RISK FACTORS FOR BREAST CANCER IN A TERTIARY HOSPITAL IN ABUJA

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DECLARATION

It is hereby declared that this work is original unless otherwise acknowledged. This work has not been presented to any other Institutution for either the award of a degree or fellowship or to any journal for publication.

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Mrs. Nwajana Adankwa Ngozi

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Date

DEDICATION

This work is dedicated to my immediate family, Mr. G.O.C. Nwajana, Tobechukwu Nwajana for their understanding and love during the duration of my studies.

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I wish to acknowledge my parents Engr. and Mrs. B.C. Mbonu who stood by me all through the study. I appreciate their support and care.

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TABLE OF CONTENTS

Chapter Three:

Chapter Four:

Chapter Five:

Chapter Six:

LIST OF ABBREVIATION

HRT	**-**	**Hormone Replacement Therapy**
DCIS	**-**	**Ductal Carcinoma In Situ**
LCIS	**-**	**Lobular Carcinoma In Situ**
B.C	-	Before Christ
BRCA 1	-	Breast Cancer Gene 1
BRCA 2	-	Breast Cancer Gene 2
BMI	-	Body Mass Index
GIT	-	Gestro Interstinal Tract
SPSS	-	Statistical Package for Social Sciences
X^2	-	Chi-square
FCT	-	Federal Capital Territory

LIST OF TABLES

ABSTRACT

Breast cancer is the commonest site specific, malignancy affecting women and the most common cause of cancer mortality in women world wide. Our knowledge about breast cancer is evolving but it is still limited with respect to its etiology and biology and with respect to its features in individual countries and cultures.

The study was conducted to identify and determine the risk factors for breast cancer in a Tertiary hospital in Nigeria. A retrospective case control study was carried out in National Hospital Abuja. A total of 544samples were used in the work comprising of 272 cases and 272 controls . The data was obtained directly from patients case file. Information obtained were; Sex, Occupation, Weight, Height, Parity, Age, Religion, Marital Status, Smoking, Family history of breast cancer, Alcohol consumption, Menarche and Oral Contraceptive history. The data was entered and analyzed using SPSS 15 version. The P value accepted as significant was set at $P < 0.05$ at 95% confidence level. Test statistics performed were chi-square (x^2) and odds ratio (OR) in order to obtain the association as well as level of risk of a given risk factor.

Females constituted 521 (95.8%) of the study population while males were 23(4.2%). Patients age ranged between 25-74 years with age groups 35-44 and 45-54 years constituting the highest frequencies of 158 (29.4%) and 160 (29.8%) respectively. Those who had early menarche were 257(51.1%) while normal menarche were 246 (48.9%). Population of women who used oral contraceptives were 110 (21.8%) while those who did not use were 395 (78.2%). Parity among

patients ranged between 0-10 children with those having 1-5 children having the highest frequency of 361 (72.8%). 264 (49.1%) of the patients consumed alcohol while 274 (50.9%) did not consume alcohol. Mother 60 (40.0%) and Sister 37 (24.7%) had the highest frequency for patient with family history. Civil servant 229 (43.5%) had the highest frequency for occupation of patients in the study. This was followed by those doing business 120 (22.8%). Housewives 96 (18.3%) Retiree 49 (9.3%) Student 18 (3.4%) and Farmers 14 (2.7%). 25 (4.6) of the patients smoked while 515 (95.4%) did not smoke. 47 (32.2%) of the patient were underweight while 99 (67.8%) were over weight. 459 (84.7%) of patients were Christians while 83 (15.3%) were practicing Islam. Finally 447 (82.9%) were married while 56(10.4%) were single and widows were 36 (6.7%) in the study.

In conclusion, Gender, Age, Parity, Early menarche, Use of oral contraceptives, Alcohol consumption, Occupation and family history of patients with breast cancer were identified as risk factors for breast cancer as well as had significant association for development of breast cancer. Smoking, Religion, Marital status and BMI of patients were not identified as risk factors for developing breast cancer in the study.

CHAPTER ONE

1.0 INTRODUCTION

Breast Cancer constitutes a major public health issue globally with over 1 million new cases diagnosed annually, resulting in over 400,000 annual deaths and about 4.4 million women living with the disease. It is the commonest site specific malignancy affecting women and the most common cause of cancer mortality in women worldwide.[1,2]

In Africa, Breast Cancer has overtaken cervical cancer as the commonest malignancy affecting women and the incidence rates appear to be rising. [3,4] In Nigeria for example, incidence rate has increased from 13.8–15.3 per 100,000 in the 1980s, to 33.6 per 100,000 in 1992 and 116 per 100,000 in 2001.[5]These increases in incidence are due to changes in the demography, socio-economic parameters, epidemiologic risk factors, better reporting and awareness of the disease.

There is an international/geographical variation in the incidence of Breast Cancer. Incidence rates are higher in the developed countries than in the developing countries and Japan. Incidence rates are also higher in urban areas than in the rural areas. While mortality rates are declining in the developed world (Americas, Australia and Western Europe) as a result of early diagnosis, screening, and improved cancer treatment programs, the converse is true in the developing world as well as in eastern and central Europe [6,7]

Breast cancer and its treatment constitute a great physical, psychosocial and economic challenge in resource limited societies as found in Africa. The hallmark of the disease in Africa are patients presenting at advanced stage, lack of adequate mammography screening programs, preponderance of younger pre-menopausal patients, and a high morbidity and mortality. [3,6]

Pregnancy associated breast cancer is defined as breast cancer diagnosed during pregnancy or lactation or one year post partum. Breast cancer and pregnancy can be classified into three main situations; these are: breast cancer that is detected during the evolution of pregnancy; breast cancer that is detected during lactation or postpartum, and pregnancy in patients who have had a previous breast cancer. Cancer complicates approximately 1 per 1000 pregnancies and accounts for one-third of maternal deaths during gestation. The prevalence of breast cancer during pregnancy is increasing due to delayed onset of childbearing. Breast cancer is diagnosed in approximately 1 in 3000 pregnancies. The incidence ranges from 0.76% to 3.8% of breast cancer cases. The median age of pregnant women affected with breast cancer is 33 years. In a recent review in Nigeria, 12% of the patients with Breast Cancer were pregnant or lactating and 74% were premenopausal, making it the most frequently occurring malignancy during pregnancy, along with cancer of the uterine cervix.[5]

1.2 INCIDENCE TRENDS WOMEN

1.2.1 Invasive breast cancer

Incidence rates of invasive female breast cancer for all races combined show three distinct phases since 1975, when broad surveillance of cancer began:

Between 1975 and 1980, incidence was essentially constant;
Between 1980 and 1987, incidence increased by almost 4% per year;
Between 1987 and 2002, incidence rates increased by 0.3% per year.[9]

Much of the long-term underlying increase in incidence is attributed to changes in reproductive patterns, such as delayed childbearing and having fewer children, which are recognized risk factors for breast cancer. The rapid increase between 1980 and 1987 is due largely to greater use of mammographic screening and increased early detection of breast cancers too small to be felt. Detecting these tumors earlier has the effect of inflating the incidence rate because tumors are being detected 1-3 years before they would have appeared if they continued to grow until symptoms developed. During the introduction of mammography, from 1980 to 1987, incidence rates of smaller tumors ($\leq$2.0 cm) more than doubled, while rates of larger tumors (3.0 cm or more) decreased 27%.[10] During this time, the trend in diagnosis of smaller ($\leq$2.0 cm) tumors continued, increasing by 2.1% per year from 1988 to 1999, and stabilized thereafter.[11] A similar time trend was seen with stage at diagnosis, with increases in the rates limited to cancers diagnosed at a localized stage. The continued, though slight, increase in overall

breast cancer incidence since 1987 may reflect increase in the prevalencement therapy (HRT).

