ASSESSMENT OF REPRODUCTIVE AND FAMILY HISTORY RISKFACTORS IN PATIENTS WITH PRIMARY BREAST CANCER ATTENDING ORCI HISTIOLOGICALLY DIAGNOSED FROM 2008 - 2014.

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Muhimbili University of Health and Allied Sciences
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By

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A Dissertation Submitted in Partial Fulfillment of the Requirements for the Degree of Master of Medicine (Clinical Oncology) of Muhimbili University of Health and Allied Sciences

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October, 2014

CERTIFICATION

The undersigned certifies that he has read and hereby recommends this acceptance by Muhimbili University of Health and Allied Sciences, a dissertation titled **"ASSESSMENT OF REPRODUCTIVE AND FAMILY HISTORY RISK FACTORS IN PATIENTS WITH PRIMARY BREAST CANCER ATTENDING OCEAN ROAD CANCER INSTITUTE HISTIOLOGICALLY DIAGNOSED FROM 2008-2014",** in (Partial) fulfilment of the Requirement for the Master Degree in Clinical oncology of Muhimbili University of health and Allied Sciences.

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Dr. Khamza Maunda – Clinical oncologist

Supervisor

_____

Date

DECLARATION AND COPYRIGHT

I, **Dr Alita Mrema** do hereby declare that this is my original work and has never been submitted for a similar or other degree award in any other university.

Signature……. Date ……

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ABSTRACT

Background.

Breast cancer is the 2nd commonest malignancy after cancer of the cervix among Tanzanian women. A lot of risk factors are associated with breast cancer and most have been researched in the western world. This research aim at assessment of reproductive and family history risk factors of primary breast cancer among female patients attending ocean road cancer institute. Most of the reproductive risk factors are hypothesized to be caused by oestrogen hormone.

It has been postulated that cumulative ovarian activities causes increased risk of breast cancer by causing cumulative effect of oestrogen on mammary glands. Oestrogen causes increased risk of neoplasia through two hypothesis;1);by increasing mitotic activity in breast tissue hence increasing probability of errors in cell division eg DNA copying errors, chromosomal translocation etc).2);by altering normal embryological development of primitive germ cells. Oestrogen cause developmental arrest of fetal germ cells which then remain dormant until puberty. At puberty gonadotropins from the pituitary stimulate both normal and dormant oestrogen arrested cells, stimulation of dormant oestrogen arrested cells can produce a germ cell neoplasia. In this case oestrogen serves as a initiator and gonadotropins as a 2nd stage promoters.

Family history of primary breast cancer among family members has shown to increase the risk of breast cancer in the same family members or members of the next generation. This due to a genetic mutation of tumour suppressor genes BRAC1 and BRAC 2 mutation and p53 genes.

Broad Objective

To assess reproductive and family history as risk factors among female patients with primary breast cancer histologically diagnosed from 2008-2014 attending ORCI.

Methodology

This study was hospital based case control study one to one age matched where by cases were female patients with primary breast cancer histologically diagnosed from 2008 to

2014 with age of 20-85yrs who gave consent. Were relatives / escortee of female patients which were diagnosed with primary cancer of the Cervix. Patients who didn't give consent or were too weak to be interviewed were excluded. There were 92 cases and 92 controls to sum up to a total of 184 people. The study was conducted at ORCI a specialized cancer centre in Tanzania. Cases and controls were recruited in the hospital as they were attending/escorting patients to the clinics and were interviewed through a structured questionnaire age. Socio demographic characteristics, patholological subtypes and cancer risk factors were clearly reported. Logistic regression, crude and adjusted odds ratio with their 95% CI were used for analysis and control of confounders

Results

This study had a total of 184 people,92 patients were cases with primary breast cancer while 92 were controls .Among the cases the larger age group constituted of patients who were between 36-45 years (33.7%),with the least number of patients being more than 65 years(4.3%).

The mean age was 48.5+/- 10.7yrs, with larger percent (23.9) from the city of Dar es salaam.

