RISK FACTORS ASSOCIATED WITH BREAST CANCER AMONG WOMEN IN TWO REFERRAL CENTRES IN NIGERIA

BY

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ABSTRACT

Breast Cancer (BC) is a common cause of death among Nigerian women. Past studies suggest that diet, lifestyle and environmental pollutants are more important risk factors in the aetiology of cancers. Identifying some of these factors is vital to directing strategies for intervention in specific locations. This study was carried out to determine risk factors associated with BC among women in two referral hospitals in Nigeria.

A case-control study was carried out among 266 women aged 20-80 years. Warri Central Hospital and University College Hospital were purposively selected based on their Management's approval to be part of the study. 35 and 30 cases of BC were recruited from the hospitals, respectively. For the controls, consenting women in Warri (111) and Ibadan (90) were enlisted from neighbouring households in the same enumeration areas as the cases. Cases and controls were matched in the ratio of 1:3 for age and duration of stay in area of residence. A semi-structured questionnaire was used to collect data on socio-demographic characteristics, family history of breast cancer, dietary pattern, nutritional status, physical activity and environmental factors. Food frequency questionnaire was used to assess high risk food intake where consumption of high calorie-containing food ≥ 3 times week was categorised as high and <3 times a week as low. Body mass index (kg/m2) and waist-to-hip ratio were used to determine respondent's nutritional status and abdominal fat, respectively. Physical activity was measured using WHO standard (where exercise for at least a three times per week was categorised as good while less than three times a week as poor). Frequency of exposure to automobile, generator, industrial fumes and effluents was categorised qualitatively as daily, occasional and rarely. Data were analysed using descriptive statistics, Chi-square test and logistic regression at 5% level of significance.

The mean age of the respondents was 48.7±11.8 years. Family history of breast cancer was reported by 6.2% of the cases and 5.0% of controls. Dietary pattern revealed that cases (69.2%) and controls (54.7%) significantly had high risk consumption pattern for high calorie containing foods. Cases were significantly more overweight than the controls (41.5% versus 21.4%). Higher proportion of controls (58.6%) than the cases (22.9%) had high risk abdominal obesity. Significantly more controls than cases had good exercise (17.9% versus 6.2%). The odds of developing breast cancer was four times higher among women who reported daily exposure to fumes from automobiles and generators than those who were rarely exposed (OR=4.40, CI=1.25-

15.57), seven times higher among women who reported occasional exposure to wastes from operating industries than those who were rarely exposed (OR=6.91, CI=2.87-16.66).

Major risk factors for breast cancer among women in Warri and Ibadan were lack of exercise, high calorie containing food intake, environmental pollutants and nutritional status. Health education to improve knowledge of self-protection against pollutants and adoption of healthy dietary habits may reduce risk of breast cancer.

Keywords: Breast cancer, Environmental pollutants, Dietary pattern.

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DEDICATION

I dedicate this dissertation to God Almighty, my parents and all cancer patients in the world.

DECLARATION

I hereby declare that this work is original. The work has neither been presented to any other faculty for the purpose of the award of a degree nor has it been submitted elsewhere for publication.

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CERTIFICATION

We certify that this work was carried out in the Department of Epidemiology and Medical Statistics, Faculty of Public Health, University of Ibadan under our supervision.

.....20/7/2014.....

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ABBREVIATIONS

IARC	-	International Agency for Cancer Research
ADH	-	Atypical Ductal Hyperplasia
ALH	-	Atypical Lobular Hyperplasia
AOR	-	Adjusted Odds Ratio
BMI	-	Body Mass Index
BRCA1	-	Breast Cancer gene 1
BRCA2	-	Breast Cancer gene 2
BRECAN	-	Breast Cancer Association of Nigeria
CBE	-	Clinical Breast Examination
CI	-	Confidence Interval
DCIS	-	Ductal Carcinoma In Situ
DCPP	-	Disease Control Priorities Project
FFQ	-	Food Frequency Questionnaire
LCIS	-	Lobular Carcinoma in Situ
OR	-	Odds Ratio
PAHs	-	Polynuclear Aromatic Hydrocarbons
SEER	-	Surveillance Epidemiology End Results
SPSS	-	Scientific Package for Social Sciences
TDLU	-	Terminal Ductal-Lobular Units
TNM	-	Tumour Node Metastases
UCH	-	University College Hospital
WHO	-	World Health Organization
WHR	-	Waist Hip Ratio

CHAPTER ONE

INTRODUCTION

1.1 Background of the Study

Breast Cancer is a type of cancer that forms in tissues of the breast, usually the tubes that carry milk to the nipple (ducts) and glands that make milk (lobules). It occurs in both men and women, although male breast cancer is rare (National Cancer Institute, 2011). There are several symptoms of breast cancer and these include swellings or lumps in the breast or in the armpit, changes in the size and shape of the mature breast, especially if it is prominently noticed in one breast; fluid or blood discharging from the nipple, especially in older women; and noticeable changes occurring in the size and shape of the nipple or a nipple that does not easily return to its normal shape. The most common types of breast cancer are: ductile carcinoma which is about 85 - 90% of all cases and lobular carcinoma which constitutes 8% of all cases, (National Cancer Institute, 2011).

The actual cause of breast cancer is unclear but studies have implicated age (Adebamowo and Ajayi, 2000), sex (McPherson et al., 2000), heredity (Bevier et al., 2012), reproductive factors (Hulka and Moorman, 2001), diet (Jemal et al., 2010), anthropometric characteristics (Adebamowo et al., 2003; Okobia et al., 2006), psychological factors (Ronit et al., 2008) and environmental factors (Adebamowo and Ajayi, 2000; Ana et al., 2010) as possible etiological factors. Evidence attributes the majority of cancers to not one single factor but various physical, environmental, and genetic factors. Factors affecting obesity, immunity, and the tumor's environment within the body, as well as exogenous environmental exposures are all examples of variables in the development of disease (American Cancer Society, 2010; National Cancer Institute, 2011). With one million new cases in the world each year, breast cancer is the most common malignancy in women and comprises 18% of all female cancers (GLOBOCAN, 2008). According to the Surveillance, Epidemiology, and End Results (*SEER*) data from 2002-2008, approximately 90% of women diagnosed with invasive breast cancer were still living five years after getting the disease; among black women, approximately 78% were still living five years after getting the disease (Altekruse et al., 2010).

Nigeria is the most populous nation in Africa with about 160 million people in 2011 (National Population Commission, 2013), and one in five black persons all over the world has Nigerian ancestry (Huo et al., 2009). Earlier studies conducted among Nigerian and African women in general, have revealed that breast cancer occurs earlier in these women compared with their Caucasian counterparts (Adebamowo and Ajayi, 2000, Odunsanya, 2001).

According to Odunsanya (2001) the disease is the most common malignancy seen in Nigerian women and its incidence rate seems to be rising. However, Nigeria has a lower incidence rate of breast cancer compared with the United States and other developed countries (Parkin et al., 2005)

The recent report of the World Health Organisation (WHO, 2012) calls for urgent action against the problem of cancer. According to the report, by the year 2020, cancer could kill up to 10 million people yearly with the number of new cases increasing from 11 million in 2002 to 15.7 million in 2020 worldwide. Breast cancer-related mortality rates are higher in developing countries as a result of late detection and diagnosis (Lawrence et al., 2010). Other attributed factors include genetics, cultural and social factors such as poverty, unequal access to prompt high quality treatment, lack of screening facilities, or lack of awareness and knowledge of the disease. Breast cancer ranks second to cervical cancer in cancer incidence and is still the second principal cause of cancer mortality among women worldwide including Nigeria (Adebamowo and Ajayi, 2000; Parkin, 2005; Okobia, 2006). However, amidst the alarming rate of incidence being reported breast cancer remains the most preventable and manageable among cancers with improved understanding of the aetiology and predisposing risk factors in specific geographical sites.

1.2 Statement of the Problem

Breast cancer is an increasingly important public health problem in developing countries of Africa (Farmer et al., 2010). It is by far the most frequent cancer among women with an estimated 1.38 million new cancer cases diagnosed in 2008 (23% of all cancers), and ranks second overall (10.9% of all cancers) globally. Incidence rates vary between women in Africa and women in Western Europe (see figure 1.1 on page 7) and are documented to be higher in developed regions of the world (except Japan) and low (less than 40 per 100,000) in most of the developing regions (GLOBOCAN, 2008).

In Nigeria, the age-adjusted incidence was 25.3 per 100, 000 women in 2001 therefore implying that if there are 30 million women older than 25years, then approximately 7,500 new cases will occur per year (Adebamowo, 2001). Furthermore, in 2010, the age-adjusted incidence was documented to be 54.3 per 100,000 Nigerian women thus representing a 100% increase over the last decade (Jedy-Agba, E., et al., 2012). It was reported by Banjo (2004) that the relative frequency of breast cancer to other female cancers from Cancer Registries in Nigeria were 35.3% in Ibadan, 28.2% in Ife-Ijesha, 44.5% in Enugu, 17% in Eruwa, 37.5% in Lagos, 20.5% in Zaria and 29.8% in Calabar. In all the

centres, except Calabar in Cross River and Eruwa in Oyo state, breast cancer rated first among other cancers. Banjo (2004) further reported that majority of cases occurred in pre menopausal women, and the mean age of occurrence ranged between 43–50 years across the regions. The youngest age recorded was 16 years.

Breast cancer is influenced by several risk factors out of which there are more relevant risk factors that may be related to breast cancer incidence in countries with rapidly increasing rates. Furthermore, even though the risks associated with diet, obesity, and exercise are not consistent between studies in the US and Europe, these factors are often cited as the cause of the increasing breast-cancer rates in developing countries (Porter, 2008). High fat intake, low vegetable intake, and low soy intake have all been implicated, but the data have not been consistent or conclusive. In one of the largest nutritional studies of women in Shanghai China, an aggregate "meat–sweet" diet was associated with only a modest increased risk of breast cancer compared with a more traditional vegetable-rich diet (Cui, et al., 2007). Risk of postmenopausal (but not premenopausal) breast cancer is documented to be increased among obese women, and physical exercise probably decreases the risk of postmenopausal breast cancer (~~American~~ Institute for Cancer, 2007).

Among women worldwide, breast cancer is the most common cause of cancer death (Chong et al., 2002; Harris et al., 2003, Okobia et al., 2006). In 2010, there were 438,000 deaths globally (Lozano, et al. 2012). High mortality rates in low resource countries are primarily due to late-stage disease presentation. For example, the high mortality rate to incidence rate (MR:IR) ratio in Africa to a large degree reflects the high proportion of women in many African countries who present with late-stage cancer. In sub-Saharan African countries, small studies indicate that up to 90% of women present with stage III or VI disease, many with large tumors (median of 10 cm) and clinically apparent lymph node metastases (Fregene and Newman, 2005). Breast cancer is responsible for about 16% of all cancer-related deaths in Nigeria (GLOBOCAN, 2002). In 2005, it caused 502,000 deaths (7% of cancer deaths; almost 1% of all deaths) worldwide (WHO, 2006).

Inadequate health care systems also contribute to high mortality rates. There are no examples of universal breast cancer ~~screening~~ in low resource countries that could down-stage breast cancer diagnoses. In addition, there are typically only a few hospitals that can administer radiotherapy and chemotherapy and very few trained oncologists (Nigeria, for instance, has approximately 100 oncologists for a population of over 140 million). National expenditure on health care overall inversely correlates with mortality from breast cancer, but there are exceptions (Igene, 2008). The effect of morbidity and mortality associated with the breast

cancer in Nigerian women is very disturbing. This alarming morbidity and mortality from breast cancer on Nigerian women in a nutshell is as a result varying environment specific predisposing factors, late presentation, poor awareness of risk factors, poor breast screening practices and high cost of treatment. In addition, psychological effects and economic consequences such as absence from work/business, lack of employment, high cost of treatment and high cost of palliative care (Adebamowo and Ajayi, 2000; Okobia et al., 2006; Osime, et al., 2008) constitute negative impact of the disease.

1.3 Justification of the Study

Every woman is at risk of developing breast cancer (American Cancer Society, 2007). Breast cancer risk is a function of genetic, lifestyle (westernization) and environmental factors. Geographical variations in incidence and mortality rates of breast cancer suggest that the known risk factors for breast cancer may vary in different geographical sites and that environmental factor which include, diet, lifestyle patterns and environmental pollutants are of greater importance than genetic factors (McPherson et al., 2001). There is no doubt that breast cancer now constitutes an important cause of morbidity and mortality and is rated second to lung cancer in both industrialised and non-industrialised nations of the world (Ogunbiyi, 2000; Olufunmilayo, 2000; Wild, et al., 2006).

The nature of the disease is such that each society, race and population must seek to define the characteristics of the disease among its people and evolve appropriate management strategy (McPherson et al., 2000). Although there has not been any significant association found between environmental exposures, dietary patterns and breast cancer in Nigeria and parts of Africa, ignoring these risk factors associated with breast cancer would be detrimental. This is because such information serves as a necessary surrogate measure to identify, track and investigate health disparities and risk factors as it relates to a particular race or geographical setting for the development of effective control programme. It is without doubt that the health professionals, especially clinicians and epidemiologists, have been the primary decision- makers in the development of breast cancer prevention policies. To enhance our understanding of the disease, there is a need to carefully evaluate earlier proposed risk factors and offer recommendations suitable for each society (Okobia, 2006).

The study sites Warri, Ibadan and its environs in Delta and Oyo States, Nigeria respectively are both unique in geographical setting and are made up of people with diverse ethnic groups, lifestyle, psychosocial factors, different dietary pattern and environmental exposures. Warri is well known for its crude oil producing capacity and the presence of oil companies like Shell, Chevron and many others which predispose residents to carcinogenic compounds.

Ibadan on the other hand is an ancient city that also has industries some of which include breweries and food industries and thus witnesses some high level of industrial activity. There are questions among researchers on the influence of environmental and psychosocial factors on cancer in general. This research therefore aimed at evaluating and comparing the risk factors associated with breast cancer among women in Warri, Delta state and Ibadan, Oyo state, Nigeria.