1.2.2 Age

From 1980 to 1987, incidence rates of invasive breast cancer increased among women aged 40-49 and 50 and older (3.5% and 4.2% per year, respectively).[11] Since 1987, rates have continued to increase among women 50 and older, though at a much slower rate. In contrast, the rates have slightly declined among women aged 40-49. There has been relatively little change in the incidence rates of invasive breast cancer in women younger than 40.

1.2.3 Race/ethnicity

During 1992-2002, overall incidence rates increased in Asian Americans/Pacific Islanders (1.5% per year), decreased in American India/Alaska Natives (3.5% per year), and did not change significantly among whites, African Americans, and Hispanics/Latinas.[11] This could be attributed to poor prognosis of aggressive tumor common in African –American women[8.]

Incidence rates of breast cancer by tumor size differed between white and African American women: African American women were less likely to be diagnosed with smaller tumors (≤ 2.0 cm) and more likely to be diagnosed with larger tumors (2.1-5.0 and > 5.0 cm) than white women.[11]

White women have a higher incidence of breast cancer than African American women after age 35. In contrast, African American women have a slightly higher

incidence rate before age 35 and are more likely to die from breast cancer at every age. Incidence and death rates from breast cancer are lower among women of other racial and ethnic groups than among white and African women.

1.2.4 In situ breast cancer

Incidence rates of in situ breast cancer have increased rapidly since 1980[11] largely because of increased diagnosis by mammography. Most of this increase represents increased detection of ductal carcinoma in situ (DCIS), which from 1998 to 2002 accounted for about 85% of the in situ breast cancers diagnosed. Incidence rates of DCIS increased more than sevenfold during 1980-2001.[12] The increase was observed in all age groups, although it was greatest in women aged 50 and older.[11,12]

Most cases of DCIS are detectable only through mammography, and the large increases in DCIS incidence rates since 1982 are a direct result of mammography's ability to detect cancers that cannot be felt. Although increase in both invasive breast caner and DCIS incidence rates have slowed since the mid-1980s,[13]the temporal increase in DCIS since 1982 is larger than the increase in invasive breast cancer.

Lobular carcinoma in-situ (LCIS) is less common than DCIS, accounting for approximately 12% of female in situ breast cancers diagnosed from 1998 to 2002.[11] Similar to DCIS, the overall incidence rate of LCIS has increased more rapidly than the incidence of invasive breast cancer.[11] This increase has been limited to women older than 40 and largely to postmenopausal women.'[12.14]

1.3 Mortality trends –women

The death rate from breast cancer in women has decreased since 1990:

Between 1975 and 1990, the death rate for all races combined increased by 0.4%annually;
Between 1990 and 2002, the rate decrease by 2.3% annually.[15]

The percentage of decline was larger among younger age groups. From 1990 to 2002, death rates decreased by 3.3% per year among women younger than 50, and by 2.0% per year among women 50 and older.[15] The decline in breast cancer mortality since 1990 has been attributed to both improvements in breast cancer treatment and to early detection.[16,17]

African American women and women of other racial and ethnic groups, however, have benefited less than white women from these advances. From 1990 to 2002, female breast cancer death rates declined by 2.4% per year in whites, 1.8% in Hispanics/Latinas, 1.0% in African Americans and Asian Americans/Pacific Islanders, and did not decline in American Indian/Alaska Natives.[18] A striking divergence in long-term mortality trends is seen between African American and white females. The disparity in breast cancer death rates between African American and white women appeared in the early 1980s; by 2002, death rates were 37% higher in African Americans than in white women.[15]

1.4 Incidence and mortality trends –men

Although breast cancer in men is a rare disease, accounting for less than 1% of breast cancer case in the US, between 1975 and 2002, the incidence rate among males increased 1.1% annually. [11] The reasons for the increase are unknown and are not attributable to increased detection. Similar to female breast cancer, the incidence of male breast cancer increases with age.[19] Men however are more likely than women to be diagnosed with advanced disease and thus have poorer survival.[19] Death rates from male breast cancer have remained essentially constant since 1975. [15]

Male breast cancer is an uncommon disease although the incidence has increased over the past 25 years. Less than 1% of all breast cancer patients are male. Rates of male breast cancer vary widely between countries: in Uganda and Zambia the annual incidence rates are 5% and 15%, respectively of all breast cancer cases. These relatively high rates have been attributed to endemic infectious diseases causing liver damage, leading to hyperestrogenism. By contrast, the annual incidence of male breast cancer in Japan is less than five per million, in parallel with the lower than average incidence of female breast cancer in that country. Jewish men are the only racial group with a higher than average incidence (2•3/100 000 per year), irrespective of living in Israel or the USA.

Risk factors for Breast Cancer include; Genetic (BRCA2, Klinefelter's syndrome), Lifestyle (Obesity, Alcohol, Estrogen intake) , Work (High ambient temperature, Exhaust emissions) and Disease (Testicular damage, Liver damage, Radiotherapy to chest. The predominant histological type of disease is invasive ductal, which forms more than 90% of all male breast tumors.[29]

1.5 PROBLEM STATEMENT

Breast cancer unlike cervical cancer has no precise etiological agent. It therefore constitutes a major public health issue globally. Our knowledge about breast cancer is evolving, but it is still limited with respect to its etiology and biology and with respect to its features in individual countries and cultures.

All efforts are geared towards early diagnosis, prompt and standardized treatment to reduce the disease burden of advanced disease in African women, majority who are worse hit in the most productive part of their life time[20]. Therefore there is the need to elicit possible risk factors for breast cancer in Nigeria.

1.6 JUSTIFICATION FOR THE STUDY

The breast is very important in the life of a woman. It is the essential part of the body which nourishes a new born. It is one of the part of the body which attracts the opposite sex amongst adults. In Africa, a woman without breast is regarded as incomplete.

Breast cancer starts with some of the cells in the breast growing abnormally and in most cases, it isn't clear what causes normal breast cells to become cancerous.[60] Doctors know that only 5-10% breast cancers are inherited yet genetic mutations related to breast cancer aren't inherited.

The study was designed to identify, determine as well as establish risk factors that predispose one to breast cancer in Nigeria. Results obtained will contribute to public health consciousness to risk factors for breast cancer in Nigeria

1.7 OBJECTIVES

General Objective:

To identify the major risk factors for Breast cancer in Nigeria

Specific Objectives:

1. To identify the risk factors for breast cancer
2. To determine the association of risk factors contributing to Breast cancer.
3. To establish major risk factors contributing to Breast Cancer in Nigeria.

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 BREAST CANCER

Cancers are group of diseases that cause cells in the body to change and grow out of control. Most types of cancer cell form a lump or mass called a tumor and are named after the part of the body where the tumor originated.

Breast cancer begins in breast tissue, which is made up of glands for milk production, called lobules, and the ducts that connect lobules to the nipple. The remainder of the breast is made up of fatty, connective, and lymphatic tissue[21]. Most breast abnormalities are benign; that is, they are not cancerous, do not grow uncontrollably or spread, and are not life-threatening.

Some breast cancers are called in situ, because they have not yet spread beyond the focus where they began. In situ breast cancers are confined within the ducts (ductal carcinoma in situ) or lobules (lobular carcinoma in situ) of the breast. Nearly all cancers at this stage can be cured. Many oncologists believe that lobular carcinoma in situ (also known as lobular neoplasia) is not a true cancer but rather is an indicator of increased risk for developing invasive cancer in the future.

Other cancerous breast tumors are invasive, or infiltrating. These cancers start in the lobules or ducts of the breast but have broken through the duct or gland walls and invade the surrounding fatty tissue of the breast.

The seriousness of invasive breast cancer is strongly influenced by the stage of the disease, that is, the extent or spread of the cancer when it is first diagnosed. There are two main staging systems for cancer. The classification of tumors developed by the American Joint Committee on Cancer (AJCC) uses information on tumor size (T), lymph node involvement (N), and the presence or absence of distant metastases (M), and is commonly used in clinical settings.[22] Once the T, N, and M are determined, a stage of I, II, III, or IV is assigned, with stage I being an early stage and stage IV being the most advanced.

