]. During this time period, an observed increase in global incidence of breast cancer by 20 percent and an increase of 14 percent in mortality was reported. The Breast Health Global Initiative in 2014, projected that there will be 19.7 million new cases of breast cancer within the next ten years with more than half occurring in the less developed countries[2].

Residence in oil exploring community: In Rivers State crude oil spillage is a common occurrence. Schmidt-Etkin reported[3] that the major source of spillage among others is the oil companies through the process of exploration, production and distribution of the products. Researchers have found out that the spilled oil and its products within the region have high concentration of heavy metals that can be detrimental to human health: Cadmium (Cd), Chromium (Cr), Copper (Cu), Iron (Fe), Nickel (Ni), and Lead (Pb) were found in water and sediments[4]. Similarly, Pb, Zinc (Zn), Cu, Ni, Cd, Cobalt (Co), Cr, Fe, and Manganese (Mn) were found in fish[5]. Strontium (Sr), Zn, Pb, Barium (Ba), and Fe were found in soil sediments and solid waste[6]. Untreated industrial waste containing toxic heavy metals especially cadmium was reported[7] at levels exceeding that considered safe for the general population[8]. Meanwhile the relationship between heavy metal pollutants and human cancer induction has long been established[9, 10].

El-Harouny et al.[11] found higher tissue and urinary concentration of cadmium in breast cancer patients compared to others, and concluded that these environmental pollutants may have a causal association with breast cancer. It has also been reported that cadmium induces deoxy-ribonucleic acid (DNA) damage in normal tissues and in breast cancer cells. The female sex hormone oestrogen, whether exogenous (as in OCP) or endogenously produced, is associated with occurrence of breast cancer, and studies have indicated that toxic heavy metals exhibit “oestrogen-like” activity on human cells[12, 13]. Researchers have also found out that heavy metal lead to nitrosative and oxidative stress –

inhibition of enzyme function, DNA synthesis and repair[14-16]; and macromolecules damage with consequent cellular apoptosis or necrosis[16, 17]. A close association between heavy metal (such as Lead and Cadmium) and breast cancer has similarly been documented[9, 10].

Alcohol Consumption: Bowlin et al.[18], had reported a dose-related 50% increase risk of breast cancer among women who consume ≥ 5g of alcohol per day. Other studies[19-22] have reported an increased risk following each 10gram increase in alcohol intake. The mechanism of this association is not well known and postulations include: through increase in estrogen level[23] and through reduction in folate intake[24]. Some researchers have reported mediation through estrogen and progesterone receptors[22, 25, 26] while others still feel alcohol act as breast tumour promoter and a weak cumulative carcinogen[27].

Tobacco Consumption: Tobacco is available in various forms such as cigarettes, cigars & cigarillos, chewing tobacco, snuffs, Hookahs, and Spliffs to name a few. Studies have suggested that tobacco has carcinogenic potential[28] and contains tumour-inducing fat-soluble substances[29].

Obesity: Obesity is said to be present when the body weight is ≥ 120% of the median weight for height or the ideal body weight. The role of hyper-insulinemia, oestrogens, and androgens in the association between obesity and breast cancer has been reported[30, 31]. Elevated type-1 insulin-like growth factors, resulting from hyper-insulinemia occasioned by insulin resistance in obese women, are reported to have anti-apoptotic and tumour promoting characteristics[32, 33]. Obesity in women carries a higher risk of breast cancer when obesity occurs in late post-menopausal period[31, 34].

Family History: The hereditary cancers are reported to be autosomal dominant in transmission; have early onset; exhibit multiple primary cancers in the affected person; are often multifocal or bilateral; 50% risk of occurrence in first degree relatives of mutant carriers; and clustering of rare cancers. The failure of DNA repair function occasioned by mutations in BRCA1 and BRCA2 genes whose role is to repair damaged DNA[35, 36] is responsible for breast cancer that develop in hereditary breast cancers due to BRCA genes.

Ionizing radiation: It was reported[37] that the risk of exposure to increased radiation when products of the earth crust are extracted, refined and used. This is applicable in the Niger Delta environment because of crude oil exploration.