1.4 Significance of the study

Identifying the risk factors associated with breast cancer in these two geographical sites would provide an opportunity to distinguish between possible roles of genetics and environment in breast cancer etiology.

The findings of the study would be communicated to the public through seminar/workshops and publications in peer-reviewed journals. This information could also assist in policy formulation in order to reduce the effects of the identified risk factors for breast cancer among women in Nigeria. Furthermore, this study would serve as a reference point to researchers and health policy making.

1.5 Research Questions

This study addressed three research questions:

1. What are the risk factors for breast cancer among women in the two referral hospitals in Nigeria?
2. Are there any differences in the profiles of identifiable risk factors between women in these two study sites?
3. Are psychosocial factors associated with breast cancer risk among women in the two study sites?

1.6 Objectives of the Study

The general objective of the study was to investigate risk factors associated with breast cancer among women in two Nigerian referral hospitals located in Warri and Ibadan.

The specific objectives of the study were to:

1. Identify risk factors associated with breast cancer among women in study sites.
2. Identify the psychosocial factors associated with breast cancer.

3. Determine differences (if any) in risk factors among women in the two study sites.

1.7 Hypothesis of the Study

With statistical level of significance set at 5% the following null hypothesis was tested:

- There are no differences in risk factors for breast cancer among women in the two referral centres in Nigeria.

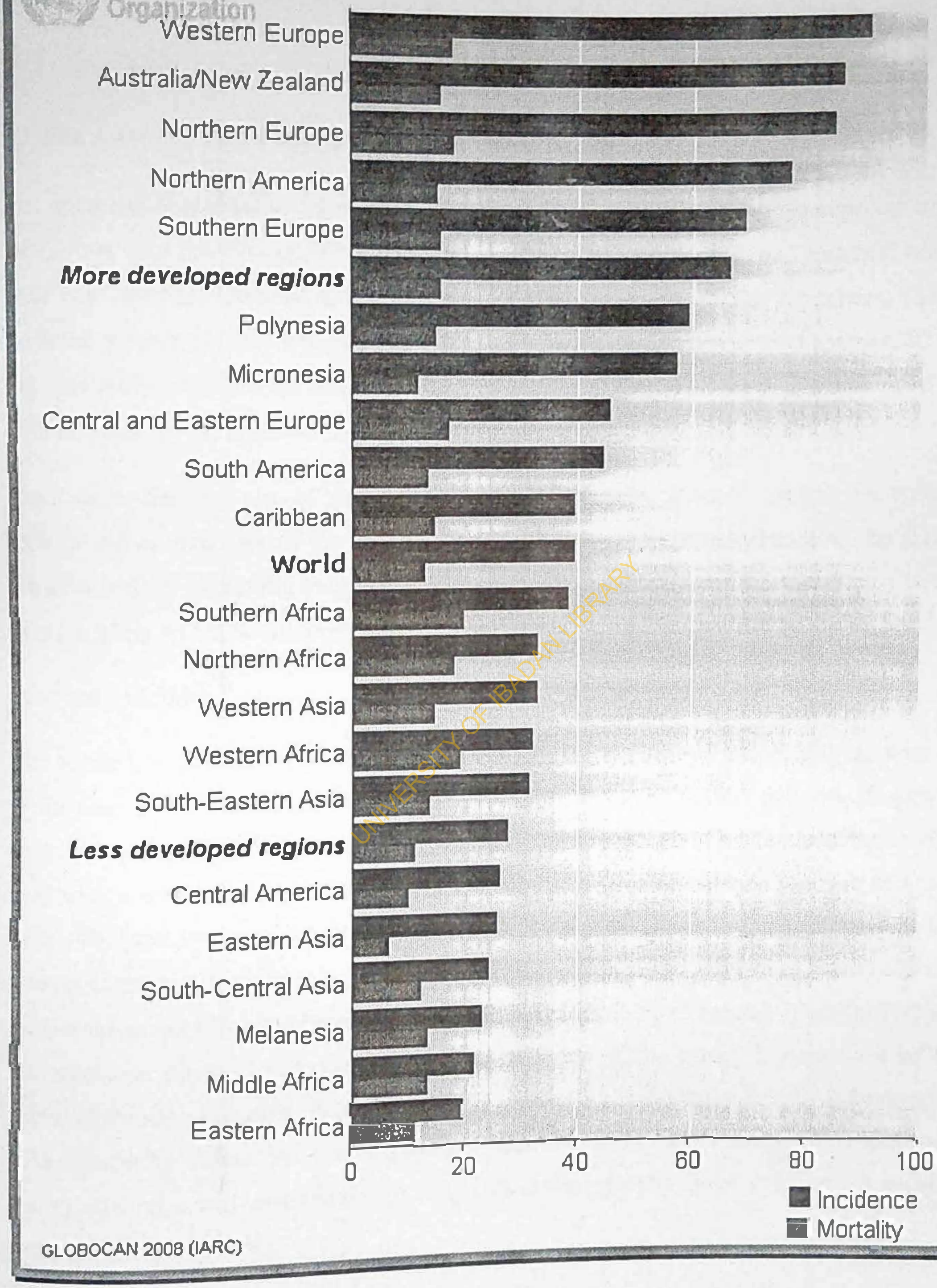

Figure 1.1. World reported Incidence and Mortality Rates of Breast (GLOBACON 2008)

CHAPTER TWO

LITERATURE REVIEW

2.1 The Anatomy and Physiology of the Female Breast

The breast is a glandular organ with lobar morphology. A breast lobe comprises a single lactiferous ~~duct~~ opening on the nipple, its segmental, sub segmental, and terminal branches with the ~~Terminal~~ Ductal-Lobular Units (TDLUs) at the end of the branching tree. The reported number of lobes within a mature breast varies considerably in the literature, 27 being the median in one detailed study (Going and Moffat, 2004). The lobes are individual units with no anastomotic connections between them.

The breast lies on top of the pectoralis major muscle. Fibrous stroma provides the background architecture of the breast. Cooper's ligaments are attached to both the fascia of the skin and the pectoralis major muscle. Carcinoma invading these ligaments may result in skin dimpling which could be subtle or obvious during visual inspection.

Internal Anatomy

The breast is composed of glandular ducts and lobules, connective tissue, and fat, with most of the benign and malignant pathology arising in the duct and lobular network (Figure 2.1). Specifically, most breast cancer is thought to originate in the TDLU. Glandular tissue and fat vary with a woman's age and weight. Lobes, lobules and acini serve to produce and secrete milk—the primary function of the breast mammary glands. Ducts and lactiferous sinuses are tubular connections between the lobes and nipples which allow milk to exit the breast. The lactiferous sinuses (located beneath the nipple) may contribute to feeling of granularity under the areola on physical examination. The parenchyma of the breast is composed of these ductal/glandular structures. Adipose tissue is present throughout the breast. A high ratio of ductal/glandular breast tissue to adipose and fibrous tissue makes detection of abnormalities during clinical breast examination (CBE) and mammography more difficult, especially in premenopausal women.

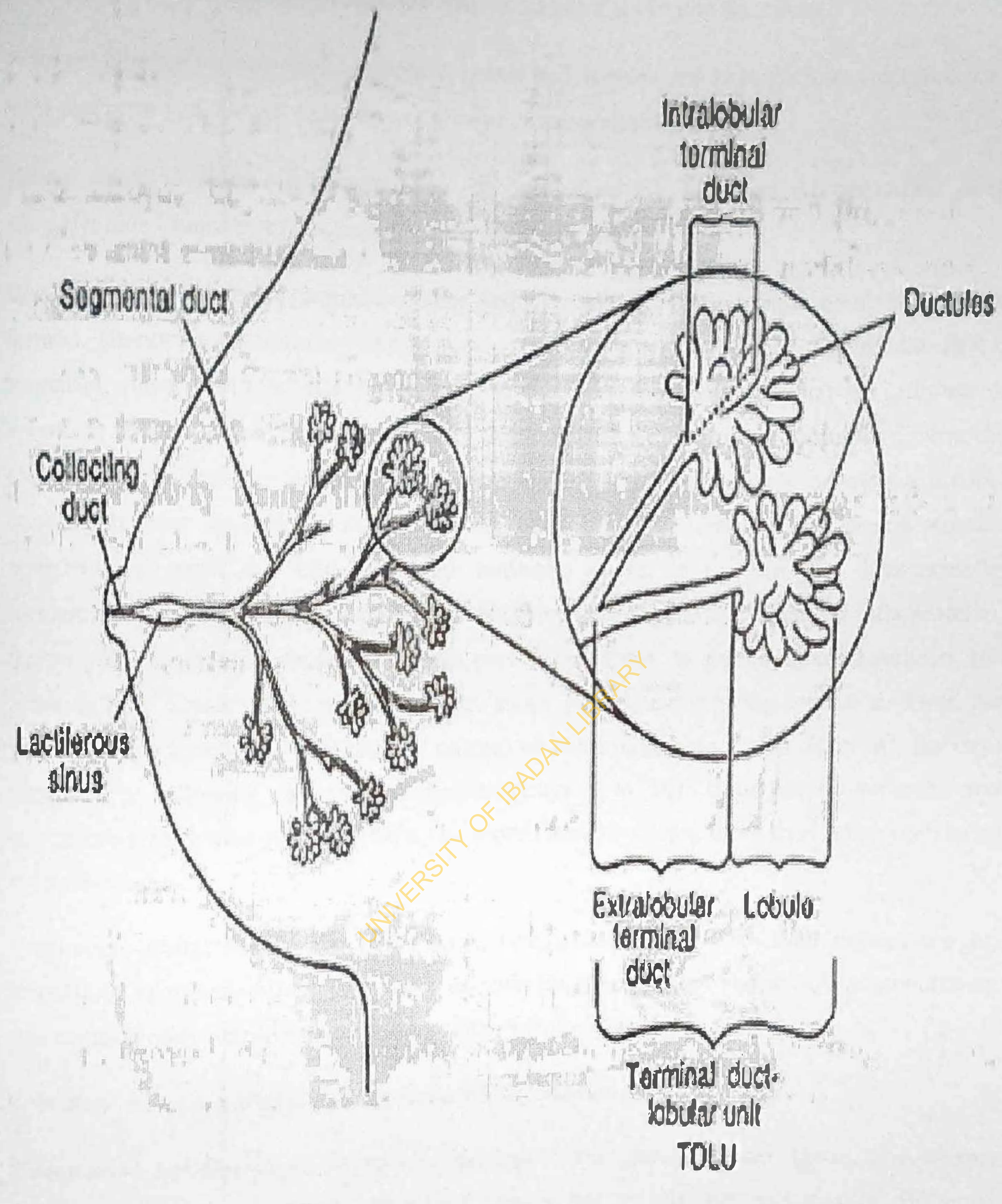

Figure 2.1. The breast is composed of glandular ducts and lobules, connective tissue, and fat. Source: A Clinical Guidebook for Women's Primary Health Care Providers.

2.2 The Stages of Breast Development

According to The American Joint Committee on Cancer and Singletary, et al. (2002), the stages of breast development are as follows:

Fetal development: Breast tissue begins to develop around the sixth week in uteri.

Prepuberty: Breasts are in resting state with ducts present but non functional.

Puberty: Ducts elongate due to estrogen; breast bud appears and is sometimes mistaken for a mass and removed. Breast buds do not always develop simultaneously.

Young adult: Effects of progesterone are influenced by initiation of ovulation; ducts elongate; side branches of ducts and lobular elements form.

~~***Maturity:***~~ Breasts become pendulous after many ovulatory cycles; lobular elements are well ~~formed.~~ Distinct morphologic changes occur with the menstrual cycle. During the first 5 menstrual days, there is minimal edema in the intralobular stroma and no mitoses or apoptosis is seen in the lobular epithelium. Intraluminal secretions are common. During the following 2 weeks, the follicular phase, the lobular acini increasingly develop a distinct double-cell layer appearance with increasing basal layer vacuolation. The stroma remains nonedematous until the third week, the midluteal phase. In the last few days prior to menstruation, the late luteal phase, there is extensive vacuolation and increased inflammation. Breast pain is more common during this part of the cycle. In premenopausal women, the breast is most sensitive to touch, or tender, about 7-14 days following ovulation. Thus, the best times for scheduling any type of clinical or mammographic breast exam are the days immediately following the start of menses (Days 5 to 10). Both require pressure and compression for better quality and may be more tolerable during these days when nodularity at its minimum.

Pregnancy: Distal ducts grow and branch; breasts enlarge to twice their normal weight; increase in ~~mammary~~ blood flow leads to vascular engorgement and areolar pigmentation; sometimes bloody nipple discharge occurs due to hypervascularity.

Lactation: Acini are dilated and engorged with colostrum and then milk.

Menopause: Lobules begin to recede, leaving mostly ducts, adipose tissue, and fibrous tissue; histologically, postmenopausal and prepubertal breasts are very similar. Hormone therapy may delay postmenopausal changes in the breast and mimic a more active physiologic or premenopausal state (ie, cyclic tenderness due to increased nodularity, etc).

2.3 Pathophysiology of Breast Cancer

Breast cancer characteristics are represented in the classification of breast tumours by the World Health Organization (Malhotra *et al.*, 2010). Traditionally, breast cancer is characterised as *in situ* or invasive regarding the integrity of basement membrane in the former case or loss of it in the second case. This concept is major prognostic value (Bombonati and Sgroi, 2011). At present, cancer *in situ* is described as ductal or lobular. The invasive cancers are classified into ductal, lobular, medullary and other, less frequent types. This classic classification retains prognostic importance and must be invariably applied when evaluating malignant breast tissue .

2.3.1 Carcinoma in situ has traditionally been classified into 2 major types: ductal and lobular. These terms denote a histologic pattern, since both types arise in the Terminal Ductal Lobular Unit (TDLU). Though ductal and lobular carcinomas were both originally thought to be precursors to invasive carcinoma, the risk for subsequently developing invasive carcinoma is quite different.