A broader system used for the staging of cancers is known as the SEER-Surveillance Epidemiology and End Results, Summary Stage system and is used more commonly in reporting cancers: [23]Local-stage used for the staging of cancers confined to the breast, regional-stage tumors have spread to surrounding tissue or nearby lymph nodes, distant-stage cancers have metastasized (spread) to distant organs.

2.2 HISTORY OF BREAST CANCER

Breast cancer is one of the oldest known forms of malignancies. The earliest known documentation on breast cancer was the Smith Surgical Papyrus (3000-2500 B.C.) written in Africa (Egypt). It described 8 cases of tumors or ulcers of the breast that were treated by cauterization, with a tool called "the fire drill." The writing says about the disease, "There is no treatment." At least one of the described cases is male. There were few other historical references to breast cancer until the first century when Celsus recognized the relevance of operations

for early breast cancer. In the second century, Galen inscribed his classical clinical observation: "We have often seen in the breast a tumor exactly resembling the animal the crab. Just as the crab has legs on both sides of his body, so in this disease the veins extending out from the unnatural growth take the shape of a crab's legs. We have often cured this disease in its early stages, but after it has reached a large size, no one has cured it. In all operations we attempt to excise the tumor in a circle where it borders on the healthy tissue".[21]

Halsted and Meyer reported their operations for the local treatment of breast cancer in 1894. Both Halsted and Meyer advocated complete dissection of auxiliary lymph node levels I to III and removal of pectoral muscle along with the breast. By demonstrating loco regional control rates after radical resection and providing the first opportunity for cure, these surgeons established radical mastectomy as state-of-the-art treatment in the early part of the 20th century. Later in the century, there was a transition from the Halsted radical mastectomy to the modified radical mastectomy (*MRM*) as the surgical procedure most frequently used for breast cancer. This procedure maintained the en bloc dissection of the breast and lymph nodes, but left the pectoralis major muscle intact.

The recognition in the 1950s that breast cancer was often a systemic disease at presentation shifted the management of primary breast cancer away from a purely surgical approach to a multidisciplinary one that uses systemic therapy, surgery and radiation. As a result surgery for breast cancer may now be managed with more conservative and less locally ablative procedures such as lumpectomy. The

past three decades has witnessed an enormous growth in the knowledge and understanding of the basic science of the disease especially the genetic and molecular basis of the disease.

2.3 PATHOPHYSIOLOGY AND TYPES OF BREAST CANCER

There are four different types of breast cancer. They are described below.

Breast cancer is either invasive or noninvasive (often referred to as in situ). There are two types of noninvasive breast cancers: ductal carcinoma in situ (DCIS) and lobular carcinoma in situ (LCIS). These two types of noninvasive breast cancers do not invade the basement membrane of the breast. As their names suggest ductal carcinoma in situ cancer cells are found in the lining of the duct whereas lobular carcinoma in situ cancer cells are found in the lobules.

There are the two types of noninvasive breast cancer described above and there are also two types of invasive breast cancer: infiltrating ductal carcinoma and infiltrating lobular carcinoma. As their names suggest, infiltrating ductal carcinoma penetrates the wall of the duct and travels to areas outside of it whereas infiltrating lobular carcinoma spreads through the wall of the lobule and also travels to areas outside of it. Infiltrating ductal carcinoma is the most common type of breast cancer, accounting for between 70%-80% of the cases of breast cancer.

Breast cancer has four stages that relate to the severity of the cancer. The following describes the types and stages of breast cancer.[24]

Stage 0—noninvasive carcinomas (LCIS or DCIS). Cancer cells have not invaded the surrounding breast tissue.

Stage I—the tumor is no more than 2 cm in size and cancer cells have not spread beyond the breast.

Stage II—either the tumor has spread to the lymph nodes under the arms but the tumor is less than 2 cm in size, or the tumor has not spread to the lymph nodes under the arms but is greater than 5 cm in size, or the tumor is between 2 and 5 cm and may or may not have spread to the nodes.

Stage III—the tumor is greater than 5 cm in size and has spread to the lymph nodes under the arms.

Stage IV—the cancer has spread to other parts of the body (metastatic cancer).

2.4 SIGNS AND SYMPTOMS

Most breast lumps aren't cancerous. Yet the most common sign of breast cancer for both men and women is a lump or thickening in the breast. Often, the lump is painless. Other potential signs of breast cancer include:

A spontaneous clear or bloody discharge from the nipple, often associated with a breast lump, Retraction or indentation of the nipple, A change in the size or contours of the breast, Any flattening or indentation of the skin over the breast, Redness or pitting of the skin over the breast, like the skin of an orange.[25]

2.5 ETIOLOGY/RISK FACTORS:

The risk factors include:

Age: The incidence of breast cancer increases with age and is rare before the age of 20 years. The breast cancer incidence in Caucasians is highest at age 50-59, after menopause, dropping after age 70. In Africa and African-Americans the peak age incidence is about one decade less, so that the majority of the patients are pre- menopausal. While numerous theories have been proposed to explain this difference, including age at menarche, time of first delivery, parity, socio-demographic factors, body mass index, and underlying genetic difference, none are completely satisfactory and more research is needed in this area.[3-5, 26-28]

Sex: Breast Cancer is 100 times more common in women than in men with male breast cancer accounting for <1% of all breast cancer cases in the United States and 0.1% of cancer mortality in men [29-31].However in Africa this situation may be different as from 5-15% of breast cancer in Uganda and Zambia may occur in males.[29,32-35] In fact, being female is the single greatest risk factors for breast cancer. Although men develop the disease, it's far more common in women.

Hormone/Pregnancy related factors: The role of estrogen in the causation of breast cancer has been extensively studied and the general opinion is that estrogen is the primary stimulant for breast epithelial proliferation. Factors that increase exposure to high or prolonged level of estrogen are therefore associated with an increased risk of developing breast cancer. [36-40] These include early menarche, late menopause, use of contraceptives and exogenous estrogen, nulliparity and

increased age at first term pregnancy. Induced abortion and spontaneous abortion do not increase the risk. Prolonged lactation and breast feeding reduce the risk. As the living standard and health care facilities in Africa improve, it is probable that age at menarche will decrease while that of menopause increases. The demands for education and a career may increase the number of women who delay childbearing, have fewer children, use contraceptives and breast feed for a shorter time. These will likely impact on the increase in the incidence of breast cancer as African countries meet the minimum development goals.

Previous Breast Disease: Individuals who have a prior history of invasive carcinoma or ductal carcinoma in situ have a 0.5%-1% per year risk of developing a new invasive breast carcinoma. Women with atypical ductal or lobular hyperplasia have a four to five times higher risk of developing breast cancer. Proliferative lesions without atypia, such as moderate hyperplasia and sclerosing adenosis, are associated with a slightly increased risk (1.5-2%). Other common non-proliferative changes such as palpable cysts, fibroadenomas and duct papillomas are not associated with a significantly increased risk.[41]

Environmental Exposures: Exposure to ionizing irradiation increases the risk of developing breast cancer. Excess breast cancer has been observed in patients given multiple fluoroscopies, radiotherapy for ankylosing spondylitis, Hodgkin's disease, or enlargement of the thymus gland and in survivors of the atomic bombings, painters of radium watch faces and X-ray technicians.[42] Environmental exposures to organic chlorines and other environmental/synthetic estrogens like

cosmetics and phytoestrogens found in food have also been postulated to increase the risk, but so far there are no conclusive evidence linking organic chlorines to breast cancer. [39, 44 ,45]

Anthropometric indices and physical activity: Height, obesity and high body mass index are risk factors especially in post menopausal women. In pre-menopausal women, obesity and high body mass index has an insignificant but inverse relationship to breast cancer risk that is reduced by physical activity. [46-48]

Diet, Alcohol and Smoking: Alcohol and Diets rich in fat especially saturated fat raises the risk while smoking does not appear to affect the risk.[49,50]

Family history and genetics: A family history of breast cancer increases a woman's risk of developing the disease. A woman is considered to be at increased risk if the family member is a first degree relation with early age of onset (< age 50), if both breasts are involved, or if she has multiple primary cancers (such as breast and ovarian cancer). Women with one, two, and three or more first-degree affected relatives have an increased breast cancer risk when compared with women who do not have an affected relative (risk ratios 1.8, 2.9 and 3.9, respectively) [51] Such women are recommended to begin breast cancer screening at an age 10 years younger than the age at which the affected relative was diagnosed.

