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Comparative study of breast cancer risk factors at Kenyatta National Hospital and the Nairobi Hospital

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Abstract Breast cancer rates in high-income countries increased sharply with industrialization and urbanization but are now declining. Rates in low-income countries are instead rising after adoption of western type lifestyles. Some breast cancer risk factors are modifiable for prevention while others are not. The purpose of this study was to find out if wearing of brassieres and psychosocial stress had association with breast cancer occurrence. It was conducted from 09/08/11 to 23/12/12. Women with newly diagnosed breast cancer were matched with controls for age. A questionnaire was administered to detail patterns of brassiere wearing and marital stability, and some known breast cancer risk factors which could be confounders. Multivariate statistical models were used to discriminate confounders, and significance calculated at 95% confidence intervals. Three hundred and thirty-nine cases and 355 controls were included. The median age for cases was 48 years, range 25 to 80 years. The median for controls was 49, range 23 to 83 years. Age at onset of menses, parity, and the number of children who breastfed for at least 12 months was similar between cases and controls. There was no difference in level of education (p=0.783), and marital status (p=0.432) between cases and controls. On the other hand intensity of brassiere use (p<0.001), occupation (p<0.001), area of residence (p=0.045) diet (p=<0.01), duration of use of hormonal contraceptives (p<0.001), and family history of breast cancer (p=0.016), had association with breast cancer occurrence.

Keywords Brassieres · Breast cancer · Risk factors · Cases · Controls · Research category · Epidemiology

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Introduction

Breast cancer is the number one cancer among women worldwide. In many developing countries it is second to carcinoma of the uterine cervix, but in others like Kenya it arguably ranks higher than cervical cancer (1). This scenario is different from decades back when breast cancer was considered to be rare among non affluent women in low-income countries. Adoption of affluent western lifestyles appears to have brought along some factors important in breast cancer causation. Some of these factors are yet to be comprehensively identified.

Evidence has pointed at various factors including high fat diets and sedentary lifestyles among others. After decades of increasing incidence, invasive breast cancer rates are declining in western countries, while at the same time increasing in low-income countries (2). Epidemiologic studies have already provided much information on important risk factors for breast cancer (3). These include age, family or personal history of breast cancer, reproductive history, and exposure to specific carcinogens. Many of these factors may be related to oestrogens, but in a series of patients seen at an oncology clinic, Lynch and Lynch documented a family history of breast cancer in only 32 of 325(9.8%) consecutively treated breast cancer patients(4). Estimates from population-based studies suggest that only 5-10% of cases are explained by inherited mutations in highly penetrant susceptibility genes such as BRCA1 and BRCA2 (5,6). These and TP53 gene abnormalities appear to be the most relevant in the clinic. Brassieres apply considerable pressure on the breasts have not been adequately studied, nor have psychosocial factors.

Breast cancer risk factors such as age and family history are nonmodifiable. Dietary risk factors and sedentary life styles are modifiable and are currently being addressed reasonably well in some high-income countries. Unfortunately, it seems that the reduction in breast cancer incidence by such measures may soon plateau and leave a sizeable proportion of women still exposed to breast cancer even in these societies.

The objectives of this study were to show breast cancer occurrence in relation to certain exposure factors, and by multivariate analysis, derive the major breast cancer associations. It also aimed at documenting the pattern of brassiere wearing in relation to breast cancer occurrence, and show if instability in a woman's marriage had a significant association with breast cancer occurrence.

Materials and methods

Cases were women with pathological diagnosis of breast cancer seen at the Kenyatta National Hospital and the Nairobi Hospital. Controls were women with other diagnoses than cancer, visiting the same hospitals and matched for age. A questionnaire was administered to interrogate known and unknown but specified risk factors. Women with tissue diagnosis of breast cancer in these hospitals were identified from wards and clinics, and were registered as cases. Once a case was identified, the investigators went through the records and verified the diagnosis, followed by administration of the questionnaire. The same was done for controls. Records were taken of residence, dietary factors, environmental or familial factors. Marital status, parity, breast feeding, and hormonal contraceptive use were also interrogated, as were educational background and occupation. Patterns of brassiere wearing were also detailed. A similar questionnaire was administered to controls.

Statistical anlysis

Data was analyzed first, by exploring population descriptive statistics. Continuous data were summarized by using means and standard deviations while categorical data were summarized by using frequencies and percentages. Multivariate logistic regression was used to evaluate factors associated with breast cancer occurrence. Significance was determined using Chi Square tests, at 95% confidence interval (Table 1).