Lobular carcinoma in situ (LCIS) is usually an incidental finding in breast tissue removed for another indication and is frequently multifocal. This lesion rarely causes clinical findings such as a mass. On palpation it feels more like a platform of dense tissue and may be seen as calcifications on mammography. It is characterized microscopically by distension of at least half of the acini in a lobular unit by a very round uniform population of small cells, which may have clear cytoplasm or nuclear vacuoles. The histological differences and clinical implications of LCIS and atypical lobular hyperplasia (ALH) are not particularly distinctive. Thus, many pathologists prefer to refer to them together as *lobular neoplasia*. The risk of the development of breast cancer is considerably less than that of Ductal carcinoma in situ (DCIS) or even atypical ductal hyperplasia (ADH), and is more similar to florid epithelial hyperplasia in fibrocystic change.

Ductal carcinoma in situ (DCIS) is considered a precursor to invasive breast cancer because it is often noted in and around invasive cancers and because invasive cancer has been noted to develop when these lesions are incompletely excised. Of the invasive carcinomas that subsequently develop, invasive ductal carcinoma is the most common type (Jacobs, et al., 2001; Shaaban et al., 2002; Page, et al., 2003). However, it is not a single entity and the risk of progression to invasive carcinoma may vary considerably based on several pathologic

features. Histologically, DCIS is characterized by a proliferation of neoplastic cells, which distend the TDLU but do not breach the basement membranes. Microscopic criteria important to the diagnosis of DCIS include architectural pattern, nuclear grade, and necrosis, and these features should be listed in the pathology report.

2.3.2 Invasive breast cancer

An invasive breast cancer is one in which there is dissemination of cancer cells outside the basement membrane of the ducts and lobules into surrounding adjacent normal tissue. Breast cancers were previously classified either as ductal or lobular types, since it was believed that ductal carcinomas arose from ducts and lobular carcinomas from lobules. It is now known that both arise from the terminal duct lobular unit (Sainsbury et al., 2000). Almost all neoplastic breast pathology arises in the Terminal Ductal Lobular Unit (TDLU). Subsequent risk of invasive breast cancer varies based on the histologic category of a benign breast lesion (Jacobs et al., 2001; Shaaban et al., 2002; Page et al., 2003).

Infiltrating lobular carcinoma - This type is characterized histologically by a monotonous population of small cells that frequently contain a cytoplasmic vacuole and that classically infiltrate in a single-file pattern. The stroma is densely sclerotic, giving this tumor a rock-hard feeling on palpation and making the cells difficult to remove. This tumor has a better prognosis than infiltrating ductal carcinoma, an increased incidence of multifocality and bilaterality, and a distinctive pattern of metastases. Tumors that do not fulfil these classic criteria should be designated as "infiltrating carcinomas with lobular features" or as "lobular carcinoma variants" since they do not have the same prognostic implications.

Infiltrating ductal carcinomas are the most common type of invasive breast cancer, accounting for 50% to 75% of cases, and are sometimes referred to as *ductal carcinoma of no special type*. There are many histologic and cytologic patterns within this category, and grading these features can give a clue to prognosis. In general, this form of breast cancer is composed of neoplastic cells that infiltrate the tissue in nests, sheets, cords, tubular structures, or as a combination of these patterns. The cells can vary in size but are usually at least twice the size of a normal ductal cell. The nuclei are enlarged and have conspicuous nucleoli. Nuclear pleomorphism and the number of mitoses may vary. The stroma is usually sclerotic. The tumour may invade vascular spaces.

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2.4 Sub molecular types of breast cancer

Breast cancer is increasingly considered to be not one disease, but a group of diseases distinguished by different molecule, subtypes, risk factors, clinical behaviours and responses to treatment. Distinct molecular subtypes of breast cancer have been identified using gene expression profiles, a process that is both complex and costly (Perou et al., 2000). More convenient approximations of molecular subtypes have been identified using biological marker including the presence or absence of estrogen receptors (ER+/ER-), progesterone receptors (PR+/ PR-), and human epidermal growth factor receptor 2 (HER2+/ HEH2-) (Reis-Filho and Pusztai, 2011). Molecular subtypes are increasingly being used for research purposes; however, questions remain about their usefulness to further tailor breast cancer treatments and predict breast cancer prognosis (Reis-Filho and Pusztai, 2011, Goldhirsch et al., 2011).

2.4.1 Luminal A: About 40% of breast cancers are luminal A, making it the most common breast cancer subtype (Perou and Borresen-Dale, 2011). These tumors tend to be ER+ and/or PR+ and HER2-. Slow growing and less aggressive than other subtypes. Luminal A tumors are associated with the most favorable short-term prognosis in part because expression of hormone receptors is predictive of a favorable response to hormonal therapy, however long-term survival is similar to or even lower than some other subtypes (Blows et al., 2010).

2.4.2 Luminal B: About lO% to 20% of breast cancers are luminal B (Blows et al., 2010, Perou and Borresen-Dale, 2011). Like luminal A tumors, most luminal B tumors are ER+ and/or PR+ but they are distinguished by either expression of HER2 or high proliferation rates (high numbers of cancer cells actively dividing) (Cheang et al., 2009).

2.4.3 Basal-like:. About 10% to 20% of breast cancers are basal-like, and the majority of basal-like breast cancers are referred to as "triple negative' because they are ER-, PR-, and HER2 (Carey et al., 2006, Voduc et al., 2010). Basal-like tumors are more common in African American women, premenopausal women, and those with a *BRCA1* gene mutation." Women diagnosed with basal-like breast cancer have a poorer short-term prognosis than those diagnosed with other breast cancer types because there are no targeted therapies for these tumors.

2.4.4 HER2 enriched: About 10% of breast cancers produce excess HER2 (a growth-promoting protein) and do not express hormone receptors (ER-and PR-) (Perou and Borresen-

Dale, 2011). Similar to the basal-like subtype, these cancers tend to grow and spread more aggressively than other breast cancers and are associated with poorer short-term prognosis compared to ER+ breast cancers (Blows et al., 2010). However, the use of targeted therapies for HER2+ cancers has reversed much of the adverse prognostic impact of HER2 expression.

2.5 Staging of Breast Cancer

The prognosis (forecast or outcome) 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:

2.5.1 The TNM classification of tumors uses information on tumor size and how far it has spread within the breast (T), the extent of spread to the nearby lymph nodes (N), and the presence or absence of distant metastases (spread to distant organs) (M). Once the T, N. and M are determined. A stage of 0, I, II, III or IV is assigned, with stage 0 being in situ, stage I being early stage invasive cancer and stage IV being the most advanced disease, The TNM staging system is commonly used in clinical settings (Edge et al., 2010).

Stage I

An invasive cancer up to 2 cm across with no evidence of spread.

Stage II

Stage IIa - An invasive cancer less than 2cm where there are cancer cells in the armpit gland, but the glands are not stuck together OR A cancer that is less than 5cm where no lymph glands are involved OR Where there are cancer cells in the armpit nodes, but the nodes are not stuck together, but there is no cancer to be found in the breast (that is, it is occult or hidden).

Stage IIb - The cancer is less than 5cm, the armpit glands contain cancer cells but the glands are not stuck together and the cancer had not spread any further. The cancer is bigger than 5cm with no cells in the armpit glands and the cancer had not spread.

Stage III

Stage IIIa is where there are cancer cells in the lymph glands and the glands are stick together, but there is no cancer to be found in the breast, OR The tumour is smaller than 5cm and the armpit glands contain cancer cells that are stuck together, but there is no evidence of

any further spread, OR The cancer is larger than 5cm and the armpit glands contain cancer cells and may be stuck together, but there is no sign of any further spread

Stage IIIb - The cancer is fixed to the skin or chest wall, the lymph nodes may or may not contain cancer, but there is no further spread.

Stage IIIc - The cancer can be any size and has spread to lymph nodes in the armpit and under the breast bone, or to nodes above or below the collarbone, but there is no further spread

Stage IV

A cancer of any size where cancer has spread to other parts of the body, for example the liver or lungs. The lymph nodes may or may not be involved.

2.5.2 The Surveillance, Epidemiology, and End Results (SEER) Summary Stage system is more simplified and is commonly used in reporting cancer registry data and for public health research and planning (Young et al., 2001).

According to this system:

- Local stage refers to cancers that are confined to the breast (corresponding to stage I and some stage II cancers in the TNM staging system).
- Regional stage refers to tumors that have spread to surrounding tissue or nearby lymph nodes (generally corresponding to stage II or III cancers, depending on size and Lymph node involvement).
- Distant stage refers to cancers that have metastasized (spread) to distant organs or lymph nodes above the collarbone (corresponding to stages IIIc and IV).

2.6 Epidemiology of Breast Cancer

Epidemiologist defines risk factors as exposures that are associated with an increase or decrease in the number of cases of illness in a population. There are several factors, both endo- and exogenous, which are known to affect the risk of breast cancer in the population. These include lifestyle factors (i.e. childbearing, breastfeeding, type of diet and obesity, use of alcohol and tobacco), hormonal status (influencing age at menarche and menstrual cycle, and determined by endogenous hormones, oral contraceptives use, and hormone replacement therapy), anthropometric characteristics, and environmental factors such as gas emissions, chemical emissions, radiation, and genetic predisposition (McPherson et al., 2001). Like

other non-communicable diseases the risk factors for breast cancer can be divided into modifiable and non-modifiable factors. Most risk factors are not modifiable, including age, family history, reproductive history, BRCA status, and breast density. The amount of lifetime exposure of breast tissue to circulating ovarian hormones is only partially under one's control—modifiable with respect to exogenous hormone use. Similarly, the age at which menarche and menopause occur is generally out of one's control (Ma et al., 2008; Pijpe et al., 2012).

Other risk factors are potentially modifiable, including obesity reduction, avoidance of use of combined estrogen and progestin menopausal hormones, reduced alcohol consumption and smoking, and increased physical activity. However, all of these factors are only weakly to moderately associated with breast cancer risk, with relative risks of <2.0. There is also mixed evidence in relation to the impact of various commonly used medications on breast cancer risk, with some emerging evidence that perhaps bisphosphonates and metformin may lower breast cancer risk (Gnant, 2010; Chlebowski et al., 2012; Rennert et al., 2012)

2.6.1 Non Modifiable Risk Factors for Breast Cancer

2.6.1.1 Age

The probability of having breast cancer increases with age (Sasieni et al., 2011). Age is the single most important non modifiable risk factor for breast cancer (McPherson et al, 2000 Compared with women in their twenties, women are ten times as likely to develop breast cancer in their thirties, forty times as likely in their forties, sixty times as likely in their fifties, and ninety times as likely after age sixty (GLOBOCAN, 2000). In theory, the more years a woman is exposed to hormones during her lifetime, the greater her risk of breast cancer. For example, women are two times more likely to get breast cancer if they reach menopause after the age of fifty four and three times more likely if they have their first child after age forty (McPherson et al., 2000).

2.6.1.2 Genetic Predisposition

Genes for breast cancer have been mapped out by genetic linkage and they are the BRCA1 (Breast Cancer 1) gene and the BRCA2 (Breast Cancer 2) gene. Women carrying germline in BRCA1 or BRCA2 have an extremely high lifetime risk for developing breast cancer. The cumulative lifetime risk for breast cancer in women with BRCA1 and BRCA2 is 50% compared with 12% for women in the general population (Liang, 2000). Mutational screening

of genes functionally related to *BRCA1* and or *BRCA2* has revealed four genes, *CHEK2*, *ATM*, *BRIP1*, and *PALB2*; mutations in these genes are rare and confer an intermediate risk of breast cancer (Turnbull and Rahman, 2008).

The breast cancer mutations also confer increased risk for early-onset breast cancer, though this may be limited to women born in or after the latter half of the 20th century (so suggesting possible interactions with lifestyle factors), a cohort study showed (Tea et al., 2013). These mutations probably account for up to 20% of the familial or inherited genetic component of disease risk (Balmaña et al., 2011). Mutations in the BRCA genes are known as high-penetrance, and confer a greater than 10-fold increase in breast cancer risk. TP53 (Li Fraumeni syndrome) also falls into this category, but is thought to account for a very low proportion of familial breast cancer due to its rarity (Turnbull and Rahman, 2008).

BRCA1 gene

The BRCA1 gene is located on chromosome 17. The gene is extremely large and complex, and there are more than 1, 000 different possible mutations. BRCA1 mutations are inherited in an autosomal-dominant fashion and are associated with an increased risk of breast, ovarian, and, to a lesser degree, prostate cancers and a 15% to 45% lifetime risk of developing ovarian cancer (Chen and Parmigiani, 2007; Dowsett, 2008; Turnbull and Rahman, 2008).

BRCA2 gene

The BRCA2 gene is localized to chromosome 13; BRCA2 is approximately twice as large as BRCA1 and is similarly complex. Alterations in BRCA2 have been associated with an increased incidence of breast cancer in both women (similar to BRCA1) and men (6% lifetime risk). BRCA2 mutations are also associated with an increased risk of ovarian cancer, pancreatic cancer, prostate cancer, and melanoma. Together, mutations of BRCA1 and BRCA2 have been linked to most hereditary breast and ovarian cancer families and approximately half of hereditary breast cancer families (Chen and Parmigiani, 2007; Dowsett, 2008; Turnbull and Rahman, 2008).

A woman's family and personal medical history are therefore critical causative predictors. The genetic contribution, confirmed by family history is one of the strongest known predictive risk factors for breast cancer; the observation of families with multiple affected family members, many of which show an autosomal dominant pattern of inheritance, are evident of this fact. Women are twice as likely to develop breast cancer if their mother or sister had breast cancer prior to age 50, and their risk doubles again if two immediate family

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members had breast cancer (McPherson et al., 2000). While this risk may reflect a genetic component of the disease, genetic mutations appear to account for only five percent of all breast cancer cases (McPherson et al., 2000; National Cancer Institute, 2002). Women also are four times as likely to develop breast cancer if they have a history of certain types of benign breast disease (McPherson et al., 2000).