Hereditary breast cancer caused by an underlying inherited gene mutation accounts for a small proportion (5-10%) of all breast cancers. The majority is accounted for by 2 germline mutations BRCA-1 (50%) and BRCA-2 (32%),

which are inherited in an autosomal dominant fashion with varying penetrance. These tumor suppressor genes are important in the processing of DNA damage and preservation of genomic integrity. BRCA-1 is located on chromosome 17q while BRCA-2 is located on chromosome 13q. [52] They are most commonly found in the European Ashkenazi Jewish population and their descendants, accounting for their relatively high prevalence in the developed world. In Europe and North America, BRCA1 is found in 0.1% of the general population, compared with 20% in the Ashkenazi Jewish population and is found in 3% of the unselected breast cancer population and in 70% of women with inherited early-onset breast cancer. [53] Up to 50-87% of women carrying a mutated BRCA1 gene develop breast cancer during their lifetime. Risks for ovarian and prostate cancers are also increased in carriers of this mutation. BRCA2 mutations are identified in 10-20% of families at high risk for breast and ovarian cancers and in only 2.7% of women with early-onset breast cancer. The lifetime risk of developing breast cancer in female carriers is 25-30%. BRCA2 is also a risk factor for male breast cancer; male carriers have a lifetime risk of 6% for developing the cancer. BRCA2 mutations are associated with other types of cancers, such as prostate, pancreatic, fallopian tube, bladder, non-Hodgkin lymphoma, and basal cell carcinoma.

Although there are claims on the Internet that breast cancer risk may be increased for women who wear underwire bras or who use antiperspirants, at present, there is no scientific evidence that shows an association between these products and breast cancer.[54] There are also claims that women who have had an abortion are at increased risk for developing breast cancer, but a recent review by a panel of

experts convened by the National Cancer Institute concluded that there is no association between medical abortion and developing breast cancer.[55] Subsequent to that review, a combined analysis of 53 studies, including 83,000 women with breast cancer, also found no link to a previous abortion, either spontaneous or induced.[56]

Despite concern that rising breast cancer incidence in the latter half of the 20th century may be caused by environmental pollutants such as organochlorine pesticides, studies to date have not found increased concentrations of organochlorines when measured in adults to be related to breast cancer risk in the general population.[57-59] Ongoing research is examining whether exposure to organochlorines during adolescence or at other critical periods may affect risk.

2.6 DIAGNOSIS

Breast self examination

To perform a breast self-exam, use a circling, massaging motion and follow a clock pattern or a wedge pattern. Alternatively, you can use a sweeping motion to examine breast tissue; sweeping your fingers from the outer part of your breast in toward your nipple.[60]

Early breast cancer causes no symptoms and is usually painless. The commonest symptom is a painless lump in the breast. Examination of the breast should be done in such a way to show respect for the privacy and comfort of the patient. A systematic approach to breast examination is important. Initial examination should start with the patient in an upright position with careful visual inspection of masses, skin and nipple changes, and asymmetries. Palpation should be done to include all the breast quadrants, the nipple-areola complex, the axillary tail and the axilla. Simple maneuvers like stretching the arms high above the head, tensing the pectoralis muscles may help accentuate asymmetries and dimpling.

Other less frequent presenting signs and symptoms of breast cancer include (1) breast enlargement or asymmetry; (2) nipple changes, retraction, or discharge, including Paget's disease; (3) ulceration or erythema of the skin of the breast including inflammatory carcinoma; (4) an axillary mass; and (5) systemic symptoms such as fatigue, cough, ascites or neo musculoskeletal discomfort.

Clinical breast examination

Unless one has a family history of cancer or other factors that place one at high risk, the American Cancer Society recommends having clinical breast exams once every

three years until age 40. After that, the American Cancer Society recommends having a yearly clinical exam.

During this exam, the doctor examines the breasts for lumps or other changes. He or she may be able to feel lumps you miss when you examine your own breasts and will also check for enlarged lymph nodes in your armpit (axilla).[60]

Mammography

Mammography is a low-dose x-ray procedure that allows visualization of the internal structure of the breast. Mammography is highly accurate, but like most medical tests, it is not perfect. On average, mammography will detect about 80%-90% of breast cancers in women without symptoms. Testing is somewhat more accurate in Postmenopausal than in premenopausal women.[61] The small percentage of breast cancers that are not identified by mammography may be missed for any of the following reasons: breast density, faster tumor growth rate, or simply failing to see the small early signs of an abnormality. Although the overwhelming majority of women who undergo screening each year do not have breast cancer, about 5%-10% of women have their mammograms interpreted as abnormal or inconclusive until further tests are done. In most instances, additional tests (Imaging studies and /or biopsy) lead to a final interpretation of normal breast tissue or benign (Non cancerous) tissue. It is especially important that women receive regular mammograms.

Recommended screening intervals are based on the duration of time a breast cancer is detectable by mammography before symptoms develop. Studies have

shown that many breast cancers are diagnosed as larger, more advanced cancers simply because too much time has elapsed from the date of the last normal mammogram.[62,63] For this reason, women should talk with their doctors about a plan for receiving regular mammograms according to recommended guidelines.

Numerous randomized trials and population-based evaluations of screening mammography have clearly shown that early detection of breast cancer through mammography greatly improves treatment options, the chances for successful treatment, and survival. [64-67] Mammography is the single most effective method of early detection, Since it can Identify cancer several years before physical symptoms develop. Treatment is more successful when cancer is discovered early.

2.7 PREVENTION

At this time, there is no guaranteed way to prevent breast cancer, which is why regular mammograms are so important. A woman's best overall preventive health strategy is to reduce her known risk factors as much as possible by avoiding obesity and weight gain, increasing physical activity, and minimizing alcohol intake.[93] Women should consider the increased risk of breast cancer associated with HRT use in evaluating treatment options for menopausal symptoms. Treatment with tamoxifen can also reduce the risk of breast cancer among women at high risk.

2.7.1 Obesity

Obesity increase risk of postmenopausal, but not premenopausal, breast cancer,[68] and other studies have found weight gain during adulthood may further increase risk. [69-71] in postmenopausal women, circulation estrogen is primarily produced in fat tissues. Thus, having more fat tissue can increase estrogen levels and the likelihood of developing breast cancer. A recent large American Cancer society study showed that women who were overweight (BMI>25) are 1.3 to 2.1 times more likely to die from breast cancer compared to women with normal weight (BMI=18.5-24.9).[72]Given the large percentage of women in the United States who are overweight, strategies to maintain a healthy body weight are important to reduce the risk of both getting and dying from breast cancer.[73]

2.7.2 Physical activity

There is evidence that supports a small protective association between physical activity and breast cancer.[68,74,75] A recent study suggests that regular physical activity, regardless of intensity, may reduce the risk of breast cancer in postmenopausal women.[75]The protective effect may be even greater among lean women, women who have carried children to term, and premenopausal women. The underlying mechanism of this potential protection is not well understood, although it has been hypothesized that the benefit may be due to the effects of physical activity on hormones and energy balance.[68,76]

2.7.3 Alcohol Consumption

Alcohol is consistently associated with increased breast cancer risk.[77,93] A meta-analysis of more than 40 epidemiologic investigations suggests that the equivalent of two drinks a day (or 24g of alcohol) may increase breast cancer risk by 21%. This increased risk is dose-dependent and exists regardless of the type of alcohol beverage consumed.[78] A recent review concluded that the most likely mechanism by which alcohol increases risk of breast cancer is by increasing Estrogen and Androgen Level s.[79] Thus, reducing alcohol intake may be a useful strategy for reducing breast cancer risk among regular consumers of alcohol.