Results

Between 9/08/11 and 23/12/12 inclusive, 363 cases and 363 controls were enrolled. Of these, 24 cases and 8 controls were excluded because of incomplete data, leaving 339 cases and 355 controls for analysis. The median age for cases was 48 years, range 25 to 80 years. The median for controls was 49, range 23 to 83 years. The median age at onset of menses for both cases and controls was 15 years with a range of 9 – 25 years for both. The median age at cessation of menses for cases was 45 years with a range recorded as 25 – 60. Further information could not be verified for the one patient who had cessation of menses recorded as having occurred at 25 and 30 years of age. The ages at cessation of menses for controls did not come out clearly either. Parity range for cases was 0-13 with a median of 3 and that for controls was 0-14 with a median of 4. The median number of cases who had breast fed children for at least a year was 3 with a range of 0-13, compared with a median of 4 and a range of 0-10 for controls (Table 2).

Table 1 Biodata.

Biodata	Cases	Controls
Age years:		
Range	25-80	23-83
Median	48	49
Age at onset of menses:		
Range	9-25	9-25
Median	15	15
Age at cessation of menses:		
Range	25-60	34-60
Median	45	47
Parity:		
Range	0-13	0-14
Median	3	4
Number of children who breastfed for at least a year:		
Range	0-13	0-10
Median	3	3

Only 38 cases (11.2%) and 57 controls (15.7%) had attained tertiary level of education. There was no correlation between breast cancer cases and controls in respect to level of education (p=0.056). Residential area was difficult to characterize in this study since the majority of cases and controls were recruited at the Kenyatta National Hospital. Over 60% of cases and controls came from low cost Nairobi residences and the adjacent parts of central Kenya. Cases from low cost Nairobi areas and central Kenya constituted 30.8% and 31% respectively. For controls the values were 21.4% and 40.3% respectively. Central Kenya and Nairobi low cost residences correlated significantly with cancer occurrence (p=0.045).

As for patterns of brassiere wearing, 24.8% of cases never wore brassieres, or only did so on important occasions, as opposed to 33.8% of controls. On the other hand, 9.1% of cases and 3.1% of controls wore brassieres all the time, even when in bed. Patterns of brassiere wearing were significantly correlated with cancer occurrence (p<0.001)

Occupation was difficult to characterize. Of note, only 9.7% of cases were recorded as housewives, compared with 22.5% among controls, and 34.5% of cases were categorized as labourers/peasants compared with 25.9% among controls. Less than 1% of cases were categorized as unemployed, as

Table 2 Exposure variables between cases and controls.