Among risk factors which were assessed, the risk which showed statistical significant was having less than three full term pregnancies, risk was three times more than for those having more than three parities with OR 3.3(CI 1.5-7.3), P value 0.003.A family history of breast cancer showed to be a risk factor for breast cancer with a p value of 0.004 but didn't show increased risk whether the relative affected was 1^{st},2^{nd} or 3^{rd} degree relative.

KEYWORDS; BRCA1& BRCA2 (Breast cancer genes 1 and 2), ORCI (Ocean road cancer institute)

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CHAPTER ONE

INTRODUCTION

Breast cancer is the most common cancer in women worldwide. It has high incidence rates in United State and United Kingdom. Based on rates from 2008-2010, 12.29% of women born in US today will be diagnosed with breast cancer sometimes during their lifetime (according to National Cancer Institute based on Surveillance Epidemiology and End Result data)

It is the 2nd commonest malignancy in women in Tanzania after carcinoma of the cervix. At ocean road cancer institute there are approximately 270 new cases annually. Multiple factors are associated with increased risk of developing breast cancer including Age> 50yrs,family history of breast cancer especially 1st degree relatives, endogenous and exogenous exposure to oestrogen, radiation exposure to younger age, high dietary fats, early menarche< 12yrs and late menopause> 55yrs,1st live birth 30yrs and above, null parity, history of not breast feeding , genetic factors such as BRAC1 and BRAC2 mutation, obesity , excessive consumption of alcohol and cigarette use.

Pathology and Natural History

Breast cancer is a heterogeneous disease growing at different rates in different patients. Tumours with poor prognosis include poorly differentiated carcinoma and inflammatory carcinoma. Well differentiated carcinomas and special tumour types (medularly, mucinous, papillary and pure tubular types) have good prognosis. Early disease without lymph node involvement survival rate is 80% for invasive ductal carcinoma and 90-95% for invasive lobular, comedocarcinoma and colloid carcinoma

Pathological Subtypes

There are several pathological subtypes but ductal carcinoma is the commonest pathological subtype of invasive carcinoma comprising of about 78% of invasive carcinoma**.** Special types with good prognosis accounts for 10%, followed by lobular carcinmoma 9%, comedocarcinomas 5%, medullary carcinoma 4%, colloid carcinoma 3%, inflammatory carcinoma 1% and carries poorest prognosis and paget's disease.

Mode of spread is through local extension, lymphatics and blood borne.

Signs and Symptoms;

Breast lump (solitary, hard & painless) spontenous nipple discharge (serous, serosanginous/bloody discharge, skin changes) unilateral eczema in paget's disease, skin erythema, edema, axillary lymphadenopathy and underlying indurations in inflammatory carcinoma.

General management includes surgery if tumour is operable, chemotherapy and hormonal therapy after completion of chemotherapy. Also targeted therapy as new methods like stratuzumab against HER2 receptors.

LITERATURE REVIEW

Worldwide breast cancer accounts for 22.9% of all cancers with exception of non melanoma skin cancers in women(by international agency for research on cancer 2008).Epidemiological studies of breast cancer focusing on age, race , ethnicity and geographical location have shown disparities(by ethn Dis 2005),for example whites have higher incidence of breast cancer than African American women but African American has higher incidence before age of 40yrs and higher mortality rates at any age (by American cancer society surveillance research 2007).

Breast cancer is becoming increasingly problem in low resource regions where incidence rates have been increasing by 5% annually (Anderson et al 2006)

Apart from being female, age is the single most important breast cancer risk .According to national cancer institute (NCI 2008) the risk between 30-39 is 0.43%, 40-49yrs risk is 1.44%, 50-59 risk is 2.63%, 60-69 yrs risk is 3.65%, based on probabilities for whole population and not individual risk factors.

Breast cancer is more than 100 times common in women than in men although men tend to have poorer outcome due to a delay in diagnosis (Male cancer treatment (NCI)2011.

Breast cancer in African countries is characterized by advanced clinical stage presentation and this is contributed by delayed presentation at medical evaluation, inadequate diagnosis by inexperienced health workers and limited available medical technology for cancer screening, diagnosis and treatment.