2.7.4 Tobacco

Most studies have found no link between active cigarette smoking and breast cancer. [77,80] Though both active smoking and secondhand smoke have been suggested to increase the risk of breast cancer in a number of studies that restrict the comparison group to women who report no exposure to secondhand smoke, this issue remains controversial.[80,81] However, no secondhand smoke is beneficial for multiple health reasons.

2.7.5 Hormone replacement therapy (HRT)

Use of combined HRT increase the risk of breast cancer.[82] the US preventive services task force has recommended against the routine use of HRT for the prevention of alcohol diseases in postmenopausal woman.[83] A woman considering HRT should discuss the benefits with her doctor and let her doctor decide that HRT is appropriate to treat specific menopausal symptoms or health problems, it

should be prescribed at the lowest effective dos and for as short a time as possible. Other treatments for these symptoms and conditions should also be considered.

2.7.6 Tamoxifen

The drug Tamoxifen has been used for many years as a treatment for some breast cancers. A large randomized trial demonstrated that Tamoxifen can also be used to reduce the risk of breast cancer in women at high risk for developing the disease.[84] After a median follow-up of more than 69 months, breast cancer risk decreased by 49% in the group that received Tamoxifen, with 22 cases of breast cancer diagnosed per 1,000 women, compared to 43cases per 1,000 in the group who did not receive Tamoxifen. A protective effect was also observed in an international randomized prevention trial.[85] In that trials, the group that receive tamoxifen reduced their breast cancer risk by 32%, with 69 cases diagnosed among 3,578 women in the tamoxifen group, compared to 101 cases among 3,566 women in the group not receiving tamoxifen. Administration of tamoxifen resulted in some risks in both trials, particularly an increased risk of endometrial cancer. A woman at increased risk of breast cancer should discuss taking tamoxifen with her doctor. It is estimated that more than two million US women could benefit from tamoxifen chemoprevention.[86]

2.7.7 Prophylactic surgery

Women at very high risk of breast cancer may elect preventive (prophylactic) mastectomy. This operation removes one or both breasts before cancer has been discovered. A recent study reported a greater than 90% reduction in risk of breast cancer in high-risk women with a family history who received prophylactic

mastectomy.[87] Subsequently studies confirmed the benefit of prophylactic mastectomy in genetically susceptible women, i.e. women with a BRCA1 or BRCA2 mutation.[88-90] While the operation reduces the risk of breast cancer, it does not guarantee that cancer won't develop in the small amount of breast tissue remaining after the operation. Prophylactic oophorectomy (surgical removal of the ovaries) also appears to reduce the risk of breast cancer, as well as ovarian cancer, in carries of BRCA mutations.[91, 92] A woman considering these operations should discuss these issues carefully with her doctor.

CHAPTER THREE

3.0 METHODOLOGY

3.1 Study Area –Abuja

Abuja is the capital of Nigeria. It is located in the centre of Nigeria in the Federal Capital Territory (FCT). It is a planned city and officially became Nigeria's capital on 12th December 1991 replacing Lagos the previous capital.As at the 2006 census the FCT has a population of 778,567. The FCT was formed on the 3rd of February 1976 from parts of former Nasarawa, Niger and Kogi State. Unlike the states in Nigeria headed by elected Governors, it is administered by a minister appointed by the president.

The territory is located just North of the confluence of Niger and Benue rivers. It is bordered by the states of Niger to the west and North, Kaduna to the Northeast, Nasarawa to the east and South and Kogi to the South west. Abuja lies between latitude 8.25 and 9.20 north of the equator and longitude 6.45 and 7.39 east of Greenwich meridian. It has a land mass of approximately 8000km^2 of which the city occupies 250sq km. It is situated within the savannah region with moderate climatic condition.

The FCT experiences three weather conditions annually; a warm humid rainy season, a blistering dry season and in between these two seasons, a brief interlude of harmattan occasioned by the North East Trade wind, with the main feature of dust haze, intensified coldness and dryness. The rainy season begins from April and ends in October with total annual rainfall ranging from 1100mm to 1600mm.

In the rainy season, daytime temperatures reach 28-30^{o}C and nighttime lows around 22-23 ^{o}C. In the day season, daytime temperatures can soar up to 40 ^{o}C and nighttime temperature as low as 12 ^{o}C resulting in chilly evenings. The FCT falls within the forest savannah mosaic zone of the west Africa sub-region. Patches of rainforest however occur in the Gwagwa plains especially in the gullied terrain to the south and the rugged south eastern parts of the territory. Predominant tribe/ ethnic group is Gbagyi other tribes are; Izon and Gede. Major occupation of the people is yam cultivation.

The FCT is currently made up of six area councils namely:- Abuja, Abaji, Gwagwalada, Kuje, Bwari and Kwali. Abuja city is further divided into districts; Central district Garki, Wuse, Maitama, Asokoro, and Gwarimpa. Most people living in Abuja are civil servants working in the ministries and parastatals. Minority are engaged in trading and business. The central district is the city's principal Business zone also known as the three arms zone because it houses administrative offices of the executive legislative and judicial arms of the federal government.

The National Hospital Abuja located within the central district was originally designed to cater for the needs of women and children in Nigeria and the West African sub-region with a view to reduce morbidity and mortality rates, and to carry out extensive research into the peculiar causes of women and children-related diseases in Africa. Being a tertiary hospital, accepts referrals from private hospital, primary health care facilities, specialist hospital as well as from other tertiary hospitals in the country. The hospital is well equipped in handling cancer

patients. The hospital offers surgery, chemotherapy, radiotherapy, ultrasound scanning service as well as clinical services.

3.2 Design of Study:

Retrospective case control study was done to identify, determine as well as establish risk factors that predisposes one to breast cancer.

3.3 Target Population:

The target populations for the study were patients diagnosed with breast cancer attending the National Hospital Abuja for treatment. The controls were patients who had same exposure as those with breast cancer but had other types of cancer like cervical cancer, prostrate cancer, GIT cancer etc.

3.4 Sample Size:

The sample size was determined using the formula;[98]

$$N = \frac{Z^2Pq}{d^2}$$

Where N = Sample size

Z = confidence limits

P= Prevalence of a previous study

d= Sampling error

q=1-P

In a work by Jamal et al [99] the prevalence was obtained to be 23% (0.23)

Where P = 23% (0.23)

Z = 1.96

d = 0.05

$$q = 1-0.23 = 0.77$$

$$N = \frac{(1.96)^2 \times 0.23 \times 0.77}{(0.05)^2} = 272$$

A total of 544 samples comprising of 272 cases and 272 controls were used in the study. The method of sampling was simple random sampling. Samples were obtained directly from the cancer records of the hospital the years 2005 to 2009 and being a retrospective study, diagnosed breast cancer patients were matched with criteria .

Exclusion criteria

Patients with no bio-data in their case files were excluded from the study.

3.5 Data Collection:

Information was collected directly from patient's case files from the cancer registry. To hasten the work, two research assistants were trained to assist in the data collection, retrieval of files and matching of the cases with controls. Data collected from patients case files were; Sex, Age, Occupation Family History, Weight, Height, Alcohol consumption, Menarche, BMI, Religion, Smoking, Marital Status parity and Contraceptive history. The data was hand filled in the prepared checklist and can be seen in Appendix I..