Variable	Cases		Controls		95% CI	OR	P value
	No	%	No	%			
Level of Education							
Primary and Below	168	49.6	163	45.0	0.9-1.7	1.3	0.783
Secondary	131	38.6	133	36.7	0.8-1.30	1.05	
Tertiary	38	11.2	57	15.7	0.40-0.9	0.6	
Unknown	2	0.6	9	2.5	0.2-8.6	1.2	
Residential Area							
Central	103	30.4	76	21.4	1.3-2.4	1.80	0.045
Nairobi low cost	105	31.0	143	10.3	0.1-0.6	0.2	
Nairobi medium cost	13	3.8	19	5.4	0.5-0.8	0.6	
Nairobi high cost	1	0.3	3	0.8	0.41-0.97	0.69	
Eastern	46	13.6	37	10.4	0.9-2.0	1.30	
Nyanza& western	31	9.1	39	11.0	0.7-1.9	1.2	
Coast	10	2.9	9	2.5	0.2-1.6	0.50	
Rift valley	25	7.4	28	7.9	0.5-1.3	0.8	
North Eastern	0	0	0	0	-	-	
Other	5	1.5	1	0.3	0.74-3.23	1.98	
Occupation							
Housewife	33	9.7	80	22.5	0.3-0.6	0.4	<0.001
Househelp	2	0.6	1	0.3	0.2-8.6	1.2	
Unemployed	3	0.9	21	5.9	0.2-0.7	0.3	
Labourer/peasant	117	34.5	92	25.9	1.5-2.7	1.9	
Large scale farmer	0	0	2	0.6	0.0-1.9	0.1	
Executive	2	0.6	7	2.0	0.8-1.97	1.1	
Artisan/businesswoman	155	45.7	126	35.5	0.8-1.6	1.1	
Secretary/clerical	12	3.5	18	5.0	0.3	1.9	
Other	15	4.4	8	2.3	0.6-2.4	1.2	
Diet							
Predominantly carbohydrates/vegetables	265	78.2	311	87.6	0.8-4.2	1.9	<0.01
Predominantly animal proteins	2	0.6	0	0	0.1-19.4	1.2	
Mixed, rich in fruits	63	18.6	24	6.8	0.2-2.0	0.7	
Others	9	2.7	20	5.6	0.1-4.3	0.4	
Marital status							
Married	254	74.9	256	72.1	0.9-1.7	1.2	0.432
Single	51	15.0	56	15.8	0.6-1.2	0.8	
Divorced/separated	32	9.4	36	10.1	0.5-1.4	0.9	
Other	2	0.6	7	2.0	0.9-1.7	1.3	
Use of hormonal contraceptives							
Never or less than a year	153	43.1	189	53.2	0.9-1.67	1.23	<0.001
For 1 – 10 years	125	36.9	104	29.3	1.05-2.11	1.48	
For Over 10 years	45	13.3	16	4.7	1.84-6.84	3.46	
Family history of breast cancer							
Yes	104	30.7	79	22.3	1.16-2.41	1.67	0.016
No	235	69.3	272	76.6	0.5-0.9	0.6	
Don't know	0	0	4	1.1	-	-	
Patterns of brassiere wearing							
Never or only during important occasions	84	24.8	120	33.8	1.0-2.0	1.5	
During most waking hours	211	62.2	199	56.0	0.4-0.7	0.5	<0.001
All the time even when in bed	31	9.1	11	3.1	1.6-7.1	3.4	

OR= Odds ratio ; 95% CI = 95% confidence intervals.

compared with 5.9% for controls. Being a housewife or unemployed appeared to correlate less with breast cancer occurrence ($p<0.001$). Diet was also difficult to categorize, with 78.2% of cases and 87.6% of controls indicating that they fed mainly on diets composed of carbohydrates and vegetables. More cases than controls (18.6% vs 6.8% respectively) indicated that they took mixed diet rich in fruits. Paradoxically, those who indicated that they took diet rich in fruits were more likely to have a diagnosis of breast cancer ($p<0.001$.)

Use of hormonal contraceptives for over 10 years correlated significantly with cancer occurrence as compared with the status never used, or used for less than 10 years ($p<0.001$). Marital status was well balanced between cases and controls and had no correlation with cancer occurrence ($p=0.432$). Cases who had never used hormonal contraceptives or only used them for less than a year were fewer than controls (43.1% vs 53.2%), and three times as many cases as controls had used hormonal contraceptives for more than 10 years (13.3 vs 4.7% respectively). Family history of breast cancer was positive among 30.7% of cases, as opposed to 22.3% of controls. It correlated significantly with breast cancer occurrence ($p=0.016$).

Discussion

Breast cancer is common globally, but the fact that rates are increasing in low-income countries like Kenya is worrying. It is possible that awareness being created in recent times, and improved diagnostic capability is pushing up the number of cases. This is also coupled with the increasing population. If on the other hand it is mainly to do with adoption of affluent western lifestyles then the affluence culprit should be identified for risk modification. Epidemiologic studies have provided much information on its important risk factors (3). These include age, family or personal history of breast cancer, reproductive history, and exposure to specific carcinogens. Age is a major risk factor (7), though in our study more than 50% of the patients were less than 50 years. Suffice it to say, the median age of occurrence of breast cancer in our local setting is on the increase, from 40 years barely 2 decades ago from our previous studies (1,8). This is in line with the increasing life expectancy, ensuring that the pool of older women with the risk to develop breast cancer is increasing. This may account for the observed increment over the years.

Age at onset of menses and age at cessation of menses may be important but were not accurately profiled in this study. Even the number of children who breastfed for at least a year did not differ between cases and controls.

There was a significant correlation between family history of breast cancer and breast cancer occurrence. Lynch and Lynch (4) documented a family history of breast cancer in 32(9.8%) of 325 consecutively treated breast cancer patients. Estimates from population-based studies suggest that only 5-10% of cases are explained by inherited mutations in highly penetrant susceptibility genes such as BRCA1 and BRCA2 (5,6). These and TP53 gene abnormalities are currently the most relevant in the clinic. To date, deleterious mutations in BRCA1 and BRCA2 account for the largest proportion of inherited breast cancers (6). TP53 and PTEN mutations, each account for fewer than 1% of cases (9). Breast cancer can cluster in families purely by chance, or as a result of shared environmental influences or shared life-style.