Age at 1st Full Term Pregnancy;

One of the risk factor associated with increased risk of developing breast ca is late age at first pregnancy. If a woman gives birth to a first child at an age of >30 yrs is associated with high probability of getting breast cancer. It is hypothesized late age at first pregnancy causes cumulative exposure to endogenous estrogens which tends to be the risk factor in breast cancer. The risk reduction is limited more to hormone receptor +ve breast cancer cells and appears to have little effect on to hormone receptor negative breast cancer cells. In a study done by **Lord et al 2008** showed women who gave birth before 25 yrs had a

36% reduced risk of breast cancer compared to nullgravida. This protective effect was restricted to ERPR+ve breast cancer but late age at 1st birth increased the risk of ERPR-VE breast cancer cells. Another study done by **LAI et al 1996** in Taiwan showed women with full term pregnancy before 30yrs at least 3 full term pregnancies had a decreased risk of developing breast cancer. In Mexico study done by **Mendoza et al 2007** on reproductive risk factors for breast cancer, Women older than 50yrs the most important risk factor was age at 1st full term pregnancy but for younger age <50yrs lactation shorter than 12months was a risk factor.

Breast Cancer and Parity;

Nullparity is considered as a risk factor of developing breast cancer. In a study done by **Lambe et al 1996** showed increased parity was associated with a pronounced decrease of breast cancer with each additional birth conferring to 10% risk reduction. Parity risk factor has been shown in recent studies to be a risk in relation to hormonal receptor status. In a study done by **Ma et al 2006** each birth reduced the risk of ER/PR+ by 11%.Neither parity or age at first birth was associated with an increased risk in ER/PR-VE cancer patients.

Gao et al 2000 did a study in shanghai China and among risk factors which were evaluated nulliparity showed to increase risk of breast cancer among both menopausal and pre-menopausal women.

Lactation Period. Lactation is one of the factors which reduce the risk of breast cancer in pre-menopausal women. It reduces the number of ovulatory cycles and hence reduce exposure to endogeneos oestrogen. In a study done by **Newcomb et al 1994** showed lactation has been associated with decreased risk of primary breast cancer in premenopausal women compared to those parous women who has not breastfed. Another study done by **Purwanto et al in 2000** showed lactation exerts a protective effect against breast cancer though there was no clear duration of lactation period. Study done by

Irmgard et al 2010 in Northern part of Tanzania showed longstanding lactation and reproductive behaviour are associated with lower risk of breast cancer in the region.

Family History of Breast Cancer;

Family history of breast cancer is one of the risk factor which predisposes to breast cancer. It is more at risk when it involves 1st degree relatives. It is due to genetic predisposition BRAC1 and BRAC2 mutations. It is passed as Autosomal dominant inheritance and transmitted through father's/mother's side. In a study done by **Slattery et al 1993** in Utah university showed women with a family history of breast cancer even if the nearest relative with breast cancer is a 3rd degree relative are at more risk of developing breast ca. Another study done by **Pharoah et al 1997** revealed increased risk of breast cancer in women with family history of breast cancer especially when a relative has been diagnosed before 50yrs of age.

PROBLEM STATEMENT

Breast cancer is the disease with rising incidence especially in the underdeveloped world like Tanzania. It has highest incidence in the developed world especially North America, Northern and Western Europe and Australia (according to American Cancer Society; Global facts and figures). It is the leading cause of female cancer deaths in western world.
The incidence rise in underdeveloped world is due to many factors among these is adaptation of the western world lifestyles including the reproductive and dietary factors which influences the modifiable risk factors.

A lot of research about the risk factors of breast cancer has been done in the developed world some showing a significant association while others do not show an association. Few studies has been published about risk factors of breast cancer among African women and none has been done in ocean road cancer institute to assess reproductive and+ family history factors as breast cancer risk which occurred in these patients.

RATIONALE

Modifiable breast cancer risk tends to differ from one population to another. The difference in incidence pattern between different populations can be attributed by different environmental factors.