3.6 Data Entry and Analysis

The statistical package used was SPSS 15. The P value to be accepted as significant was set at $P< 0.05$ at 95% confidence level. Data was entered as

variables. Continuous variables like parity were grouped with an interval of 5, age with an interval of 10 .

Patients with breast cancer were matched with controls who had some exposure to risk factors obtainable for breast cancer but had other types of cancer other than breast cancer; cervical cancer, prostrate cancer, cancer of the gastrointestinal tract and skin cancers.

Test statistics performed were chi-square (X^2) and odds ratio (OR). The chi-square was used to determine the association for the risk factor contributing to breast cancer while the odds ratio was used to establish the risk factor.

3.7 Study Hypothesis and Decision rules

Ho - There is no relationship or association between breast cancer and the given risk factor.

HA - There is a relationship or association between breast cancer and the given risk factor.

Decision rules

1. If $P < 0.05$, then there is significant association but if $P > 0.05$, then there is no association.
2. If $OR > 1$ then, it is a risk factor but if $OR < 1$, it is not a risk factor.

3.8 Ethical consideration

Copies of the proposal was sent to the Health Research Ethics Committee (HREC) of the National Hospital Abuja and their approval letter is in appendix II.

3.9 Limitations of study.

The study being a retrospective study, it had the following limitations;

- Inadequate information in patient's case file which may be due to inadequate clerking of patients or misplacement of patients case notes. This was observed while trying to obtain the BMI of the patients. Only patients with their BMI known were recorded.
- Problem of memory recall as some patients failed to remember age at menarche and family history of breast cancer resulting to fewer data obtained. Those with family history were recorded.
- Matching of the case to appropriate controls took much time as controls had to be exposed to risk factors obtainable for Breast cancer. Matching was done with respect to age, sex, occupation, family history, alcohol consumption, weight, height.
- Collecting the required data took time as required parameters had to be searched in the case files rather than being obtained from a computer.
- Some of the patients were referrals and their case notes had little or no bio-data in them. Those without bio-data were replaced.

However these limitations were overcome by replacing case files, which had sufficient bio-data in them.

CHAPTER FOUR

4.0 RESULTS

Table One: Gender of patients

		Cases	N (%)	Control	N (%)	Total	N (%)
Gender	Female	267	98.2	252	93.4	521	95.8
	Male	5	1.8	18	6.6	23	4.2
Total		272	100	272	100	544	100

	Value	df	P value
Pearson Chi-Square	7.675	1	.006
N of Valid Cases	544		

		95% Confidence Interval	
	Value	Lower	Upper
Odds Ratio for Gender (Female / Male)	3.786	1.385	10.350

Error

X^2 =7.675 df = 1 P= 0.006 OR = 3.786

A total of 544 patients were used in the study,267 (98.2%) of the cases were females, while 5 (1.8%) were males. 254(93.3%) of controls were females while 18 (6.6%) were males.The chi-square result of 7.675 at one degree of freedom and odds ratio of 3.786 are statistically significant.

Table two: Age of patients

		Cases	N (%)	Control	N (%)	Total	N (%)
Age group in years	25-34	32	11.9	29	10.8	61	11.4
	35-44	98	36.6	60	22.3	158	29.4
	45-54	74	27.6	86	32.0	160	29.8
	55-64	40	14.9	81	30.1	121	22.5
	65-74	24	9.0	13	4.8	37	6.9
Total		268	100	269	100	537	100

	Value	df	P value
Pearson Chi-Square	27.348	4	.000
N of Valid Cases	537		

$X^2 = 27.348$, df = 4, P= 0.000

The cases wthin the age groups 25-34 are 32 (11-9%), 35-44 are 98(36.6%) 45-54 are 74(27.6%), 55-64 are 40 (14.9%), 65-74 are 24(9.0%) while the controls within same age groups are 29(10.8%), 60(22.3%), 86(32.0%), 81(30.1%) and 13(4.8%) respectively. The chi-square result of 27.348 at 4 degrees of freedom is statistically significant.

Table Three: Menarche of Patients

		Cases	N (%)	Control	N (%)	Total	N (%)
Menarche	Early	102	40.6	155	61.5	257	51.1
	Normal	149	59.4	97	38.5	246	48.9
Total		251	100	252	100	503	100

	Value	df	P value
Pearson Chi-Square	21.920	1	.000
N of Valid Cases	503		

		95% Confidence Interval	
	Value	Lower	Upper
Odds Ratio for Menarche (Early / Normal)	1.316	.874	1.981

$X^2 = 21.920$ df =1 P=0.000

Odd ratio (OR) = 1.316

A total of 503 patients were used in the study,102 (40.6%) of the cases and 155 (61.5%) of the control had early menarche while 149 (69.4%) of cases and 97 (38.5%) of control had normal menarche. The chi-square result of 21.920 at 1 degree of freedom and odds ratio of 1.316 are statistically significant.

Table Four: Use of Oral Contraceptives by patients

		Cases	N (%)	Control	N (%)	Total	N (%)
Use of contraceptives	Oral Contraceptive	44	17.3	66	26.4	110	21.8
	Don't use	211	82.7	184	73.6	395	78.2
Total		255	100	250	100	505	100

	Value	df	P value.
Pearson Chi-Square	6.197	1	.013
N of Valid Cases	505		

		95% Confidence Interval	
	Value	Lower	Upper
Odds Ratio for Use of contraceptives (Oral Contraceptive / Don't use)	1.288	1.070	1.552

$X^2 = 6.197$ df = 1 P=0.013

OR = 1.288

A total of 505 patients were considered,44(17.3%) of case and 66(26.4%) of control used oral contraceptive, while 211(82.7%) of cases and 184(73.6%) of control did not use oral contraceptive. The chi-sqare result of 6.197 at 1 degree of freedom and odds ratio of 1.288 are statistically significant.

Table Five: Parity of Patients

		Cases	N (%)	Control	N (%)	Total	N (%)
Parity	0	32	13.1	14	5.6	46	9.3
	1-5	155	63.5	206	81.7	361	72.8
	6-10	57	23.4	32	12.7	89	17.9
Total		244	100	252	100	496	100

	Value	df	P value
Pearson Chi-Square	21.147	2	.000
N of Valid Cases	496		

$X^2 = 21.147$, df= 2, P=0.000

Patients without a child were 32(13.1%) for cases and 14(5.6%) for controls. Patients with 1-5 children are 155(63.5%) for cases and 206 (81.7%) for controls. Patients with 6-10 children are 57 (23.4%) for cases and 32 (12.7%) for controls. The chi-square result of 21.147 at 2 degrees of freedom is statistically significant.

Table six: Family History of Breast Cancer among patients

		Cases	N (%)	Control	N (%)	Total	N (%)
Family history	Sister	18	34.0	19	19.6	37	24.7
	Mother	21	39.6	39	40.2	60	40.0
	Aunt	12	22.6	20	20.6	32	21.3
	Cousin	2	3.8	19	19.6	21	14.0
Total		53	100	97	100	150	100

	Value	df	P value
Pearson Chi-Square	9.062	3	.028
N of Valid Cases	150		

Patients who had a sister with breast cancer were 18 (34.0%) for cases and 19(19.6%) for control while those whom had mothers with breast cancer were 21 (39.6%) for cases and 39 (40.2%) for controls. Patients who had aunt with breast cancer were 12 (22.6%)z for cases and 20 (20.6%) for control, while those who had cousin with breast cancer were 2 (3.8%) for cases and 19 (19. 6%) for controls. The Chi-square result of 9.062 at 3 degree of freedom is statistically significant.