Materials and methods

This study aimed to determine the relationship between exposure to non-hormonal risk factors, (alcohol consumption, tobacco usage, obesity, and hereditary/family History), environmental pollutants (Oil spillage, radiation and telecommunication mast) and breast cancer among women resident in Port Harcourt within the last 15 years.

Null Hypothesis: There is no significant difference between cases and controls in their exposure to individual breast cancer risk factors among women in Port Harcourt in the last 15 years.
Subjects and Methods: Clinically and histologically confirmed breast cancer patients as cases; and matched and selected other non-cancer patients from the out-patient clinics of the same facilities as controls.

Study Sites: The study was carried out in the out-patient clinics of public tertiary health care facilities in Port Harcourt: The University of Port Harcourt Teaching Hospital (UPTH); Kelsey Harrison Specialist Hospital (KHSH); Braithwaite Memorial Specialist Hospital (BMSH), Military Hospital, and some other private clinics in 2016.

Research Design: This was a hospital-based case control study. Cases and controls were individually matched on a ratio of 1:1 based on age and sex. Cases and controls were recruited over a 3-month period from October to December 2016, and data was collected via an interviewer-administered questionnaire for respondents that were not literate and for those that were, it was self-administered.
Study Population: The respondents were made
up of female patients aged 20 years and above. The study was carried out among all patients with histologically confirmed breast cancer (as cases) and non-cancer patients (as controls) in the out-patient clinics and wards of the same public tertiary hospitals. The sample size was determined using the formula for sample size calculation for case-control studies and a total of 213 participants was gotten for each group[38].

$$n = \left(\frac{r+1}{r}\right)\frac{(\bar{P})(1-\bar{P})(Z_{\beta}+Z_{\alpha/2})^2}{(P1-P2)^2}$$

Methods of Data Analysis: Data was analysed using IBM Statistical Package for Social Sciences (SPSS) Vs 21 and presented in tables. Descriptive analysis was carried out for demographic characterization; Mantel-Haenszel Chi Square test was done to test for risk of association between the dependent variable (breast cancer) and the independent variables above, (P- value was set at ≤ 0.05).

Validity/Reliability of Instrument: The study instrument was pre-tested among similar group of cases and control (at Federal Medical Centre, Yenagoa and The Niger Delta University Teaching Hospital, Okolobiri), and necessary corrections made before use.

Ethical Considerations: The approval of the ethical committee of The University of Port Harcourt was sought and obtained. Permission was also sought in writing to carry out the study from other centres and informed consent was obtained from the participants prior to data collection.

Results

The age range with the highest number 68 (31.9%) of cases was 30-39years; and the age range with the least number of cases was ≥70years as shown in Table 1a. The mean age for the cases was 44.67±13.41years and that for the control group was 46.11±13.76 years. Table 1a above shows that only 1 (0.5%) participant in the control group had no formal education, otherwise all others had at least a primary education. In all, those with tertiary education appear to be in the majority in both the cases 114 (53.5%) and control 104 (48.8%) group, followed by participants with secondary education. There were no statistical differences (P≤ 0.05) between the controls and the cases.

Table 1a: Socio-demographic characteristics among cases and controls

This table shows the age distribution and educational status of participants for both cases and control.

Variables	**Cases (%)**	**Control (%)**	**Total (%)**		
	(n=213)	**(n=213)**		X^2	**p-value**
Age (years)					
20-29	25 (11.7)	23 (10.8)	48 (11.3)	0.0035	0.953
30-39	68 (31.9)	56 (26.3)	124 (29.1)	0.5934	0.4411
40-49	47 (22.1)	57 (26.8)	104 (24.4)	0.4636	0.4959
50-59	37 (17.4)	37 (17.4)	74 (17.4)	0.0203	0.8867
60-69	24 (11.3)	28 (13.2)	52 (12.2)	0.0802	0.777
≥70	12 (5.6)	12 (5.6)	24 (5.6)	0.0625	0.8025
Mean age	44.67±13.41	46.11±13.76			
Education					

None	0 (0.0)	1 (0.5)	1 (0.2)	0.6666	*1.000
Primary	36 (17.0)	48 (22.5)	84 (19.7)	0.877	0.349
Secondary	63 (29.65)	60 (28.2)	123 (28.9)	0.0122	0.912
Tertiary	114 (53.5)	104 (48.8)	218 (51.2)	0.221	0.6382

*Fisher Exact

The dominant religion of respondents in the study was Christianity amounting to 203 (95.31%) for cases and (205) 96.24% for controls. Most of the respondents were married 167(78.40%) for cases and 156 (73.24%) for the control group respectively. The participants in the study as shown in table 1b above belonged to twelve different occupations, with slightly more than a third 78 (36.62%) cases and 83 (38.97%) controls being business women. However, observed differences were not statistically significant (P≤ 0.05).