This study aims at improving the knowledge of, reproductive and family history factors as risks in development of breast cancer among ocean road cancer institute female patients.
It will also help to know socio demographic factors and common pathological subtypes of breast cancer seen in our patients.

BROAD OBJECTIVE

To assess reproductive and family history factors as breast cancer risk among female patients with primary breast cancer attending ocean road cancer institute histiologically diagnosed from (2008-2014).

Specific Objectives

1. To assess the socio-demographic characteristics of patients with primary breast cancer attending ORCI.

2. To assess the disease profile of patients with primary breast cancer attending ORCI

3. To assess the reproductive and risk factors for breast cancer among patients attending ORCI

4. To assess the family history as risk factor for breast cancer among patients attending ORCI

CHAPTER TWO

METHODOLOGY

Study Area.

The study was conducted at ocean road cancer institute a referral cancer centre in Tanzania. It is located in Dar es Salaam in the Ilala Municipality. It receives patients from other government referral hospitals throughout the country. Some patients are referred from private hospitals. The centre attends to about 4000 – 5000 new cancer patients per year. Also this cancer centre does screening of carcinoma of the cervix and carcinoma of the breast for women.

Researches through department of epidemiology are done as well as training of undergraduate and postgraduate students in cancer field

Study Design.

Case control study design. Age matched one to one case control study. Controls were escortee / relatives of patients with carcinoma of the cervix who were free from cancer. Cases were female patients with primary breast cancer attending the clinic and those admitted. Both cases and controls were interviewed through a structured questionnaire where the socio demographic characteristics, both reproductive and family history factors were clearly asked and documented.

Study Population.

92 female patients with primary breast cancer aged 20yrs to 85yrs attending ocean road cancer institute(histiologically diagnosed from 2008-2014) and 92 relatives of patients with cancer of cervix who were free from cancer of any type.

Sample Size Calculation.

Use following parameters

P1 = estimated prevalence of reproductive risk factor = 19%

P2 = estimated prevalence of reproductive risk factor = 6%

$N = [Z_{1-\alpha/2}\sqrt{2\underline{p}(1-\underline{p})} + Z_{1-\beta}\sqrt{p1(1-p1)+p2(1-p2]^2/\delta^2}$

- N = sample size
- $Z_{1-\alpha/2}$ = significance level (0.05)=1.96
- $Z_{1-\beta}$ = power of the study (80%)=0.842
- P1 and p2 = pre-study estimates
- $\underline{P} = (p1 + p2)/2$
- δ = standardized difference (relevant difference) – p1-p2=19%-6%=13%
- P=19%+6%/2=12.5%
- $N=1.96\sqrt{2(12.5)(100-12.5)} +0.842\sqrt{19(100-19)+6(100-6)/13^2}$
- N=100
- 100 cases and 100 controls. But in this study a total of 92 cases and 92 controls were recruited.

Statistical Analysis

The data analysis was done using the SPSS version 16 for windows. Logistic regression analysis was employed to adjust for confounders and estimated odds ratio with their crude and adjusted 95% confidence interval were used for analysis. P-value of <0.05 was considered to be statistically significant.

Selection Criteria

Inclusion Criteria

Female patients with primary breast cancer attending ocean road cancer institute aged 20-85 yrs from 2008-2014 (histological diagnosed) who consented to be interviewed while cases were relatives/escortee of patients with primary cancer of the cervix who were free from cancer.

Exclusion Criteria.

Patients/relatives who were too weak to be interviewed and who didn't give consent.

Sampling Technique.

Women histologically diagnosed with primary breast cancer between 2008-2014 were randomly selected in the clinic and in the wards, and interviewed through structured questionnaire.

Ethical Consideration

Ethical clearance to conduct the study was sought from Muhimbili University of Health and Allied Sciences Ethical Review Board. Permission to do the study was seeked from ocean road cancer institute.