Table Seven:Occupation of patients

		Cases	N (%)	Control	lN (%)	Total	N (%)
Occupation	Civil servant	97	37.9	132	48.9	229	43.5
	Housewife	55	21.5	41	15.2	96	18.3
	Student	10	3.9	8	3.0	18	3.4
	Business	73	28.5	47	17.4	120	22.8
	Farmer	4	1.6	10	3.7	14	2.7
	Retiree	17	6.6	32	11.9	49	9.3
Total		256	100	270	100	526	100

	Value	df	P value
Pearson Chi-Square	20.051	5	.001
N of Valid Cases	526		

$X^2 = 20.051$, df = 5 P= 0.001

Patients who are civil servants were 97(37.9%) for cases and 132(48.9%) for controls while housewives were 55(21.5%) for cases and 41(15.2%) for controls. Students were 10(3.9%) for cases and 8(3.0%) for controls while those doing business were 73(15.2%) for cases and 47(17.4%) for controls. Farmers amongst the patients were 4(1.6%) for cases and 10(3.7%) for controls while retirees were 17 (6.6%) for cases and 32(11.9%) for controls. The Chi-square result of 20.051 at 5 degrees of freedom is statistically significant.

Table eight: Alcohol consumption by patients

		Cases	N (%)	Control	N (%)	Total	N (%)
Alcohol consumption	Yes	158	59.0	106	39.3	264	49.1

	Value	df	Pvalue
Pearson Chi-Square	20.878	1	.000
N of Valid Cases	538		

		95% Confidence Interval	
	Value	Lower	Upper
Odds Ratio for Alcohol consumption (Yes / No)	2.222	1.574	3.137
N of Valid Cases	538		

X^2 = 20. 87 df =1 P= 0.000

OR = 2.222

A total of 538 patients considered showed that 158 (59.0%) of cases and 106 (39.3%) of control took alcohol while 110 (41.0%) of cases and 164 (60.7%) of cotrols, did not take alcohol. The Chi-square result of 20.878 at 1 degree of freedom as well as odds ratio of 2..22 are satistically significant.

Table Nine: Smoking amongst patients

		Cases	N (%)	Control	N (%)	Total	N (%)
Do you smoke?	Yes	15	5.6	10	3.7	25	4.6
	No	255	94.4	260	96.3	515	95.4
Total		270	100	270	100	540	100

	Value	df	P value
Pearson Chi-Square	1.049	1	.306
N of Valid Cases	540		

		95% Confidence Interval	
	Value	Lower	Upper
Odds Ratio for Do you smoke? (Yes / No)	1.529	.675	3.468
N of Valid Cases	540		

$X^2 = 1.049$, df = 1, P = 0.306

OR = 1.529

A total of 540 patients were considered, 15 (5.6%) of cases ad 10(3.7%) of controls, smoked while 255 (94.4%) of cases and 260 (96.3%) controls did not smoke.The chi-square result of 1.049 at 1 degree of freedom is not statistically significant though the odds ratio of 1.529 is significant.

Table Ten: BMI Status of patients

		Cases	N (%)	Control	N (%)	Total	N (%)
Status of BMI	Underweight	28	30.4	19	35.2	47	32.2
	Overweight	64	69.6	35	64.8	99	67.8
Total		92	100	54	100	146	100

	Value	df	P value
Pearson Chi-Square	.352	1	.553
N of Valid Cases	146		

		95% Confidence Interval	
	Value	Lower	Upper
Odds Ratio for Status of BMI (Underweight / Overweight)	.806	.395	1.645
N of Valid Cases	146		

$X^2 = 0.352$, df = 1, P = 0.553

OR = 0.086

Out of 146 patients considered, 28 (30.4%) of cases and 19 (32.2%) were underweight while 64 (69.6%) of cases and 35 (64.8%) of controls were over weight. The chi-square result of 0.352 at 1 degree of freedom as well as odds ratio of 0.553 are both statistically not significant

Table Eleven: Religion of patients

		Cases	N (%)	Control	N (%)	Total	N (%)
Religion	Christianity	233	85.7	228	83.8	459	84.7
	Islam	39	14.3	44	16.2	83	15.3
Total		272	100	272	100	544	100

	Value	df	P value
Pearson Chi-Square	.356	1	.551
N of Valid Cases	544		

		95% Confidence Interval	
	Value	Lower	Upper
Odds Ratio for Religion (Christianity / Islam)	1.153	.722	1.842
N of Valid Cases	544		

X 2 = 0.356, df = 1, P = 0.551

OR = 1.153

In a total of 544 patients, Christians were 233 (85.7%) for cases and 228 (84.7%) for controls while those practising Islam were 39 (14.3%) for cases and 44 (16.2%) for controls. The chi-square result of 0.356 at 1 degree of freedom was statistically not significant though the odds ratio of 1.153 is statistically significant.

Table Twelve: Marital Status of patients

		Cases	N (%)	Control	N (%)l	Total	N (%)
Marital status	Married	230	85.5	217	80.4	447	82.9
	Single	34	12.6	22	8.1	56	10.4
	Widow	5	1.9	31	11.5	36	6.7
Total		269	100	270	100	539	100

	Value	df	P value
Pearson Chi-Square	21.726	2	.000
N of Valid Cases	539		

$X^2 = 21.726$, df = 2, P = 0.000

A total of 539 patients were considered in the study, those who were married had 230 (85.5%) for cases, 217 (80.4%) for controls, while singles had 34 (12.6%) for cases and 22 (8.1%) for controls. Widows had 5(1.9%) for cases and 31 (11.5%) for controls. The chi-square result of 21.726 at 2 degrees of freedom is statistically significant.

CHAPTER FIVE

5.0 DISCUSSION

Gender of patients showed that 267 (98.2%) cases of breast cancer were females while 5(1.8%) cases were males. A result of 7.675 indicated a significant association with breast cancer. The odds ratio for gender is approximately 3.8.This shows a risk of 3.8 times of having breast cancer amongst females than males. This is consistent with a table by Hulka *et al* 2001[96] showing factors that increase the relative risk for breast cancer in women, indicated that the highest relative risk factor of 4.0 is the female factor for breast cancer. This finding concurs with studies by Fentiman *et al* 2001[29] and Weiss *et al*, 2005[31] revealing that breast cancer is 100 times more common in women than in men, with men breast cancer accounting for < 1% of all breast cancer mortality in men. In addition, women having one or several risk factors may not necessarily mean they have to develop breast cancer as most women with breast cancer have no known risk factor other than simply being a female[60]. This showed that in the study, breast cancer is most common in females than in males.

The age groups 35-44 and 45-54 of cases with breast cancer had the highest frequencies of 98 (36.6%) and 74 (27.6%) respectively. This indicated that most patients presenting with breast cancer were premenopausal. Similarly when compared with works by Adebamowo *et al*, 2006[5]and Newman, 2005[27] revealed the peak age incidence in Africans and African- American to fall between 40-49 years, while it is a decade more amongst Caucasians. Cases with age groups 25-

34 and 55-64 showed lesser frequencies of 32 (11.9%) 40 (14.9%) respectively while cases with age group 65-74 showed the least frequency of 24 (9.0%). A result of 27.348 revealed significant association for breast cancer. This finding agrees with a work by Ijaduola and Smith which shows that incidence of breast cancer increase with age though rare before 20 years of age and drops after menopause[26]. A report in Breast cancer facts and figures 2005-2006 showed a woman's risk of developing breast cancer at different ages. At 30years and above, a woman has 1 in 230 chance, while by 79 years and above, 1 in 8 chances. Hence besides being female, age is the most important risk factor for breast cancer.[94] This finding agrees that women presenting with breast cancer are mostly pre-menopausal and have a greater risk of developing breast cancer than post-menopausal women.