2.6.2 Modifiable Risk Factors for Breast Cancer

2.6.2.1 Reproductive Factors

There have been several studies showing a relationship between reproductive factors and the risk of breast cancer. It has been shown that risk increases with decreasing age at menarche, increasing age at first pregnancy, increasing age at menopause, and low parity (Gao et al., 2000; Clavel-Chapelon F and the E3N-EPIC Group., 2002; Garcia-Closas and Brinton, 2006). Hormones, especially estrogens, play a crucial role in the development and growth of breast cancer, and they may be the common factor behind the many reproductive variables associated with breast cancer (Sasco, 2001, Ma et al., 2006). Studies also suggest that extended breastfeeding for a lifetime total of six years or more reduces the risk of breast cancer, at least among premenopausal women (Lipworth, 2000; Parkin, 2011). A large body of research has explored the link between breast cancer and two common hormonal supplements: oral contraceptives and hormone replacement therapy (Parkin, 2011; Kaaks et al., 2013; Moorman et al., 2013). Oral contraceptives are associated with a small increase in breast cancer risk that persists for ten years after women stop taking them, but the cancers diagnosed among users are likely to be less advanced than breast cancers diagnosed among non-users (McPherson et al., 2000; Sasco, 2001; Parkin, 2011). Hormone replacement therapy is associated with a small increase in risk for each year of use, which continues for four years after therapy is stopped (McPherson et al., 2000; Reeves et al., 2006).

2.6.2.2 Anthropometric Factors

Several anthropometric factors play a role in breast cancer risk. A study published in December 2011 estimated that around 9% of breast cancers in women in the UK in 2010 were linked to excess bodyweight (Parkin and Byold, 2011). Increasing height is associated with an increasing risk in both pre- and post-menopausal women. Increased weight (measured by body mass index – BMI) decreases breast cancer risk before menopause, and increases risk after menopause (Friedenreich, 2001). Greater central adiposity has been associated with an approximate doubling of breast cancer risk among post-menopausal women in cohort studies (Morimoto et al., 2002) independent of BMI. Morimoto et al.,

(2002), documented a statistically significant trend of increasing breast cancer risk with increasing waist and hip circumferences but not waist/hip ratio, was observed although the finding was limited to women who had never used hormone replacement therapy. In a study conducted by Okobia et al., 2006 among Nigerian women, waist hip ratio was found to be a significant predictor of risk for breast cancer in women and thus was also reported in another study by Adebamowo et al., (2003) where a positive association between obesity and breast cancer risk among postmenopausal women in Nigeria was found. In contrast, obese pre-menopausal women have been documented to have a 20% reduction in breast cancer risk (Reeves et al., 2006).

2.6.2.3 Lifestyle and Physical Activity

That lifestyle changes can change the risk of developing breast cancer is supported by several lines of evidence. First, rates of breast cancer incidence vary widely by geographical sites around the world. Only a small part of these differences is due to genetics, few chemical or other carcinogen exposures have been linked to risk, and the remainder of the cases are, therefore, due to individual health and lifestyles behaviours (IARC, 2002, McTiernan, 2003). Second, within country changes overtime in breast cancer incidence have been paralleled by great lifestyle and health behaviour changes (McTieman, 2000; 2003). Third, experimental animal and human models provide confirmation of observable effects of several lifestyle behaviours on breast biology (IARC, 2002). The International Agency for Research on Cancer (IARC) estimates that 25% of breast cases worldwide are due to overweight/obesity and a sedentary lifestyle (IARC, 2002). An American Cancer Society cohort study of 495, 477 women followed for 16years found that the risk of breast cancer mortality increased significantly with increasing level of obesity; compared with women with a body mass index (BMI) under 25.0, those with BMIs of 25-29.9, 30-34.9, 35-39.9 and ≥40 had relative risk (RR) of breast cancer mortality of 1.34, 1.63, 1.7, and 2.12, respectively (Calle, et al., 2003). Thus, lifestyle changes to correct these factors might be expected to have a major impact on public health.

The life style in women has significantly deteriorated in the last 20 years. Women are more likely to be obese, consume sub-optimum diet, have early menarche, have fewer children, breast feed less often and perform less physical activity. Others include regular alcohol consumption of which two or more drinks per day increases risk by about 40%. On the aspect of smoking, although several studies in the past suggested an association (both positive and negative) between exposure to tobacco smoke and breast cancer risk, there is no convincing evidence of such a link. IARC now states that there is limited evidence that tobacco smoking

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causes breast cancer (Cogliano et al., 2012). Epidemiological studies have consistently shown a significant association between alcohol consumption and breast cancer and a recent IARC report concluded that this association is causal (Baan et al., 2007). There is considerable evidence from epidemiological studies that alcohol consumption increases breast cancer risk (Key et al., 2006). A meta-analysis of cohort studies reported that breast cancer risk in drinkers was 22% higher than that in non-drinkers and that risk did not differ significantly by beverage type or menopausal status. The relative risk for breast cancer increased by 10% for each additional 10g of alcohol consumed per day (Key et al., 2006) ranging from about 7-12% (Hamajima et al., 2002; Key et al., 2006; Allen et al., 2009). This is possibly due to the higher levels of some sex hormones in the bloodstream of alcohol consumers than non-consumers (Rinaldi et al., 2006). A study published in December 2011 estimated that more than 6% of breast cancers in women in the UK in 2010 were linked to alcohol consumption (Parkin, 2011).

Many studies have looked at the association between physical activity and breast cancer, showing a 15-20% risk reduction for the most active women, with the strongest association shown for post-menopausal women (Monninkhof et al., 2007). The vigorousness of activity may be important; a Canadian case-control study showed light-intensity activity did not reduce breast cancer risk (Kobayashi et al., 2013). The effect of physical activity on breast cancer risk may be due to how it affects hormone levels, with a recent European Prospective Investigation of Cancer (EPIC) study showing lower levels of oestrogen and testosterone in post-menopausal women who reported higher levels of physical activity (Chan et al., 2007). A study published in December 2011 estimated that more than 3% of breast cancers in women in the UK in 2010 were linked to inadequate physical activity (less than 150 minutes moderate physical activity per week) (Parkin, 2011).

2.6.2.4 Environmental Factors

Exposure to certain environmental substances and conditions may also increase a woman's risk of developing breast cancer. Currently there is conflicting evidence regarding the risk of environmental exposure to organochlorines (some exert a weak estrogenic effect), tobacco smoke, as well as night shift work. Research is ongoing in these and other areas of our current environment with potential for effecting breast cancer risk (American Cancer Society, 2013). Environmental factors known to affect cancer risk (either beneficially or detrimentally) include exposure to hydrocarbons gas flares, ultraviolet radiation, and certain occupational and chemical exposures. Every year, at least 200,000 people die worldwide from cancer related to their workplace. Millions of workers run the risk of developing cancers

such as lung cancer and mesothelioma from inhaling asbestos fibres and tobacco smoke, or leukaemia from exposure to benzene at their workplaces. Currently, most cancer deaths caused by occupational risk factors occur in the developed world (World Health Organization, 2007). It is estimated that approximately 20,000 cancer deaths and 40,000 new cases of cancer each year in the U.S. are attributable to occupation (United States National Institute for Occupation Safety and Health- Occupation Cancer, 2010). Polycyclic aromatic compounds which have been found to be carcinogenic are very common in the environment and are largely present in the atmosphere, rivers, oceans, soils, and processed foods (Adebamowo and Ajayi, 2000).

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2.6.2.5 Psychological Factors

The relationship between "body and mind" is an old issue. Numerous scientific publications documented the relationship between stressful life events, depression and/or anxiety and the development of breast cancer (Jacobs and Bovasso, 2000; Duijts et al., 2007; Kruk and Aboul-Enein, 2004; Lillberg et al., 2003; Glaser and Kiecolt-Glaser, 2005). A review of experimental in- vivo and in -vitro studies explaining how psychological factors are associated with immune dysfunctions and the development of malignant cells was made and

these studies took into account the type and severity of the event, the effect of accumulated events and the burden of the psychological distress developed by the event. These series of studies provide some evidence of the pathways through which psychological stress could contribute to the increase of cancer risk. However, despite the fact that some empirical evidence regarding the interaction between the endocrine system, psychological distress and the aetiology of the disease has been suggested, the subject is still under dispute. It is also probable that personality characteristics and personal resources, as well as coping skills and social support are playing an important role in these associations (Glaser and Kiecolt, 2005).

Epidemiologic evidence for a stress–breast cancer association

Stress exposure has been proposed to contribute to the etiology of breast cancer. However, the validity of this assertion and the possible mechanisms involved are not well established. Epidemiologic studies differ in their assessment of the relative contribution of stress to breast cancer risk, while physiological studies propose a clear connection but lack the knowledge of intracellular pathways involved (Antonova et al., 2011). A meta-analysis was performed by Duijts and colleagues (Duijts et al., 2003). Twenty-seven studies published between 1966 and December 2002 examining the relationship between stressful life events and breast cancer risk were analyzed. The studies encompassed a wider variety of research designs and included ten retrospective case–control studies, four prospective case–control studies, nine limited prospective cohort studies, and four prospective cohort studies. The findings concluded that variables significantly associated with breast cancer risk are an increased number of stressful life events (OR = 1.77, 95% CI = 1.31 to 2.40), death of a significant other (OR = 1.37, 95% CI = 1.10 to 1.71), and death of a relative or friend (OR = 1.35, 95% CI = 1.09 to1.68). Prospective studies showed a higher summary OR associated with stressful life events than retrospective design studies (OR = 2.46, 95% CI = 0.98 to 6.18 and OR = 1.93, 95% CI = 1.13 to 3.31, respectively). This was attributed to the fact that possible factors showed a statistically significant association with stress (for example, OR = 2.22, 95% CI = 1.39 to 3.56 for stressful life events), whereas studies that did not control for such factors did not report an association when pooled (for example, OR = 1.04, 95% CI = 0.90 to 1.20 for stressful life events).

The effect of work-related stress on breast cancer risk was assessed in some recent prospective cohort studies. In a study by Kuper and colleagues, the effect of job strain on breast cancer incidence was examined among 36,332 Swedish women participating in the Women's Lifestyle and Health Cohort Study, followed for an average of 13 years (Kuper et al., 2007). The results showed that both low job control and high job demands were

associated with breast cancer risk among women working full-time, whereas an even stronger association was observed among women exposed to both of these variables.

According to Chida and Hamer (2008) and Chrousos (2009), stress can be acute (short-lived) or chronic (repetitive or occurring over an extended period of time). There appears to be a tendency towards stronger associations being observed in studies looking at certain types of stressful life events and breast cancer incidence, compared with those studies examining chronic stress such as work-related stress, caregiving stress, or everyday/total stress. Variability between studies may also stem from the distinctive time windows of relevant exposure to stress examined. The latency period between stress exposure and breast cancer initiation is unknown. In general, the process of breast cancer development is estimated to occur over 10 to 20 years (Land et al., 2003). In agreement with this, a study by Lillberg and colleagues found that breast risk is most strongly correlated with life events that have occurred within 11 years prior to diagnosis (Lillberg et al., 2003).

A time-associated factor was taken into consideration in a study conducted by Eskelinen and Ollonen, (2010) to investigate the possibility that exposure to stress at certain periods of development may have a stronger impact on breast physiology. Women diagnosed with breast cancer were found to be significantly more likely to have undergone stress due to losses or social deficits in childhood and adolescence, for example. Similarly, death of a mother during a girl's childhood was found to be significantly associated with increased breast cancer risk in a prospective cohort in the Baltimore Epidemiologic Catchment Area Study (Jacobs and Bovasso, 2000). Finally, in a registry study and a prospective cohort study looking at association of stress caused by exposure to the Holocaust or to the siege of Leningrad with breast cancer risk or mortality, respectively, stress among women younger than 18 years old was found to be associated with the highest risk and mortality of breast cancer (although the association in the Leningrad study did not reach statistical significance) (Koupil et al., 2009). These studies also suggest that the cancer-causing effects of stress may be fairly specific to the breast. In both cases, all types of cancer were examined, and breast cancer showed the strongest association with stress.

2.6.2.6 Diet and Nutritional Status in Relation to Breast Cancer

The prevalence of obesity and physical inactivity are increasing in several African countries, and especially in urban sites, as a result of increased consumption of calorie-dense food and declines in energy expenditures at work and in daily life (Kamadjeu et al, 2006; Abubakari et

al, 2008; Agyemang et al, 2009, Mokhtar et al, 2001; and Popkin, 2006). Mannisto et al in 2005 documented that only a few consistent findings on individual foods or nutrients that influence breast cancer risk have emerged. Further, since people do not consume individual foods but certain combinations of them, the analysis of dietary patterns may offer an additional aspect for assessing associations between diet and diseases such as breast cancer and to examine whether the relationships between dietary patterns and breast cancer risk are consistent across populations. Mannistos et al (2005) examined the risk of breast cancer with two dietary patterns, identified as "Vegetables" (VEG) and "Pork, Processed Meat, Potatoes" (PPP), common to all cohorts of the DIETSCAN project. During 7 to 13 years of follow-up, three of the cohorts--the Netherlands Cohort Study on diet and cancer (NLCS), the Swedish Mammography Cohort (SMC), and the Ormoni de Dieta nella Eziologia dei Tumori (Italy-ORDET)--provided data on 3271 breast cancer cases with complete information on their baseline diet measured by a validated food frequency questionnaire. After adjustment for potential confounders, VEG was not associated with the risk of breast cancer across all cohorts. PPP was also not associated with the risk of breast cancer in SMC and ORDET, but a high PPP score tended to be inversely associated with breast cancer in the NLCS study (RR = 0.69; 95% CI, 0.52-0.92, highest versus lowest quartile). PPP differed in one aspect between the cohorts: butter loaded positively on the pattern in all cohorts except NLCS, in which butter loaded negatively and appeared to be substituted by low-fat margarine loading positively. The results supported the suggestion derived from traditional epidemiology that relatively recent diet may not have an important role in the etiology of breast cancer.