Informed consent to participate in the study was requested from study participants. These participants were assured of confidentiality and the questionnaire didn't have any client's name, only codes were used, therefore assuring that information provided was confidential. The benefits were stated clearly in the consent form, though risks were not expected in this study. Also all clients were informed that, there was no financial gain obtained by participating in this study.

Consenting Process.

Clients who were randomly picked from the clinic and the wards were educated to participate in the study. Participation required signed informed consent. Participants were provided with information on potential benefits of participating. The consent form addressed the purpose of the study and their willingness to participate in the study. It was made clear that, acceptance or refusal to participate in the study will have no outward consequences and that they are free not to participate in the study at any time and they are also free not to answer a question if they feel uncomfortable about the question.

Confidentiality.

Clients were assured of confidentiality and the questionnaire didn't have any client's name only the code numbers therefore assuring that information provided was confidential.

CHAPTER THREE

RESULTS

DESCRIPTION OF STUDY PARTICIPANTS AND THEIR SOCIAL DEMOGRAPHIC CHARACTERISTICS

Table 1: Social demographic characteristics of the case group and control groups.

	Case group(%) n=92	**Control Group (%) n=92**	**X^2/t**	***p*- Value**
Age (Years)				
Less than 35	8 (8.7)	11 (12)		
36 to 45	31 (33.7)	27 (29.3)		
46 to 55	24 (26.1)	26 (28.3)	1.99	0.73
56 to 65	25 (27.2)	21 (22.8)		
More than 65	4 (4.3)	7 (7.6)		
(Mean Age ± SD)	48.5 ± 10.7	49.1 ± 10.6	0.41	0.68
Marital Status				
Divorced	12 (13)	6 (6.5)		
Married	59 (64.1)	74 (80.4)	6.41	0.09
Single	9 (9.8)	4 (4.3)		
Widowed	12 (13)	8 (8.7)		
Education level				
Illiterate	23 (25)	26 (28.3)		
Primary school	47 (51.1)	63 (68.5)		
Secondary school	15 (16.3)	2 (2.2)	17.44	0.001
College/University	7 (7.6)	1 (1.1)		
Occupation				
Self Employed	31 (33.7)	27 (29.3)		
Employed	7 (7.6)	18 (19.6)	5.58	0.067
Unemployed	54 (58.4)	47 (51.1)		

This case control study comprised of 92 patients with primary breast cancer which were one to age matched with 92 controls. Among the cases the age group of 36 to 45 yrs constituted a larger number of female patients with breast cancer accounting about 33.7%, followed by the age group of 56-65yrs which contributes about 27.1%,with least number of patients in the age group of more than 65yrs(4.3%).The mean age was 48.5 yrs with standard deviation of 10.7yrs.

64.1% of breast cancer patients were officially married constituting a larger group, with the minority being single constituting about 9.8%. Majority of the cases had universal primary education constituting about 51.1% while only 7.6% had college or university education. Majority of the study participants were unemployed accounting for 58.4% while 7.6% were employed either in the government or primary sector.