257 (51.1%) of patients had early menarche of 9-11 years in both cases and control and while 246 (48.9%) had normal menarche at 12 years for both cases and control. A result of 21.920 revealed significant association with breast cancer when compared with Fentiman , 2001[29] in his work; fixed and modifiable risk factors, presented early menarche as a fixed factor associated with increased risk of breast cancer amongst age, family history, late menopause and at first full term pregnancy. The odds ratio revealed a 1.3 times risk of breast cancer in females with early menarche. In the same view, when compared with a table of factors that increase relative risk for breast cancer in women by Hulka *et al* 2001[96] on breast cancer hormones and other factors, reveal risk of menarche to fall between 1.1-2.0. This finding agrees with Hulka et al, 2001[96] who attributed the

risk factor to the effect of breast hormone (estrogen) and which experts believe that exposure of breast tissue to estrogen gives a greater likelihood of developing Breast cancer.[60] This findings indicate that females with early menarche are at risk of developing breast cancer.

Oral contraceptive use by patients in showed that 110 (21.8%) of both cases and control, took oral contraceptives while 395(78.2%) of both cases and controls did not take. A result of 6.197 showed significant association. This finding is consistent with works by Okobia *et al*, 2006[40] and Colditz, 2005[37], who are of the opinion that estrogen is the primary stimulant for breast epithelial proliferation hence factors which increase exposure to high or prolonged level of estrogen are associated with increased risk of developing breast cancer.[37] The odds ratio reveal approximately 1.3 times the risk of developing breast cancer by those who take oral contraceptive and it concurs with that by Hulka *et al* 2001[96]. Experts believe that the use of oral contraceptives is associated with an increased risk of breast cancer in pre-menopausal women and the risk is greater for women who use oral contraceptives for four or more years before their first full term pregnancy.[60] In addition recent use of oral contraceptive may slightly increase the risk of breast cancer in post menopausal women.[95] The finding totally agrees that prolonged use of oral contraceptives amongst pre-menopausal women raises the risk of having breast cancer.

Parity among patients showed a significant association with breast cancer with a result of 21.147 when compared with a similar work by Basu, *et al*, 2005[36] on Genes related to estrogen action in reproduction and breast cancer revealed a

strong association of 27.3 between parity and breast cancer.This finding agreed with Hulka *et al,* 2001[96] in his work; Breast cancer: hormones and other risk factors, which showed that nulliparity and fewer number of pregnancies may increase a womans's risk of breast cancer by affecting the endogenous reproductive hormones her body produces.

Family history of breast cancer showed the highest frequency for mother 60(40.0%) for both cases and control while sister accounts for 37 (24.7%) for both cases and controls. Aunt had 32 (21.3%) and cousin had 21(14.0%). In a total of 150 patients with a family history, first degree relatives;- mother and sister accounted for more than half of the patients in both case and controls. A result of 9.06 revealed a significant association when compared with a work by Loman *et al* 2001[97] on family history of breast cancer and ovarian cancer and BRCA1 and BRCA2 mutation in a population-based series of early onset cancer, a significant association was found with family history and breast cancer especially first degree relatives(mother, sister) having an increasing risk of developing breast cancer among the relatives. Inaddition Bucholz *et al* 2002[52] in a work; evidence of haplotype insufficiency in human cells containing a germline mutation in BRCA1 or BRCA2 in 2002, attributed inherited breast cancer (5-10%) to 2 germline mutation, BRCA1 and BRCA1 which are inherited in an autosomal dominant fashion with varying peretrance. This finding reveals that family history of people who had first degree relatives; mother and sister that had breast cancer, were at greater risk of developing breast cancer.

Occupation being a socio-demographic variable, revealed a significant association withbreast cancer with a result of 20.05. Patients who were civil servants are 229(43.6%), housewives 96(18.3%), Retirees 49 (9.3%) or in Business 120 (22.8%) for both controls cases may be considered not to be physically active compared to farmers 14 (1.7) who are physically active hence prone to living a sedentary life style, thus increasing the risk of developing breast cancer due to the nature of work they perform. This result is in accordance with the works by Hulka *et al*, 2001[96] and Adesunkanmi *et al*,2006[6] which revealed physical inactivity as a modifiable associated risk factor . This finding indicates that occupations which makes one physically inactive increases ones risk of having breast cancer.

Alcohol consumption by patients had 264 (49.1%) of both cases and control consuming alcohol while 274 (50.9%) of both cases and control not consuming alcohol. A result of 20.878 revealed significant association when compared with a work by Dumitrescu *et al* 2005[48] in the etiology of alcohol induced breast cancer, alcohol consumption showed a significant association of 25.65. The odds ratio further revealed a 2.2 risk of developing breast cancer by alcohol which is slightly higher than Hulka *et al*, 2001[96] table of factors that increase the related risk of cancer in women, alcohol falls between 1.1-2.0 . Hence the finding strongly suggests that alcohol consumption is a strong risk factor for breast cancer.

Smoking had no association with breast cancer. Studies by Hamajima *et al* 2002[77] reveal no link between active cigarette smoking and breast cancer. Though researchers suggest that active smoking and exposure to second hand smoke

increase the risk of breast cancer, in a number of studies that restrict comparison group to women who report no exposure to second hand smoke, the issue remains controversial[80,81]. This finding showed that smoking was not associated with breast cancer. With respect to BMI, the result revealed no association with breast cancer. Though studies reveal obesity increases risk for post menopausal but not pre-menopausal breast cancer[68]. BMI is not identified as a risk factor in the study, this could be attributed to less data obtained from patients cases files.

Religion did not show any association though it had an odds ratio of 1.15. It is not identified as risk factor for breast cancer. Also previous works did not reveal any link of religion to breast cancer. Finally, marital status showed a significant association, studies however have not revealed any link or association to breast cancer. It may be identified as a risk factor for breast cancer though more research is needed in this area to justify marital status as a risk factor for breast cancer.

CHAPTER SIX

6.0. CONCLUSION

In the study gender showed an odds ratio of approximately 3.8 with a significant association with breast cancer. It is thus established that being a female is a single greatest risk factor for developing breast cancer. On the other hand, age revealed that incidence increase with age and drops after menopause. In addition age revealed a significant association with breast cancer and thus established as the most important risk factor for breast cancer besides being female.

Early menarche revealed a strong association with breast cancer with 1.3 time risk of developing breast cancer in females. This risk as explained by experts is attributed to exposure of circulating estrogen hormone responsible for the proliferation of epithelial cells of the breast tissue. Thus early menarche is an established strong risk factor of breast cancer. Furthermore, oral contraceptive use was found to have a significant association with breast cancer, it also had approximately 1.3 times risk of developing breast cancer. Thus from the study oral contraceptives is established as a risk factor for breast cancer.

Parity among patient revealed a strong association with breast cancer and in conjuction with other works revealed that nulliparity and fewer number of pregnancies increase a woman's risk of breast cancer. Thus parity is a risk factor of breast cancer. More also occupation among patients revealed a significant association with breast cancer in conformity with other works, indicate physical inactivity a factor associated with breast cancer. Family history revealed

significant association with increasing risk of developing breast cancer among relatives, especially first-degree relatives; mother and sister.

Alcohol consumption showed a significant association with breast cancer and a 2.2 risk of developing breast cancer. Thus it is an established risk factor for developing breast cancer.

Finally, Smoking, Religion, BMI and Marital status of patients were not identified as risk factors for breast cancer and also did not reveal any association with breast cancer. They are not risk factors for breast cancer.

6.1 RECOMMENDATIONS

The following recommendations are made to improve the health consciousness of the public on risk factors for breast cancer;

1. Health Education: To increase the awareness of causes and prevention amongst teenagers, young and old women in rural as well as urban areas, through community health workers, mass media, social groups-women August meeting etc.
2. Provision of free routine clinical breast examination by health professional, clinicians regularly to detect early cases of breast cancer as well as treat them in community health facilities and primary health care centres.
3. Intersectoral collaboration by government agencies and philanthropic organizations, should show empathy about the plight of patients by providing regular financial and material support such as free drugs, procurement of mammography and radiotherapy machines etc for screening, diagnosis and treatment.

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