A meta-analysis showed a slight reduction in breast cancer risk for a higher intake of dietary fibre, although risk reductions were not shown for the main subtypes of fibre, and were only seen when intake of fibre was at least 25g/day. On average, women in Britain consume around 16g/day of fibre (Aune et al., 2012). Higher intake of fruit is associated with a small decrease in breast cancer risk, a meta-analysis showed; both the fibre and the antioxidants contained in fruit may be responsible for this effect (Aune et al., 2012). No association has been shown between vitamin supplements and breast cancer, as shown in a comprehensive systematic review (Misotti and Gnagnarella, 2013). In another study documented by Adebamowo et al (2005), they examined data from the Nurses' Health Study II to evaluate the association between major dietary patterns and the risk of breast cancer among pre-menopausal women. Further, they derived "Western" and "prudent" dietary patterns from the responses of 90,638 premenopausal women, aged 26 to 46 years at baseline in 1991, who completed validated food frequency questionnaires in 1991 and 1995. These patterns were then evaluated for their associations with risk of breast cancer. During 8 years of follow-up,

710 cases of invasive breast cancer were documented. The multivariate RR (95% CI) comparing highest to lowest quintiles of cumulative average score was found to be 0.90 (0.68-1.18, p-value, test for trend = 0.54) for the prudent dietary pattern and 0.97 (0.71-1.33, p-value, test for trend = 0.97) for the Western dietary pattern. Their findings suggest that there is no overall association between dietary patterns and risk of breast cancer but they recommended further evaluation. A combined analysis of eight cohort studies representing 351, 825 women (7, 377 breast cancer cases), however, found no association between intake of vegetables and fruits and risk of breast cancer (Smith-Warner, et al., 2001). Some studies have pointed to a high intake of meats as a risk factor for breast cancer, but other studies have not supported this. Part of the discrepancy in findings may be the different levels of carcinogens and mutagens included in meat in different sites around the world.

2.7 Risk Factors Associated with Breast Cancer in Nigeria

Breast cancer is the most common surgical condition women worry about in a list of eleven comparable conditions (Odunsanya, 2001). Among Nigerian women, some of the factors preventing early hospital presentation and thus increasing mortalities are thought to include inadequacy of systems protecting and promoting women's health and cultural taboos regarding the female body. It additionally adds to delay in presentation and treatment (Adebamowo and Ajayi, 2000; Okobia et al., 2006). Lack of knowledge about breast cancer has also been identified as an important factor preventing women from participating in breast cancer screening (Adenike and Omuemu, 2009).

Few studies have examined risk factors for breast cancer in Nigerian women. The established risk factors for breast cancer include age, sex, age at onset of menarche, age at first full-term pregnancy, parity, breast feeding, age at onset of menopause, obesity and physical activity (Adebamowo and Ajayi, 2000; Okobia, et al., 2006; Huo, et al., 2009). The direction of change in these risk factors in Africa is towards increasing incidence of breast cancer. Age at onset of menarche is reducing because of improved nutrition and reduced physical activity. Increased demands for education and modern lifestyle choices are delaying the age at first full-term pregnancy and the fertility rate of African women, which is also contributing to reduced total lifetime breast feeding duration. Studies have also examined the association with family history and reproductive factors in sub-Saharan Africa. Analysis of African breast cancer cases and controls studied in Ibadan by "Adebamowo, et al., (2003)" showed an association with height (adjusted odds ratio 1.05, 95% confidence interval 1.01 to 1.08), a marker for nutrition in early life and with waist hip ratio (adjusted odds ratio 2.67, 95% confidence interval1.05 to 6.80).

The study carried out by Ana et al., 2010 in Port Harcourt and Ibadan demonstrated that people living in highly industrialized communities have increased environmental risk and thus a higher probability of developing cancers. The majority of those exposed were women, who are normally responsible for food preparation and cooking, and infants/young children who are usually with their mothers near the cooking site. Rapid urbanization and industrialization of Warri, and its environs between 1968 and 1990 created pollution potentials that are as high as the sources of pollution. The Warri Refinery and Petrochemical Company at Ekpan is the largest in Nigeria and have a processing capacity of 125,000 barrels per day of crude oil. Nigeria'. The metallic components in crude oil are in the form of metalloporphyrin chelates, transition metal complexes, organometallic compounds, carbonyl acid salts of polar functional groups and colloidal minerals. Other inorganic constituents of crude oil are sulphur, nitro- gen and oxygen (Achi and Shide, 2004). It is expected that refinery effluents will contain some of these metals and inorganic substances in reasonable quantity. These environmental pollutants which are environmentally mobile tend to accumulate in organisms, and become persistent because of their chemical stability or poor biodegradability (Emoyan et al., 2005).

2.8 Prevention of Breast Cancer

Prevention involves actions aimed at eradicating, eliminating or minimizing the impact of disease and disability, or if none of these are feasible, retarding the progress of the disease and disability. There are three levels of prevention that can be instituted to combat cancer especially breast cancer burden and they include primary prevention, secondary prevention and tertiary prevention. Prevention of exposure to cancer-causing agents or risk factors, including infections, tobacco use, and obesity, is by far the most feasible and cost-effective approach to cancer control in Africa (Jemal et al, 2011).

Primary Prevention

Primary prevention involves health promotion on the complete removal of aetiological factors for breast cancer, maintenance of healthy lifestyle and diet, reduced exposure to possible carcinogen like chemicals, effluents that are easily found in the environment. Each year on February 4 ,world cancer day, and the month of October commonly called the pink month for breast cancer, these bodies collaborates with other organizations to promote ways, and strategize on how to ease global cancer burden. 'Together it is possible' is the 2012 theme for world cancer day reinforcing the fact that it is only by every person, organization, and government individually playing their part that the world would be able to prevent and reduce the cancer burden. In Nigeria, ignorance, poor awareness poverty and low socio

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economic status militate against primary prevention. There is an urgent need for a well defined consistent non-sporadic, well articulated national and local Breast Cancer Awareness Campaign Strategy in Nigeria (Healthy Life for All Foundation, 2006). Health promotion should include increasing level of physical activity of Nigerians and preventing obesity. This involves promoting cycling, walking, physical fitness in schools and community (Disease Control Priorities Project, 2007).

Secondary Prevention

Secondary prevention of breast cancer involves early diagnosis, screening programmes, and campaign. Early diagnosis of breast cancers and breast lesions can be achieved by special repeated breast examination by the woman herself or a doctor. All women over age of twenty should be advised to examine their breast monthly. Non availability of breast cancer research centres, lack of clinical services for breast cancer and non availability of imaging facilities reduce the efficiency of secondary prevention for breast cancer in Nigeria. Due to inadequate knowledge and perception of the effects of breast cancer, screening measure is very poorly applied in many African countries. Although there have been attempts to teach self breast examination to women in some African countries, available evidence indicates that such measures have never been integrated into public policies (Odunsanya et al., 2001; Abdel-Fattah et al., 2007). Mammography and mammographic screening are relatively new breast imaging modalities in the developing world; however, the capacity to perform mammography is gradually becoming widespread in Nigeria (Akinola et al, 2011). In order to determine the level of awareness of mammography and mammographic screening amongst women in Nigeria, a structured questionnaire was administered to 555 consecutively recruited women who visited various clinics at the Lagos State University Teaching Hospital, Ikeja, between January 2009 and June 2009 by Akinola et al (2011). Only 20% of all subjects were aware of the recommendation that they should receive routine mammography and mammographic screenings on an annual or biannual basis, depending on their age, and of the side effects associated with the procedure. The authors found a rather low level of awareness about mammography and mammographic screening, indicating the need to educate women about the risk of breast cancer and the importance of screening as a tool for the early detection and treatment of this condition.

Tertiary Prevention

Tertiary prevention of breast cancer can be attained through early treatment, offering of palliative care and rehabilitative services where necessary. Tertiary prevention encompasses the treatment of the diseases after it has occurred. These include surgical extirpation of the

tumour, and adjuvant treatment with chemotherapy, radiotherapy, and hormone treatment. It is noteworthy to know that tertiary prevention is not cost-effective in many Africa populations due to late stage in which the women often present. When affected women present late, only palliative treatment with radiotherapy can be done and case fatality is usually high. This problem is compounded by lack of resources especially in the rural sites. Many affected women even die before they receive treatment (Okonofua and Iribbogbe, 2006).

2.9 Breast cancer control programmes in Nigeria

The Federal Ministry of Health and many non governmental organizations in Nigeria are involved in the control (prevention and management) of breast cancer. Some of these organizations include; The STOP Cancer Foundation which help increase access to information and education to people on the prevention management and control of cancer as well as creating access to treatment and early detection of cancer, Breast Cancer Association of Nigeria (BRECAN) a leading a not-for-profit and non-governmental organisation galvanising action against breast cancer in Nigeria. BRECAN is increasingly improving the lives of many touched by breast cancer who would have succumbed to the disease due to ignorance and lack of support and the Africa Cancer Care Incorporation which includes a group of individuals, devoted to bridging cancer care disparities in the United States of America and Africa. They are made up of advance practice nurses, cancer survivors, community workers, educators, nurses, pharmacists, physicians, physician assistants, radiographers, researchers, reverends, social workers, and other concerned citizens of the world.

2.10 Review of Case Control Studies on Breast Cancer Aetiology

Adebamowo et al, in 2003 conducted a case control study to examine the relationship between waist–hip ratio and the risk of breast cancer in an urban Nigerian population. There were 234 breast cancer patients and 273 population based controls recruited between March 1998 and August 2000 using nurse interviewers in urban South Western Nigeria. Multivariable logistic regression showed a significant association between the highest tertile of waist–hip ratio and the risk of breast cancer (odds ratio=2.67, 95% confidence interval=1.05–6.80) among postmenopausal women. No association was found in premenopausal women.

Okobia (2006) conducted a study aimed at evaluating the risk factors for breast cancer in Nigerian women. A case-control design recruiting 250 women with breast cancer and their

age-matched female controls was adopted for the study. Both cases and controls were drawn from four University Teaching Hospitals in Mid-Western and South-Eastern Nigeria. Data on the clinical and epidemiological characteristics of the respondents were collected using interviewer-administered structured questionnaires followed by the anthropometric measurements. The mean ages of the cases and controls were 47.1 and 46.1 years, respectively. Fifty-seven percent of the cases were premenopausal while 43% were postmenopausal. Using conditional logistic regression, the effects of the various risk factors for breast cancer in the study population were assessed. Positive family history of breast cancer in first- and second-degree relatives was associated with a 15-fold increased risk of breast cancer [Odds ratio (OR) = 14.99, 95% Confidence interval (CI), 1.98, 113.47]. Also, waist-hip ratio (WHR) (OR = 2.10, 95% CI 1.44, 3.06), and higher level of education (OR = 1.31, 95% CI 1.07, 1.61) conferred increased risk of breast cancer. Alcohol consumption was associated with some increased risk of breast cancer, these were not statistically significant. He therefore concluded family history is a significant predictor of breast cancer risk in Nigerian women.

In another case control study by Okobia (2006) to evaluate the role of anthropometric variables in breast cancer susceptibility in midwestern and southeastern Nigeria, the result showed that WHR is a significant predictor of breast cancer risk in Nigerian women and measures to sustain increased physical activity and ensure healthy dietary practices was recommended to reduce the burden of obesity in the population. Study participants were 250 women with breast cancer who were receiving treatment in the surgical outpatient clinics and surgical wards of four university teaching hospitals located in Mid-Western and South-Eastern Nigeria, while the controls were 250 age-matched women without breast cancer or other malignant diseases being treated for other surgical diseases in the same institutions between September 2002 and April 2004. Waist:hip ratio (WHR) was associated with a significant 2.5-fold increased risk of premenopausal breast cancer (odds ratio [OR] = 2.56, 95% confidence interval [CI] 1.48–4.41] and a 2-fold increased risk of postmenopausal breast cancer (OR = 2.00, 95% CI 1.04–2.53). Increasing height conferred a modestly non significant increased risk of premenopausal breast cancer (OR = 1.59, 95% CI 0.98–2.58).

A case–control study was conducted from April 1997 to April 1998 in Tehran, Iran by Ebrahimi et al. (2002). Demographical data and risk factor related information were collected using a short structured questionnaire. Odds ratios (ORs) and 95% confidence intervals (CIs) were derived from logistic regression analysis. In all, 286 women with breast cancer and 249 control women were interviewed. In multivariate analysis, only marital status (never married: OR 4.24, 95% CI 1.70–10.57 [P = 0.002]; (never married: OR 4.24, 95% CI 1.70–10.57 [P =

0.002]; widowed/divorced: OR 1.71, 95% CI 1.05–2.68 [P = 0.03]) and family history (positive family history of breast cancer: OR 2.95, 95% CI 1.15–7.59 [P = 0.02]) were associated with significantly increased risk for breast cancer. The findings of the study suggest that family history and marital status may have an impact on the incidence of breast cancer in Iranian women widowed/divorced: OR 1.71, 95% CI 1.05–2.68 [P = 0.03]) and family history (positive family history of breast cancer: OR 2.95, 95% CI 1.15–7.59 [P = 0.02]) were associated with significantly increased risk for breast cancer.

In order to thoroughly analyze risk factors of breast cancer (BC) in premenopausal Uruguayan women, Alvaro L Ronco et al (2012) conducted a case-control study at the Pereira Rossell Women's Hospital, Montevideo, where 253 incident BC cases and 497 frequency-matched healthy controls were interviewed on menstrual and reproductive story, were administered a short food frequency questionnaire and undertook a series of body measurements necessary to calculate body composition and somatotype. Odds ratio (OR) coefficients were taken as estimates of relative risk derived from unconditional logistic regression. Among the classical risk factors, only the family history of BC in first degree relatives was significantly associated with risk of premenopausal BC. Interestingly, this risk factor was found to be stronger in women of ages >40, late menarche, early age for their first delivery, short time between menarche and first delivery, and with high parity, although heterogeneity was detected only for age and parity. High consumption of red meat was positively associated with the disease risk, in the same way as fried foods. Conversely, a high intake of plant foods displayed a protective effect. Except for hypertension, none of the analyzed components of metabolic syndrome were associated to BC risk. Particular increases of risk for premenopausal BC were found for family history in first degree relatives in certain subsets derived from the menstrual-reproductive history.