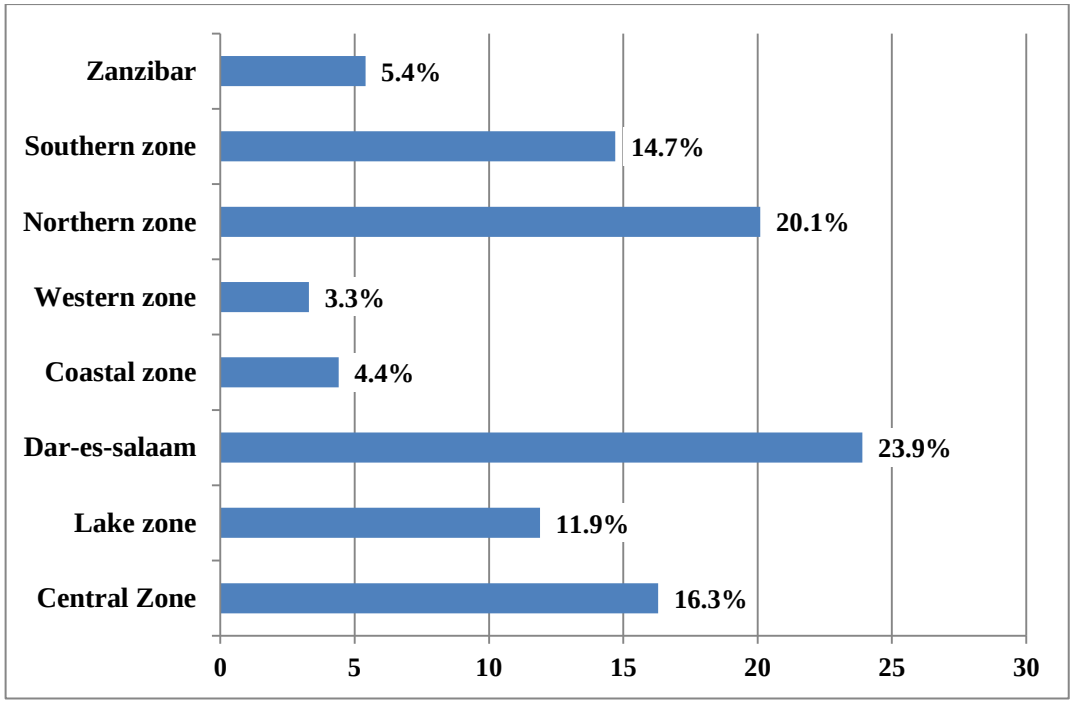

Figure 1: Bar graph showing residence of study population by respective zones

Among the breast cancer patients large percent were from Dar-es-salaam (23.9%), followed by patients from northern zone (20.1%) with least number of patients coming from western zone accounting for about 3.3%.

DISEASE PROFILE FOR PATIENTS WITH PRIMARY BREAST CANCER;

HISTIOLOGY	FREQUENCY	PERCENTAGE
INFILTATING DUCTAL CARCINOMA.	75	81.5%
APOCRINE CARCINOMA	2	2.2%
CARCINOMA NON OTHER SPECIFIC(NOS).	1	1.1%
MISSING HISTIOLOGIES	2	2.2%
INFLAMMATORY CARCINOMA.	1	1.1%
LOBULAR CARCINOMA	4	4.4%
MEDULLARY CARCINOMA	3	3.3%
MUCINOUS CARCINOMA	1	1.1%
PAPILLARY CARCINOMA	1	1.1%
SPINDLE CELL CARCINOMA	1	1.1%
UNDIFFERENTIATED CARCINOMA	1	1.1%

Among patients with primary breast cancer 81.5% had histiopathology of infiltrating ductal carcinoma, followed by lobular carcinoma 4.4%,with least histiopathology of inflammatory carcinoma, mucinous carcinoma, papillary carcinoma, spindle cell carcinoma, undifferentiated carcinoma and carcinoma non other specific constituting 1.1% in each group.

Table 2: Distribution of Reproductive history risk factor and the relationship between the Reproductive History risk factor and Breast cancer

Reproductive history	**Case N (%)**	**Control N (%)**	**Total**	***p*** **(X^2)**
Age at first pregnancy (Yrs.)				
<30	25 (28.6)	22 (24.4)	47 (26.6)	
>30	62 (71.3)	68 (75.6)	130 (73.4)	0.611
Total	**87 (100)**	**90 (100)**	**177 (100)**	
Ever given birth				
Yes	87 (94.6)	90 (97.8)	177 (98.9)	
No	5 (5.4)	2 (2.2)	2 (1.1)	0.248
Total	**92 (100)**	**92 (100)**	**184 (100)**	
Number of children				
1 to 3	43 (49.4)	24 (26.7)	67 (37.9)	
More than 3	44 (50.6)	66 (73.3)	110 (62.1)	0.002
Total	**87 (100)**	**90 (100)**	**177 (100)**	
Ever Breastfeed				
Yes	84 (91.3)	90 (97.8)	174 (94.6)	
No	8 (8.7)	2 (2.2)	10 (5.4)	0.051
Duration of breastfeeding (months)				
<12	3 (3.6)	2 (2.2)	5 (2.9)	
>12	81 (96.4)	88 (97.8)	169 (97.1)	0.28
Total	**84 (100)**	**90 (100)**	**174 (100)**	

Among female patients with breast cancer the risk factor which showed to be statically significant is having less than three full term pregnancies with a P value of 0.002. Other risk factors like age at menarche, age at menopause, age at first full term pregnancy, nulliparity, breast feeding and duration of breastfeeding didn't show any statistical significance hence were not proven to be risk factors for developing breast cancer in my study population.