The relationship between exposure to non-hormonal risk factors (alcohol consumption, tobacco usage, obesity, and hereditary/family history) and breast cancer among women in Port Harcourt at least within the last 15 years is presented in Table 2 above. Table 2 indicates that there was no association between alcohol consumption and developing breast cancer (OR=0.99, 95% CI=0.64-1.52). Women who were exposed to tobacco use showed increased risk of developing breast cancer (OR=1.13, 95% CI=0.54-2.36) compared to those women respondents who were not exposed to tobacco use. However, the relationship was not statistically significant (p>0.05). The odd of developing breast cancer among women respondents who were obese was only slightly higher in cases when compared to controls as OR was 1.06 (95% CI=0.67-1.67).

Table 1b: Socio-demographic characteristics among cases and controls continue

Table 1b shows the religious affiliations of participants, their marital status and occupation

Variables	**Cases (%) (n=213)**	**Control (%) (n=213)**	**Total (%)**	X^2	**p- value**
Religion					
Christianity	203 (95.31)	205 (96.24)	408 (95.77)	0.0004	0.9838
Islam	10 (4.69)	8 (3.76)	18 (4.23)	0.0093	0.9232
Marital Status					
Single	34 (15.28)	35 (16.43)	69 (16.20)	0.0024	0.9608
Married	167 (78.40)	156 (73.24)	323 (75.82)	0.1863	0.6660
Separated	5 (2.35)	13 (6.10)	18 (4.23)	1.5999	0.2059
Widow	0 (0.0)	1 (0.47)	1 (0.23)	0.1875	*1.000
Divorced	7 (3.29)	8 (3.76)	15 (3.52)	0.0111	0.9160
Occupation					
Accountant	2 (0.94)	5 (2.35)	7 (1.64)	0.2188	*0.6424
Business	78 (36.62)	83 (38.97)	161 (37.79)	0.0507	0.8217
Civil servant	58 (27.23)	51 (23.94)	109 (25.59)	0.1851	0.6670
Farmer	7 (3.29)	9 (4.23)	16 (3.76)	0.0104	0.9186
Fishing	0 (0.0)	3 (1.41)	3 (0.70)	0.5626	*0.4642

Health worker	14 (6.57)	11 (5.16)	25 (5.87)	0.0601	0.8063
House-Keeping	7 (3.29)	7 (3.29)	14 (3.29)	0.1071	0.7434
Law Practice	1 (0.47)	2 (0.94)	3 (0.70)	0.0563	*1.000
Retired C/S	3 (1.41)	4 (1.88)	7 (1.64)	0.0239	*1.000
Self employed	5 (2.35)	7 (3.29)	12 (2.82)	0.0139	0.9060
Students	35 (16.43)	27 (12.68)	62 (14.55)	0.4551	0.4999

* Fisher Exact

Hereditary/family history of breast cancer or other cancers, did not appear to be a risk factor for developing breast cancer (OR=0.90, 95% CI=0.44-1.80), and the relationship was not statistically significant (p>0.05).

Exposure to crude oil spillage does not appear to be a risk factor for developing breast cancer (OR=0.84, 95% CI=0.54-1.31), and the relationship between risk of developing breast cancer and exposure to crude oil spillage was not statistically significant (p>0.05). Women who reported exposure to radiation via telecommunication mast showed increased risk of developing breast cancer (OR=1.09, 95% CI= 0.71-1.66) compared to those women respondents who were not exposed to telecommunication mast. However, this difference was not statistically significant (p≤0.05).

Table 2: Association between non-hormonal risk factors and breast cancer among cases and controls

Table 2 Illustrates the Mantel-Haenszel odd ratio, 95% Confidence interval and p-value for alcohol consumption, tobacco usage, family history and obesity for both cases and controls.