CHAPTER THREE

METHODOLOGY

3.1 Study site

The study was carried out in two sites namely Warri, Delta state which is in south southern Nigeria and Ibadan, Oyo state which is in south western Nigeria (see figure 3.1 below). The hospitals used in these sites were the Warri Central Hospital and University College Hospital, Ibadan.

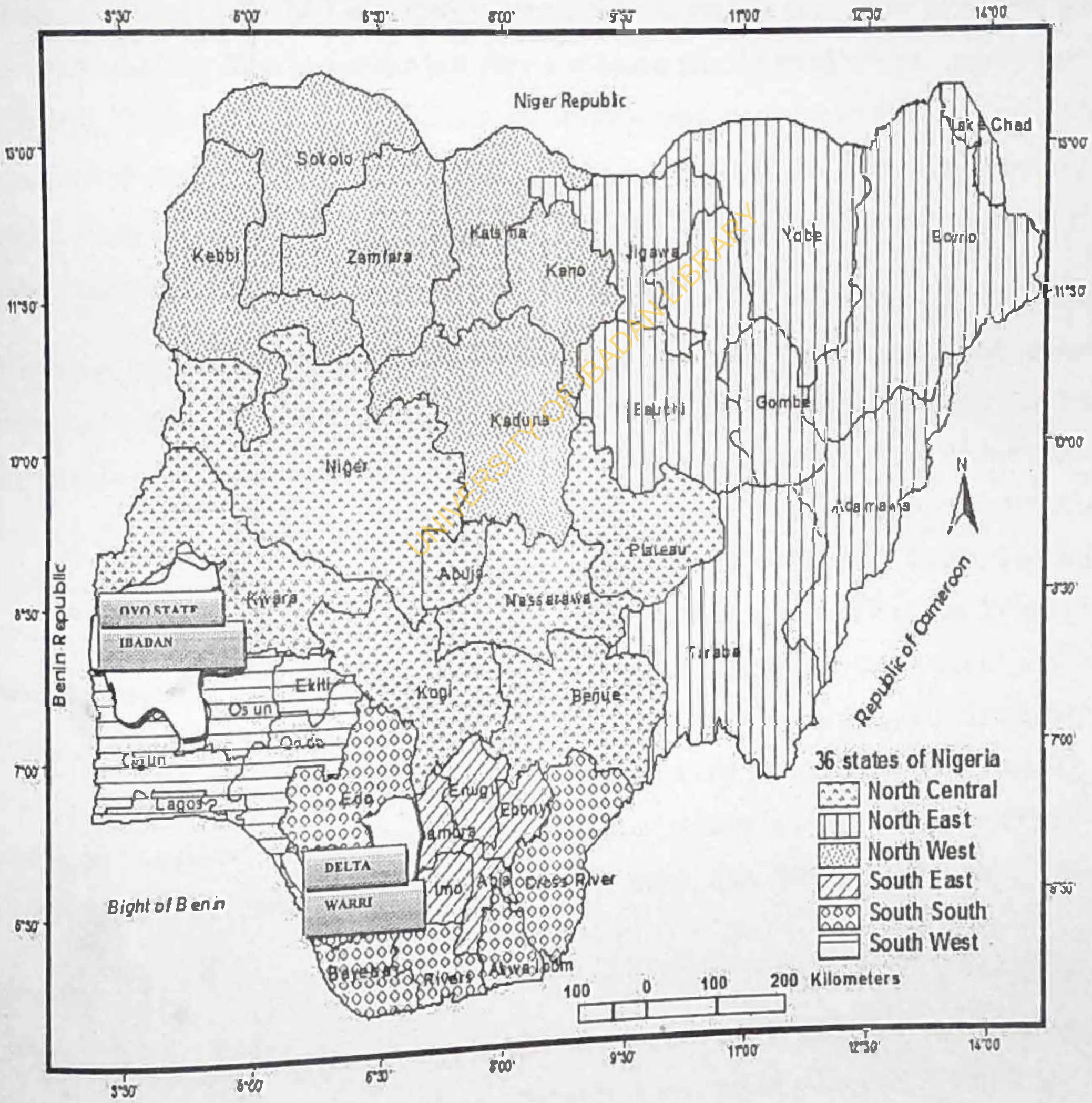

Figure 3.1: Map of Nigeria showing study sites in pink colours

Warri

Warri is one of Nigeria's oldest riverine towns in Delta state which is located on latitude 5° North, and longitude 5° East of the Greenwich meridian. For the purpose of this study, Warri and its environ included Warri north, Warri southwest, Warri south, Udu, Ughelli north, Ughelli south and Uvwie local government sites. The 2006 population census estimates the population of these local government sites to be 1,429,190 out of which 705,224 are females of all age groups.

The Warri central hospital is located at the heart of Warri near the Nigerian Port Authority. It is the only hospital capacitated with resources to diagnose breast cancer. The Warri Central Hospital is owned by the Delta state government and readily accessible by people within the geographical site. The hospital has a fifty bed space female ward where surgery patients are admitted. There are about five doctors and seven nurses available to attend to patients during breast clinic at the surgical out patients unit. Other hospitals like Shell, Chevron and NNPC staff clinics are privately operated within the study site with preference given to staff and family members alone thus not readily accessible by the public.

The economic base of Warri lies in the presence of oil and gas industries and refinery. The town is well known for a lot of ethnic violence and political tensions. Of particular significance is the environmental hazards residents are exposed to. These include gas flaring and venting, air and water pollution. The principal catchment sites for the Warri Central Hospital include Uvwie, Warri South, Udu, Ughelli North and Ughelli South. The women in Warri and its environs practice farming and trading as major occupation. The kind of farming involves majorly cassava produce and these women basically trade in food products like garri, fish and other household items either in small scale or large scale. Transportation is mainly by land and water. The common religious groups in the site are Christianity, Islam, and Traditionalists. The main language of communication is pidgin English. Ethnic groups dominant in Warri and environs include Urhobo, Isoko, Ijaw, Itsekiri, and Igbo.

Ibadan

Ibadan is the largest indigenous city south of the Sahara and is located at an altitude generally ranging from 152m to 213m with isolated ridges and peaks rising to 274m. It is the state capital of Oyo state which is near the forest grassland boundary of southwest of Nigeria on longitude 3^0 East of the Greenwich meridian, and Latitude 7^0 North of the equator. It is at a distance of about 145km North East of Lagos. Oyo state is divided into thirty-three (33) Local Government Site. It comprises largely the Yoruba speaking tribe and other ethnic

groups. Ibadan is dominantly a civil service city with some level of industrial activity, private businesses, and other forms of trade and peasant jobs. The estimated population is 2.6 million people (National Population Commission, 2006). Religious groups in the city are the Christians, Muslims and traditionalists.

The University College Hospital (UCH), Ibadan is the premier tertiary health institution in Nigeria and serves as a referral centre for majority of cancer patients in the country. It is located in Ibadan North LGA, of Oyo state. Experts in cancer management and modern facilities for cancer diagnosis and treatment such as radiotherapy machines and mammogram are available and operational in the hospital. Breast cancer patients are admitted based on the type of treatment at either the surgery out patient ward or radiotherapy ward. The surgery ward has about seventy bed space while the radiotherapy clinic ward has about thirty bed space. Catchment sites for UCH include these LGAs: Ido, Akinyele, Ona-Ora, Egbeda, Oluyole, Lagelu, Ibadan East, Ibadan North East, Ibadan South West, and Ibadan South East. However because of availability of modern radiotherapy equipment, patients are referred from different states in the country and neighbouring countries.

3.2 Study design

A case-control study matching for age and duration of stay in residence was conducted. The ratio of cases to controls was 1:3.

Definition of a case: Women with histologically confirmed malignant breast cancer.

Definition of a control: Women without histologically confirmed malignant breast cancer or history of cancer.

3.3 Study population

The study population consisted of women with breast cancer recruited from both Warri Central Hospital, Delta State and University College Hospital, Ibadan, Oyo State. Cases were aged twenty years and above. Comparable controls were community-based and selected from communities where cases resided matching for age and duration of stay in site of residence.

Inclusion criteria

Cases include women:

1. Aged from twenty years and above.
2. Histologically diagnosed with breast cancer.
3. Who must have lived for at least five years or more in the study site.

4. Who gave consent to participate in the study.

Controls include women:

1. Within ±5years of age as the corresponding case.
2. With absence of any type of cancer and breast disease.
3. Who must have lived for at least five years and more in the study site.
4. Gave consent to participate in the study.

Exclusion criteria for cases include women:

1. Whose address could not be obtained.
2. Critically ill.

3.4 Sample size determination

The sample size for this study was determined using the formula for estimating the sample size for case-control studies. The formula is given as:

$$n = \frac{(Z_{\alpha/2} + Z_{\beta})^2 \times \square(1-\square)(r+1)}{(d)^2 r}$$ (Kelsey et al., 2003)

Where;

P_1= proportion of exposed individuals who develop the disease

P_2= proportion of unexposed individuals who develop the disease.

□ = weighted average of P_1 and P_2

d = magnitude of differences one wishes to detect

r = odds ratio

n = minimum sample size

α = standard deviation a specific population

Taking;

$(Z\alpha/2 + Z\beta)2 = 7.849$

d = 0.45

r = 3

□ (1-□) = 1.2

Computing,

$$n = \frac{(7.849) \times (1.2)\,(3+1)}{(0.45)^2\,(3)}$$

$n = 62.0167$

$n = 62$ to the nearest whole number.

Taking no response rate to be 5%

$$\text{Adjusted sample size} = \frac{100 \times n}{100 - 5} = \frac{100 \times 62}{100 - 5} = \frac{6200}{95} = \text{approximately } 65$$

Thus the resulting minimum sample size for one group (ie all cases) is 65,

Therefore, taking a ratio of 1:3;

The ~~minimum sample~~ size becomes 65: 195 for the total cases and controls respectively.

3.5 Sampling technique

Cases were recruited from the radiotherapy unit and the surgical outpatient department of the study site hospitals. Cases were recruited purposively from the hospitals during clinic days. At the Warri Central Hospital, breast clinic day was usually every Wednesday at the surgical outpatient (SOP) clinic. Here eligible breast cancer patients who gave inform consent to be part of the study were recruited consecutively. In Ibadan, cases were recruited from the Radiotherapy unit every Mondays, Tuesdays and Thursdays while on Wednesdays and Fridays, cases were recruited from Surgical Out-patient (SOP) clinic.

Controls were also purposively selected based on inclusion criteria from enumeration sites where cases were resident. A list of residential sites in the local government sites where cases reside was identified and these sites were visited for recruitment of controls. For every single case, three controls was recruited with strict adherence to the criteria that controls must be within ±5years of age as the case and must have lived in that site for the same period of time that the case has lived to control for confounders.

3.6 Data collection techniques

The data collection tool was a semi-structured, interviewer-administered questionnaire (see appendix 1) which was translated to yoruba (see appendix 2 for details). The questionnaire development was based on preliminary review of literatures. It was also reviewed and face

validated by experts in related fields in the faculty. The respondents were interviewed to ascertain possible exposures to breast cancer risk factors. The questionnaire had seven sections labelled section A – G and was designed to obtain information on:

1. Socio-demographic characteristics (section A)
2. Family history of breast cancer and other cancers (section B)
3. Dietary pattern (section C) using food frequency questionnaire (FFQ). The food items were majorly high calorie containing foods. This FFQ was included in the main questionnaire to elicit information on diet pattern and frequency of consumption.
4. Anthropometry measurements (section D) including body mass index (kg/m^2) and waist-to-hip ratio (WHR) were used to determine the nutritional status and abdominal fat respectively in accordance with the world health organization (WHO) standard: Body weight was measured to the nearest 0.1kg using a calibrated weighing scale. Height was measured to the nearest 0.1cm at the highest part of the head using a flat ruler while the participant was standing straight without wearing shoes and leaning against a wall. The waist measurement was made with a flexible tape at the approximate midpoint between the lower margin of the last palpable rib and the top of the iliac crest (WHO, 2008). Hip was measured using flexible tape around the widest portion of the buttocks (WHO, 2008).
5. Lifestyle risk factors (section E) to assess the extent to which the participants engaged in physical exercise [using WHO standard, exercise for at least three times per week was considered good while less than three times a week was considered as poor (WHO, 2012)], alcohol use and smoking.
6. Environmental exposures (section F) for breast cancer risk where frequency of exposure to automobile, generator and industrial fumes was categorised qualitatively as daily, occasionally and rarely.
7. Psychological risk factors for breast cancer (section G).

Pre-test of the questionnaire

A Pre-test was carried out on 5 cases and 15 controls in both Warri and Ibadan respectively to test the comprehensiveness and clarity of the questionnaire/ conduct of the interview. The questionnaires were administered by trained research assistants for the purpose of this study.

3.7 Data Management and Statistical Analysis

The dependent variable in this study was breast cancer status while the explanatory variables included site, educational level, occupation, marital status, family history of breast and other cancer types, waist-to-hip ratio (WHR), body mass index (BMI), frequency of consumption of some selected food items, lifestyle, environmental and psychosocial factors.

Data entry, cleaning and analysis was carried out using SPSS version 15.0 statistical software (SPSS Inc. USA). Descriptive statistics such as frequencies, mean and standard deviation were used to summarise the data. The statistical difference between categorical variables was tested using Chi-square test. Logistic regression was used to determine independent predictors of breast cancer. For all inferential analysis, statistical significance was set at 5%.