Women who wore brassieres all the time, even when in bed were significantly associated with breast cancer occurrence as compared with those who never wore brassieres, or those whomonly did so on important occasions ($p<0.001$). The wearing of brassieres, particularly underwire types or those that fit tightly, has been proposed to increase the risk of breast cancer. Singer and Grismaijer published their report in the book called 'Dressed to Kill', which describes a study they conducted (10). They reasoned that brasieres cause physical constriction that reduce lymphatic circulation, resulting in the retention of carcinogenic toxins. Unfortunately their work was never accepted for publication, and to date, there have been no scientifically valid studies that support the claim that brassieres may be associated with breast cancer occurrence. Ours does. To add to their theory, carcinogens released from blocked lymphatics may cause epigenetic changes impacting on cellular downstream signaling that may culminate in cancer. This may be made even easier if they acted on an already defective gate keeper gene in concert with Knudson's 'double hit hypothesis'.

Level of education was interrogated in our study as a marker of affluence which could be a confounder. There was however no difference between cases and controls ($p=0.783$). Only about 11% of cases and 16% 0f controls had attained tertiary level of education. The reason was that the majority of cases and controls were recruited from the Kenyatta National Hospital which serves a significant number of the less educated, poor population as compared with the Nairobi Hospital which is a high cost, private hospital.

Area of residence significantly pointed to Nairobi low cost areas and central Kenya as being associated with cancer occurrence ($p=0.045$). This variable was however difficult to categorize, and the majority of cases and controls came from Nairobi low cost areas and central Kenya. Occupation was also found difficult to classify in a meaningful way. However the unemployed and househelps appeared to be less exposed ($p<0.001$). Housewives were registered to be at risk. Distinction between housewives and househelps may require that one looks more closely at their backgrounds. Househelps in affluent neighbourhoods should be as exposed as their affluent employers, if not more.

Diet was most interesting with diet rich in fruits correlating significantly with cancer occurrence ($p<0.001$). Studies on diet and breast cancer risk have yielded varied results, only diets causing postmenopausal obesity being associated with reproduceable breast cancer risk (11). Unfortunately for this population it was impossible to draw clear dietary distinctions among a population whose diet is expected to be basically similar. The large international variation in breast cancer rates, in which countries with high-fat diets have higher rates than countries like Japan and less developed countries with low-fat diets, suggested that high-fat intake may be associated with increased breast cancer risk (12). However, pooled analysis of seven prospective epidemiologic studies does not indicate any association between fat intake and breast cancer risk in adult women in more developed countries (13). There may be a moderate protective effect from high vegetable consumption, but results of meat, fibre, and fruit consumption have been inconsistent. However, a positive association between alcohol consumption and breast cancer risk has been consistently demonstrated, and the risk appears to be linearly related to the amount of alcohol consumed (14).

Marital status was used to interrogate stability in marriage and possibly emotional status but was found to be of no association($p=0.432$). Links between psychosocial stress and cancer have been postulated (15-17). However, epidemiological evidence linking psychosocial stress and cancer has been found weak in several studies (17-19)

Use of hormonal contraceptives for at least 10 years was a significant exposure factor that correlated with breast cancer occurrence,(CI 95%; HR 1.48:1.05-2.11, $p<0.001$). Many of the risk factors of breast cancer are associated with increased lifelong exposure to female reproductive hormones, including in utero exposure to high concentrations of oestrogens (20). Current users of hormonal therapy to manage menopause are at a higher risk of breast cancer than women who have never used these preparations. Hormone therapy for the menopause occurs at a time when a woman is at high and increasing background risk for breast cancer. Among current and recent users of hormonal therapy, the risk of breast cancer increases with increasing duration of use and this excess diminishes after cessation of use (21,22). Use of oral contraceptive agents, especially by women with a positive family history of breast cancer, appears to increase breast cancer risk as well (23).

In conclusion, in this study we looked at a number of factors known to be associated with breast cancer occurrence, and there was a general correlation with the majority, but brassiere use is now included. Our numbers are small, but these factors may not necessarily be acting in isolation. If they are acting together then these results cannot be ignored.

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