Risk Factors/Variables	**Cases**	**Control**	**Total**	**Odd Ratio (Mantel-Haenszel X2)**	**95% Confidence Interval (CI)**	**p-value**
Alcohol Consumption						
Yes	65	65	130	0.99	0.64-1.52	0.968
No	146	144	290	0		
Total	**211**	**209**	**420**			
Tobacco usage						
Yes	19	18	36	1.13	0.54-2.36	0.862
No	194	196	390	-0.03		
Total	**213**	**213**	**426**			
Obesity						
Yes (≥35kg/m^2)	154	154	308	1.06	0.67-1.67	0.892
No (<35kg/m^2)	53	56	109	-0.06		
Total	**207**	**210**	**417**			

Family history of breast cancer						
Yes	19	21	40	0.9	0.44-1.80	0.868
No	191	189	380	-0.11		
Total	**210**	**210**	**420**			
Family history of other cancers						
Yes	20	23	43	0.94	0.73-1.90	0.122
No	186	182	368	-0.25		
Total	**206**	**205**	**411**			

Table 3: Other environmental risk factors of breast cancer among cases and controls

Table 3 illustrates the odd ratio, 95% confidence interval and p-value for exposure to crude oil spillage; exposure to radiation from medical sources and exposure to telecommunication mast for both cases and controls.

Risk Factors/Variables	**Cases**	**Control**	**Total**	**Odd ratio (Mantel-Haenszel (X^2)**	**95% Confidence Interval (CI)**	**p-value**
Residence in oil exploring community/oil spillage within the last 15years						
Yes	59	68	127	0.84	0.54-1.31	0.491
No	148	144	292			
Total	**207**	**212**	**419**			
Exposure to radiation (medical)						
Yes	15	17	32	0.85	0.39-1.86	0.809
No	190	184	374			
Total	**205**	**201**	**406**			
Exposure to Telecommunication mast (Residence within 10 meters of mast)						
Daily	78	74	152	1.09	0.71-1.66	0.759
Not at all	126	130	256			
Total	**204**	**204**	**408**			

Discussion

This study has looked at non-hormonal factors associated with cancer of the breast. It was observed that cases who were obese, used tobacco, and lived within 10 meters of a telecommunication mast were at a slightly increased risk of developing cancer of the breast than controls. However, these observed differences were not statistically significant. These observed risk factors are modifiable factors and as such lifestyle changes should be encouraged in women of all ages. Findings from this study with respect to tobacco use is in agreement with findings from other studies which have implied that tobacco may have carcinogenic abilities[28]. Likewise, obesity has long been associated with a higher risk of developing cancer especially in older women[31, 34]. Exposure to non-ionizing radiation via telecommunication mast has also been associated with adverse health effects, but not enough evidence to causally link it with cancers[39, 40].

This study did not observe any association between residency in an oil producing area and cancer of the breast unlike a previous ecologic study which assessed discrepancies between environmental risk factors and cancers in two Nigerian cities Ibadan in South West Nigeria and Port Harcourt which is the area of study in this work. Environmental data were obtained reviewed for these 2 cities and a ten-year cancer record was also obtained from the main tertiary health institutions there. They found levels of polycyclic aromatic hydrocarbon in the air was higher in Port Harcourt than Ibadan locality ($p < 0.05$)[41].

Conclusion

Though this study showed no significant risk association between some of these environmental factors and breast cancer. There is a need for more research in this area. Besides, future research on this subject should favour population-based data and large analytical studies that will produce better evidence, in terms of generalization and ability to demonstrate causality.

Conflict of interest: None.

Ethical issues: The approval of the ethics review committee of the University of Port Harcourt and the University of Port Harcourt teaching Hospital were obtained before commencement of study.

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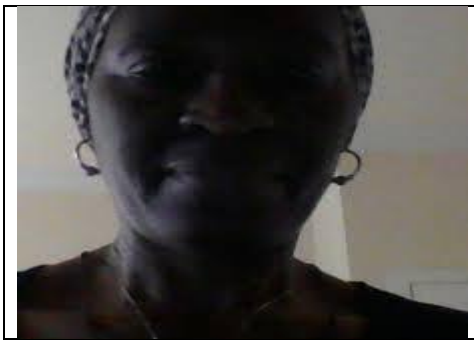

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