For logistic regression analysis, the dependent variable which was breast cancer was categorised as Cases - coded as 1, and Controls – coded as 0. Only significant explanatory variables from Chi-square test where included in the logistic regression from which the Odds ratio and 95% Confidence Interval (CI) were obtained.

Variables definition

- WHR $\geq$ 0.85 implied high abdominal fat while < 0.85 implied low abdominal fat (WHO, 2008).
- BMI categorization according to WHO standard were as follows:

  Normal weight = 18.5 – 24.9 kg/m^2

  Overweight = 25 – 29.9 kg/m^2

  Obesity = 30kg/m^2 and above.
- For the purpose of this study, consumption pattern of high calorie foods greater than or equal to three times a week was categorised as high risk and less than three times a week was categorised as low risk.

3.8 Ethical consideration

Ethical approval for the study was obtained from the Warri Central Hospital Ethical Review Committee, Delta State Ministry of Health and the Institutional Review Board of the University of Ibadan and University College Hospital, Ibadan. The questionnaire was fully explained to the participants in a manner and language that enabled easy comprehension. Data was collected with the following taken into consideration:

- **Confidentiality of data:** Respondents were assured of the confidentiality of the information obtained from them. In addition, serial number was used for identification rather than names.
- **Beneficence to participants:** Participants were made to understand that findings of this study would be beneficial and only made available to the Ministry of Health, appropriate authorities and other policy makers for appropiate preventive strategies.
- **Non-Maleficence to participants:** The study did not subject participants to harm of any sort whether physical, social or mentally. The study only required them to willingly answer questions and permit measurements of hip, waist, height and weight.
- **Voluntariness and Informed consent:** The study was made completely voluntary with written informed consent obtained from the individual.

3.9 Study limitations

A major limitation of this study was recall bias which is typical for case control studies. Cases most times readily remember and either under or overestimate their level of exposure to factors that are understood to be involved in the etiology of their specific disease process. This leads to more false positive exposure histories in case groups and is often a source of differential misclassification (Webb et al., 2005).

CHAPTER FOUR

RESULTS

There were a total of 266 respondents, 146 from Warri, Delta state and 120 from Ibadan, Oyo state. The number of cases and controls were 35 cases and 111 controls for Warri and 30 cases and 90 controls for Ibadan. The mean age of the cases and the controls were 48.65±12.3 years and 48.75±11.6 years respectively. The respondents' age ranged between 20-80years.

4.1 Socio Demographic characteristics of respondents

Table 4.1 shows the socio demographic characteristics of the respondents. There were more cases 35(53.8%) in Warri than Ibadan 30(46.2%), thus because of the matching ratio more controls in Warri 111(55.2%) than Ibadan 90(44.8%). Among the cases, highest proportion had secondary education 23(35.5%) followed by tertiary 19(29.2%), primary 12(18.5%) and no formal education 11(16.9%) while in the controls, highest proportion had tertiary education 81(40.3%) followed by secondary 70(34.8%), primary 27(13.4%) and no formal education 23(11.4%). In all the socio demographic characteristics studied, only marital status showed significant differences between cases and controls (p=0.04). Figure 4.1 presents a chart showing the age distribution of the respondents. Highest proportion (66%) was within 40-49years old while lowest proportion within 20-29years old.

Table 4.1: Socio Demographic characteristics of respondents

Variable	Cases N=65 n(%)	Controls N=201 n(%)	Total N=266 n(%)	p value
Site				
Warri	35(53.8)	111(55.2)	146(54.9)	0.85
Ibadan	30(46.2)	90(44.8)	120(45.1)	
Educational level				
No formal education	11(16.9)	23(11.4)	34(12.8)	0.31
Primary	12(18.5)	27(13.4)	39(14.7)	
Secondary	23(35.4)	70(34.8)	93(35.0)	
Tertiary	19(29.2)	81(40.3)	100(37.6)	
Occupation				
Skilled	18(27.7)	58(28.9)	76(28.6)	0.44
Semi skilled	9(13.8)	17(8.5)	26(9.8)	
Unskilled	38(58.5)	126(62.7)	164(61.7)	
Marital status				
Married	46(70.8)	151(75.1)	197(74.1)	0.04*
Single/never married	7(10.8)	7(3.5)	14(5.3)	
Seperated	0.0	10(5.0)	10(3.8)	
Widowed	12(18.5)	33(16.4)	45(16.9)	

* Significant at 5% level of significance

4.2: Relationship between marital status and the respondents (case-control) by study sites

The relationship between marital status and the respondents by study sites is presented in Table 4.2. None of the cases had any form of separation from their spouses compared to controls whose proportion was 7(6.3%) in Warri and 3(3.3%) in Ibadan. Highest proportion of cases was single/never married in Warri and Ibadan (14.3% versus 5.4%) compared to the controls (6.7% versus 1.1%) respectively. Marital status showed no significant difference for breast cancer risk between the respondents (case-control) in both study sites when compared, $p>0.005$.

Table 4.2: Relationship between marital status and the respondents (case-control) by study sites

Variable	Warri				Ibadan			
	Cases N=35 n(%)	Controls N=111 n(%)	OR (95%CI)	p value	Cases N=30 n(%)	Controls N=90 n(%)	OR (95%CI)	p va
Marital status								
Married	25(71.4)	87(78.4)	0.69	0.13	21(70.0)	64(71.1)	0.18	0.2
Single	10(28.6)	24(21.6)	(0.29-1.63)		9(30.0)	5(28.9)	(0.05-0.6)	

Table 4.2: Relationship between marital status and the respondents (case-control) by study sites

Variable	Warri				Ibadan			
	Cases N=35 n(%)	Controls N=111 n(%)	OR (95%CI)	p value	Cases N=30 n(%)	Controls N=90 n(%)	OR (95%CI)	p va
Marital status								
Married	25(71.4)	87(78.4)	0.69	0.13	21(70.0)	64(71.1)	0.18	0.2
Single	10(28.6)	24(21.6)	(0.29-1.63)		9(30.0)	5(28.9)	(0.05-0.6)	

Table 4.2: Relationship between marital status and the respondents (case-control) by study sites

Variable	Warri				Ibadan			
	Cases N=35 n(%)	Controls N=111 n(%)	OR (95%CI)	p value	Cases N=30 n(%)	Controls N=90 n(%)	OR (95%CI)	p va
Marital status								
Married	25(71.4)	87(78.4)	0.69	0.13	21(70.0)	64(71.1)	0.18	0.2
Single	10(28.6)	24(21.6)	(0.29-1.63)		9(30.0)	5(28.9)	(0.05-0.6)	

Table 4.2: Relationship between marital status and the respondents (case-control) by study sites

Variable	Warri				Ibadan			
	Cases N=35 n(%)	Controls N=111 n(%)	OR (95%CI)	p value	Cases N=30 n(%)	Controls N=90 n(%)	OR (95%CI)	p va
Marital status								
Married	25(71.4)	87(78.4)	0.69	0.13	21(70.0)	64(71.1)	0.18	0.2
Single	10(28.6)	24(21.6)	(0.29-1.63)		9(30.0)	5(28.9)	(0.05-0.6)	

4.3 Family history of breast and other cancers

The relationship between family history of breast and other cancers among cases and controls is presented in Table 4.3. Few (5.3%) and (3.4%) of the respondents reported a family history of breast and/or other types of cancers, respectively. More cases 4(6.2%) than controls 10(5.0%) mentioned family members have had breast cancer. There were no significant differences in history of breast (OR=1.25, 95% CI=0.38-4.14) and other cancers (OR=0.38, 95% CI=0.05-3.07) between cases and controls.

Table 4.3: Family history of breast and other cancers

Variable	Cases N=65 n(%)	Controls N=201 n(%)	Total N=266 n(%)	OR (95%CI)	p value
Family history of breast cancer					
Yes	4(6.2)	10(5.0)	14(5.3)	1.25	0.71
No	61(93.8)	191(95.8)	252(94.7)	(0.38-4.14)	
Family history of other types of cancer					
Yes	1(1.5)	8(4.0)	9(3.4)	0.38	0.34
No	64(98.5)	193(96.0)	257(96.6)	(0.05-3.07)	

Table 4.3: Family history of breast and other cancers

Variable	Cases N=65 n(%)	Controls N=201 n(%)	Total N=266 n(%)	OR (95%CI)	p value
Family history of breast cancer					
Yes	4(6.2)	10(5.0)	14(5.3)	1.25	0.71
No	61(93.8)	191(95.8)	252(94.7)	(0.38-4.14)	
Family history of other types of cancer					
Yes	1(1.5)	8(4.0)	9(3.4)	0.38	0.34
No	64(98.5)	193(96.0)	257(96.6)	(0.05-3.07)	

4.4 Family history of breast and other cancers by study sites

The relationship between family history of breast and others cancers among cases and controls within both study sites compared is presented in Table 4.4. A lower proportion of cases 1(2.9%) compared to 8(7.2%) controls had family history of breast cancer in Warri while in Ibadan, there were more cases 3(10.0%) compared to controls 2(2.2%) who had family history of breast cancer. Only a case (3.3%) compared to none in controls had family history of other types of cancer in Ibadan. There was no significant difference between history of breast and other cancers among cases and controls when both study sites were compared.

Table 4.4: Distribution of family history among cases and controls by study sites

Variable	Warri				Ibadan			
	Cases N=35 n(%)	Controls N=111 n(%)	OR (95%CI)	p value	Cases N=30 n(%)	Controls N=90 n(%)	OR (95%CI)	p value
Family history of breast cancer								
Yes	1(2.9)	8(7.2)	0.38	0.35	3(10.0)	2(2.2)	4.89	0.07
No	34(97.1)	103(92.8)	(0.05-3.14)	(Fisher's)	27(90.0)	88(97.8)	(0.78-30.8)	(Fisher
Family history of other types of cancer	0.0	8(7.2)	-	0.20	1(3.3)	0.0	-	0.25
Yes	35(100)	103(92.8)		(Fisher's)	29(96.7)	90(100.0)		(Fisher'
No								

4.5 Consumption pattern of selected calorie containing food

The consumption pattern for some selected high calorie containing food items by cases and controls is presented in Table 4.5. It was found that there was a higher proportion of controls than cases who had high consumption pattern for egusi(melon)/ogbono (44.3% versus 20.0%), fresh meat (93.0% versus 83.1%) and canned foods like tin tomatoes, canned corn, sardines, etc (21.4% versus 4.6%). On the other hand, more cases 45(69.2%) than controls 110(54.7%) had high consumption of frozen chicken.

Table 4.6: Consumption pattern of selected calorie containing food

Food Items	Cases N=65 n(%)	Controls N=201 n(%)	Total N=266 n(%)	OR (95% CI)	p value
Egusi (melon)/Ogbono					
Low	52(80.0)	112(68.7)	164(61.7)	3.18	<0.0001*
High	13(20.0)	89(44.3)	102(38.3)	(1.64-6.2)	
Groundnut/cashew nut					
Low	55(84.6)	159(79.1)	214(80.5)	1.45	0.33
High	10(15.4)	42(20.9)	52(19.5)	(0.68-3.09)	
Palm/Vegetable oil					
Low	5(7.7)	11(5.5)	16(6.0)	1.44	0.51
High	60(92.3)	190(94.5)	250(94.0)	(0.48-4.31)	
Butter/Mayonnaise					
Low	44(67.7)	143(71.1)	187(70.3)	0.85	0.60
High	21(32.3)	58(28.9)	79(29.7)	(0.47-1.55)	
Fresh meat					
Low	11(16.9)	14(7.0)	25(9.4)	2.72	0.02*
High	54(83.1)	187(93.0)	241(90.6)	(1.77-6.34)	
Frozen chicken					
Low	20(30.8)	91(45.3)	111(41.7)	0.54	0.04*
High	45(69.2)	110(54.7)	155(58.3)	(0.30-0.97)	
Smoked fish					
Low	35(53.8)	124(61.7)	159(59.8)	0.72	0.26
High	30(46.2)	77(38.3)	107(40.2)	(0.4:-1.27)	
Suya					
Low	59(90.8)	172(85.6)	231(86.8)	1.66	0.28
High	6(9.2)	29(14.4)	35(13.2)	(0.66-4.19)	
Canned foods					
Low	62(95.4)	158(78.6)	220(82.7)	5.62	0.00*
High	3(4.6)	43(21.4)	46(17.3)	(1.68-18.8)	
Tin tomatoes					
Low	56(27.2)	150(74.6)	206(77.4)	2.12	0.05
High	9(13.8)	51(25.4)	60(22.6)	(0.98-4.58)	

* Significant at 5% level of significance

4.6 Anthropometric indices of respondents

Respondents' anthropometric indices are presented in Table 4.6. The prevalence of obesity was 45.5% and was significantly more among controls (51.2%) than cases (27.7%)(<0.0001). The overall prevalence of high abdominal fat (WHR) (≥0.85) was 44.4%. Significantly more cases (78.5%) than controls (48.3%) had high abdominal fat (<0.0001).

4.6 Anthropometric indices of respondents

Respondents' anthropometric indices are presented in Table 4.6. The prevalence of obesity was 45.5% and was significantly more among controls (51.2%) than cases (27.7%)(<0.0001). The overall prevalence of high abdominal fat (WHR) (≥0.85) was 44.4%. Significantly more cases (78.5%) than controls (48.3%) had high abdominal fat (<0.0001).

Table 4.6: Anthropometric indices of respondents

Variable	Cases N=65 n(%)	Controls N=201 n(%)	Total N=266 n(%)	OR (95% CI)	p value
BMI					
Normal	20(30.8)	55(27.4)	75(28.2)	1.18	<0.0001*
Overweight	45(69.2)	146(72.6)	191(71.8)	(0.64-2.17)	
WHR					
High abdominal fat	51(78.5)	97(48.3)	148(55.6)	3.91	<0.0001*
Low abdominal fat	14(21.5)	104(57.1)	118(44.4)	(2.03-7.5)	

* Significant at 5% level of significance

4.7: Respondents anthropometric indices by study site

A comparison of the anthropometric indices between cases and controls by study site is presented in Table 4.7. Prevalence of obesity was significantly higher among controls than cases in Warri (34.2% versus 28.6%) and Ibadan (72.2% versus 26.7%) respectively. High abdominal fat was significantly higher among cases than controls in Warri (77.1% versus 41.4%) and Ibadan (80.0% versus 56.7%) respectively.