Table 3: Odds ratio of breast cancer and 95% confidence intervals associated with Reproductive history risk factors among breast cancer patients and Controls

Reproductive history	**Crude**			**Adjusted**		
	OR	95% CI	***p***	OR	95% CI	***p***
Age at first pregnancy						
<30	1 (Ref)			1 (Ref)		
>30	0.8	0.4 – 1.6	0.549	0.7	0.32 – 1.56	0.395
Ever given birth						
Yes	1 (Ref)					
No	1	0.06 – 16.7	0.98			
Number of children						
1 to 3	1 (Ref)			1 (Ref)		
More than 3	2.7	1.4 - 5	0.002	3.3	1.5 – 7.3	0.003
Ever Breastfeed						
Yes	1 (Ref)					
No	4.3	0.46 - 39	0.197			
Duration of breastfeeding						
>12	1 (Ref)			1 (Ref)		
<12	1.6	0.26 - 10	0.598	3.9	0.4 – 37.7	0.23

Of all the risk factors assessed in this study after adjusting for confounders, having more than three full term pregnancies reduces the risk of getting breast cancer by three fold, with p value of 0.003 with CI (1.5-7.3),OR 3.3.

Table 4: Distribution of Reproductive history risk factor and the relationship between the Family History risk factor and Breast cancer

Family history	**Case N (%)**	**Control N (%)**	**Total**	***p* (X^2)**
Family member with BC				
Yes	16 (17.4)	4 (4.4)	20 (11)	
No	76 (82.6)	88 (95.6)	164 (89)	0.004
Total	**92 (100)**	**92 (100)**	**184(100)**	
Which family member affected				
First degree	8 (50)	2 (50)	10 (50)	
Second degree	6 (37.5)	2 (50)	8 (40)	0.732
Third degree	2 (12.5)	-	2 (10)	
Total	**16 (100)**	**4 (100)**	**20 (100)**	

Family history of breast cancer as a risk factor showed statistical significance with p value of 0.004 but didn't show increased risk when the relative affected was either first degree, second degree or a third degree relative when comparing the control group and cases (p value 0.732.)

CHAPTER FOUR

DISCUSSION

Among female patients with primary breast cancer the age group between 35-46 years consisted of larger group of about 33.7% with mean age of 48.5years.This study group is of pre menopausal age. The study finding is consistent with the study done by Somdyala et al 1998-2002,that demonstrated breast cancer among African women tend to occur in premenopausal women with incidence peaking between the age of 35-45.The same findings were found by Elgali et al 2010 who researched, breast cancer burden in central Sudan. Among African population breast cancer is more diagnosed a decade earlier than in western countries.

Also in a study done by Adebamowo et al 1999 a case control study of epidemiological risk factors for breast cancer among Nigerian women showed African population has a low median age at presentation compared to western population, breast cancer among young women comprises of a higher proportion of the cases presenting in clinics than among older women.

In this study majority of study participants had universal primary education constituting for 51.1% and only 7.6% had higher learning education.

Also the large percent of participants were from the city of Dar es salaam constituting for about 23.1% with the lowest percent 3.3% from western zone, this might have been contributed by increased awareness of population in the city through media advertisements.

Disease profile among breast cancer patients, 81.5% had infiltrating ductal carcinoma, followed by lobular carcinoma which accounted for 4.4%.

In a study done by Ebughe et al in Nigeria; Most of the patients were young, with a mean age of 45.06 years, and 30-39 years being the commonest age group (38.3%). Invasive ductal carcinoma was the most prevalent histological type contributing for (85.2%).

In this case control study, it was found the only risk factor that were significant is parity, having more than three full term pregnancies was protective against breast cancer with odds ratio of 3.3,CI(1.5-7.3) and p value of 0.03.These findings tally with the study done in Japan by Tamakoshi et al 2005 which assessed the impact of menstrual and reproductive factors on breast cancer risk and they found that there was a significant decline in the risk of breast cancer with increased parity among parous women trend p=0.01.Women with four or more parities had 69% lower risk than uniparous women. It was also found that there was no apparent association of breast cancer risk with age at menarche and age at menopause.

Also a population based study done by Lambe et al 1996 in Sweeden which investigated Parity, age at 1st and last birth on breast cancer risk showed also the risk of breast cancer decline with the number of children born. Women who have given birth to five or more children had half the risk of women who didn't give birth.

Also in a study done by Mah et al 2006,each birth reduced the risk of ER/PR+VE participants by 11%.Neither parity nor age at 1st birth was associated with increased risk in ER/PR-VE patients.

Another study done by Adami et al 1980, which assessed age at 1st birth, parity and risk of breast cancer in Swedish population, showed that increasing number of births protects against breast cancer.

Other menstrual and reproductive factors like ,age at first full term pregnancy, nulilparity, breast feeding and duration of breast feeding didn't show any statistical significance probably due to difference in cultural, environmental and, genetically, factors among African Tanzanian women and other population.

In a study done by Hongpan et al 2014 in china, on reproductive factors and breast cancer risk among BRCA1/BRCA2 mutation carriers, results showed reproductive factors may be associated with breast cancer risk only among BRCA1 mutation carries. In conclusion late age at menarche, late age at first full term pregnancy; breast feeding protects against breast cancer in BRCA1 mutation carriers only. Hence an association might have been missed among my study participants due to lack molecular/genetic data. It is possible that majority

of my study participants didn't have BRCA1 mutation carriers and that is why an association could not be elucidated.

Another risk factor which showed to be statically significant was family history of breast cancer with p value 0.004, though this study was not able to show its relationship with closeness of the relative affected and possibly a larger study with genetic screening would help to improve these results.

In a study done by Slattery et al 1993 in Utah University, it showed there was an increased risk of developing breast cancer was demonstrated even if the relative affected is the 3rd degree relative.

CHAPTER FIVE

CONCLUSION

Breast cancer appeared to have affected female patients at a younger age compared to the western counterparts. Since the incidence of breast cancer is rising in underdeveloped countries like Tanzania screening programmes, mass education and awareness about breast cancer should be highly encouraged.

STUDY LIMITATIONS

- Since its an observational study (case control) it was prone to recall bias.
- Time and resources were limited

RECOMMENDATION

Further study with a larger sample size is required; some risk factors might have not shown an association because the power of the study was small.

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APPENDICES

Appendix I: Questionnaire

1. File number ……..

2. Age of the interviewee……..

3. Marital Status 1)-Married
   2)-Single
   3)-Divorced/separated
   4)-Widow

4. Where do you reside?

5. What is your occupation?
   1) Employed (a) Private (b) Government
   2) Not employed
   3) Self employed.

6. What is your highest level of education 1)Illiterate
   2) Primary school
   3) Secondary school
   4) College/university
   5) Post graduate/Masters

7. Age at 1st full term pregnancy 1) >30yrs
   2) <30yrs

8. Have you ever given birth? 1)Yes

2) No

9. How many children do you have? 1)1-3

2)>3

10. Have you ever breast fed? 1) Yes

2) No

11. How long have you breast fed: 1)<12 months

2)>12 months

12.Any family member with breast cancer; 1) Yes

2) No

13. Which family member is affected; 1) 1st degree relative

2) 2nd degree relative

3) 3rd degree relative

14. At what age was she diagnosed with breast cancer? 1) >50yrs

2) <50yrs

15. Which pathological subtype of breast cancer does the patient has? (From the file)