Table 4.7: Respondents anthropometric indices by study site

Variable	Warri				Ibadan			
	Cases N=35 n(%)	Controls N=111 n(%)	OR (95% CI)	p value	Cases N=30 n(%)	Controls N=90 n(%)	OR (95% CI)	p value
BMI								
Normal	10(28.6)	47(42.3)	0.54	0.08	10(33.3)	8(8.9)	5.13	<0.00
Overweight	25(71.4)	64(57.7)	(0.24-1.24)		20(66.7)	82(91.1)	(1.79-14.65)	
WHR								
High abdominal fat	27(77.1)	46(41.4)	4.77	<0.01	24(80.0)	51(56.7)	3.06	0.02*
Low abdominal fat	8(22.9)	65(58.6)	(1.98-1.44)	*	6(20.0)	39(43.3)	(1.14-8.21)	

* Significant at 5% level of significance

4.8: Respondents lifestyle based on physical activity, alcohol intake and cigarette smoking

The lifestyle of respondents is presented in Table 4.8. Significantly, a higher proportion of controls 36(17.9%) compared to cases 4(6.2%) reported to have engaged in exercise for at least three times a week. There were 18(27.7%) cases compared to 49(24.4%) controls who reported they took alcohol but this difference was not a significant relationship.

4.8: Respondents lifestyle based on physical activity, alcohol intake and cigarette smoking

The lifestyle of respondents is presented in Table 4.8. Significantly, a higher proportion of controls 36(17.9%) compared to cases 4(6.2%) reported to have engaged in exercise for at least three times a week. There were 18(27.7%) cases compared to 49(24.4%) controls who reported they took alcohol but this difference was not a significant relationship.

Table 4.8: Respondents lifestyle based on physical activity, alcohol intake and cigarette smoking

Variable	Cases N=65 n(%)	Controls N=201 n(%)	Total N=266 n(%)	OR (95% CI)	p value
Exercise at least 3x a week					
Yes	4(6.2)	36(17.9)	40(15.0)	0.3	0.02*
No	61(93.8)	165(82.1)	226(85.0)	(0.1-0.88)	(Fisher's)
Exercise when younger					
Yes	14(21.5)	51(25.4)	65(24.4)	0.68	0.36
No	51(76.9)	150(69.7)	201(71.4)	(0.35-1.31)	
Do you take alcohol					
Yes	18(27.7)	49(24.4)	67(25.2)	1.19	0.59
No	47(72.3)	152(75.6)	199(74.8)	(0.63-2.23)	
Ever smoked cigarettes?					
Yes	0.0	2(1.0)	2(0.8)	-	1
No	65(100.0)	199(99.0)	264(99.2)		(Fisher's)

* Significant at 5% level of significance

4.9 Respondents' physical activity by study site

The physical activity reported among cases and controls in both study sites compared are presented in Table 4.9. There were more controls 35(31.5%) than cases 3(8.6%) in Warri who reported that they exercised for at least three times a week and this difference was significant (OR=0.2, 95% CI = 0.06-0.71). In Ibadan, there was one case each among cases (3.3%) and controls (1.1%) who said they exercised for at least three times a week but this showed no significant difference.

4.9 Respondents' physical activity by study site

The physical activity reported among cases and controls in both study sites compared are presented in Table 4.9. There were more controls 35(31.5%) than cases 3(8.6%) in Warri who reported that they exercised for at least three times a week and this difference was significant (OR=0.2, 95% CI = 0.06-0.71). In Ibadan, there was one case each among cases (3.3%) and controls (1.1%) who said they exercised for at least three times a week but this showed no significant difference.

Table 4.9: Respondents physical activity by study site

riable	Warri				Ibadan			
	Cases N=35 n(%)	Controls N=111 n(%)	OR (95% CI)	p value	Cases N=30 n(%)	Controls N=90 n(%)	OR (95% CI)	p va
ercise at least 3x veek								
Yes	3(8.6)	35(31.5)	0.2	0.01*	1(3.3)	1(1.1)	3.07	0.41
No	32(91.4)	76(68.5)	(0.06-0.71)	(Fisher's)	29(96.7)	89(98.9)	(0.19-50.64)	(Fishe

* Significant at 5% level of significance

4.10: Frequency of exposure to some environmental pollutants among cases and controls

The frequency of exposure to some environmental pollutants among cases and controls is presented in Table 4.10. Significantly, higher proportion of the cases 61(93.8%) than controls 142(70.6%) was always exposed to fumes from exhaust of cars, motor bikes and generators. There were significantly more controls 12(6.0%) than cases 2(3.1%) who reported daily exposure to insecticides and pesticides. More cases 47(72.3%) than controls 72(35.8%) reported to have been sometimes exposed to effluents from industries. A higher proportion of controls 33(16.4%) reported to have been daily exposed to ~~telecommunication~~ masts.

Table 4.10: Frequency of exposure to some environmental pollutants among cases and controls

Frequency of exposure to environmental pollutants	Cases N=65 n(%)	Controls N=201 n(%)	Total N=266 n(%)	OR (95% CI)	p value
Fumes from exhaust of cars and motorbikes, generators					
Daily	61(93.8)	142(70.6)	203(76.3)	6.34	<0.0001
Sometimes	4(6.2)	59(29.4)	63(23.7)	(2.20-15.22)	(Fisher's)
Smoke from cooking with firewood					
Daily	17(26.2)	58(28.9)	75(28.2)	0.87	0.64
Sometimes	48(73.8)	143(71.1)	191(71.8)	(0.46-1.64)	
Insecticides/pesticides					
Daily	2(3.1)	12(6.0)	14(5.3)	0.07	0.01*
Sometimes	63(96.9)	189(94.6)	252(94.7)	(0.01-0.33)	
Effluents from industries					
Daily	4(6.2)	17(8.5)	21(7.9)	0.71	<0.0001*
Sometimes	61(93.8)	184(91.5)	245(92.1)	(0.23-2.19)	
Telecommunication mast					
Daily	1(1.5)	33(16.4)	34(12.8)	0.08	<0.0001*
Sometimes	64(98.5)	168(83.6)	232(87.2)	(0.01-0.59)	
Rarely					

* Significant at 5% level of significance

Table 4.10: Frequency of exposure to some environmental pollutants among cases and controls

Frequency of exposure to environmental pollutants	Cases N=65 n(%)	Controls N=201 n(%)	Total N=266 n(%)	OR (95% CI)	p value
Fumes from exhaust of cars and motorbikes, generators					
Daily	61(93.8)	142(70.6)	203(76.3)	6.34	<0.0001
Sometimes	4(6.2)	59(29.4)	63(23.7)	(2.20-15.22)	(Fisher's)
Smoke from cooking with firewood					
Daily	17(26.2)	58(28.9)	75(28.2)	0.87	0.64
Sometimes	48(73.8)	143(71.1)	191(71.8)	(0.46-1.64)	
Insecticides/pesticides					
Daily	2(3.1)	12(6.0)	14(5.3)	0.07	0.01*
Sometimes	63(96.9)	189(94.6)	252(94.7)	(0.01-0.33)	
Effluents from industries					
Daily	4(6.2)	17(8.5)	21(7.9)	0.71	<0.0001*
Sometimes	61(93.8)	184(91.5)	245(92.1)	(0.23-2.19)	
Telecommunication mast					
Daily	1(1.5)	33(16.4)	34(12.8)	0.08	<0.0001*
Sometimes	64(98.5)	168(83.6)	232(87.2)	(0.01-0.59)	
Rarely					

* Significant at 5% level of significance

4.11: Frequency of exposure to some environmental pollutants among cases and controls by study site

The frequency of exposure to environmental pollutants among cases and controls in both study sites are presented in Table 4.11. A higher proportion of cases [(33(94.3%) and 28(93.3%)] than controls [(89(80.2%) and 53(58.9%)] in both Warri and Ibadan respectively were always exposed to fumes from cars, bikes, generators. In Ibadan, lower proportion of cases 2(6.7%) reported that they were sometimes exposed to fumes from vehicles, generators and bike compared to controls 37(41.1%). More cases in Warri were always 3(8.6%) and sometimes 29(82.9%) exposed to effluents from industries compared to controls who were always 9(8.1%) and sometimes 55(49.5%) exposed ($\chi^2 = 14.00$, $p<0.0001$). Also, in Ibadan, a higher proportion of cases was sometimes 18(60.0%) exposed to effluents from industries compared to controls 17(18.9%) ($\chi^2 = 18.46$, $p<0.0001$).

Table 4.11: Frequency of exposure to some environmental pollutants among cases and controls by study site

Frequency of exposure to environmental pollutants	Warri				Ibadan			
	Case N=35 n(%)	Control N=111 n(%)	OR (95% CI)	p value	Case N=30 n(%)	Control N=90 n(%)	OR (95% CI)	p valu
Fumes from exhaust of cars and motorbikes, generators								
Daily	33(94.3)	89(80.2)	4.8	0.05	28(93.3)	53(58.9)	9.77	<0.0001
Sometimes	2(5.7)	22(19.8)	(0.91-18.31)	(Fisher's)	2(6.7)	37(41.1)	(2.19-43.57)	(Fisher'
Insecticides/pesticides								
Daily	1(2.9)	6(5.4)	0.51	0.82	1(3.3)	6(6.7)	0.48	<0.0001
Sometimes	34(97.1)	94(94.6)	(0.06-4.43)		29(96.7)	84(93.3)	(0.06-4.18)	
Effluents from industries								
Daily	3(8.6)	9(8.1)	1.06	<0.0001*	1(3.3)	8(8.9)	0.35	<0.0001
Sometimes	32(91.4)	102(91.8)	(0.27-4.16)		29(96.7)	82(91.1)	(0.04-2.95)	
Telecommunication mast								
Daily	0	21(18.9)	-	<0.0001*	1(3.3)	12(13.3)	0.22	0.09
Sometimes	35(100)	90(81.1)			29(96.7)	78(86.7)	(0.03-1.80)	

* Significant at 5% level of significance

4.12: Respondents experience of some psychosocial factors

Table 4.12 shows frequency distribution of the responses to questions on psychosocial issues experienced by respondents before onset of the disease among cases and controls. There were 19(29.2%) cases who reported having stressful daily activities compared to 110(54.7%) controls..More than half the cases 37(56.9%) reported that they relax for less than eight hours a day compared to controls 122(60.7%) while 28(43.1%) of cases said they relax for more than 8hours a day compared to controls 79(39.3%). The respondents were asked if they have ever lived with someone who had breast cancer, 3(4.6%) cases compared to 16(8.0%) controls reported to have lived with someone with breast cancer in the past. Significant differences were found for experience of loss of a close relative, loss of job, and divorce of parents between cases and controls. More of controls than cases reported to have experienced of loss of close relative, 121(60.2%) versus 22(18.5%), loss of job, 32(15.9%) versus 0.0, and divorce of parents when growing up, 29(14.4%) versus 3(4.6%).

Table 4.12: Respondents experience of some psychosocial factors

Variable	Cases N=65 n(%)	Controls N=201 n(%)	Total N=266 n(%)	OR (95% CI)	p value
How strenuous is your daily activity					
Stressful	19(29.2)	110(54.7)	129(48.5)	0.34	<0.0001*
Not stressful	46(70.8)	91(45.3)	137(51.5)	(0.19-0.62)	
Estimate of time relaxed daily					
< 8 hours	37(56.9)	122(60.7)	159(59.8)	0.86	0.59
8 hours +	28(43.1)	79(39.3)	107(40.2)	(0.49-1.51)	
Ever lived with someone who had breast cancer					
Yes	3(4.6)	16(8.0)	19(7.1)	0.5	0.36
No	62(95.4)	185(92.0)	247(92.9)	(0.16-1.98)	(Fisher's)
Loss of a close relative					
Yes	22(33.8)	121(60.2)	143(53.8)	0.34	<0.0001*
No	43(66.2)	80(39.8)	123(46.2)	(0.19-0.61)	
Ever lost a spouse					
Yes	12(18.5)	31(15.4)	43(16.2)	1.24	0.56
No	53(81.5)	170(84.6)	223(83.8)	(0.6-2.59)	
Ever lost your job					
Yes	0.0	32(15.9)	32(12.0)	-	<0.0001*
No	65(100.0)	169(84.1)	234(88.0)		(Fisher's)
Parents ever been divorced					
Yes	3(4.6)	29(14.4)	32(12.0)	0.29	0.04*
No	62 (95.4)	172(85.6)	234(88.0)	(0.08-0.98)	(Fisher's)
Ever been separated from your spouse					
Yes	3(4.6)	19(9.5)	22(8.3)	0.46	0.22
No	62(95.4)	182(90.5)	244(91.7)	(0.13-1.62)	(Fisher's)
Personal economic crisis					
Yes	7(10.8)	29(14.4)	36(13.5)	0.72	0.46
No	58(89.2)	172(85.6)	230(86.5)	(0.3-1.72	
Fear of getting breast cancer					
Yes	4(6.2)	10(5.0)	14(5.3)	1.25	0.71
No	61(93.8)	191(95.0)	252(94.7)	(0.38-4.14)	(Fisher's)

* Significant at 5% level of significance

4.13: Respondents experience of some psychosocial factors in both study sites compared

The respondents' experience of some psychosocial factors among cases and controls in both sites is presented in Table 4.13. In Warri, relatively lower proportions of cases experienced all the psychosocial factors considered compared to controls. Significant difference was found for 'How strenuous is your daily activity?' and 'ever lost a job?. In Ibadan significant difference was found for loss of a close relative and a higher proportion of controls 54(60.0%) than cases 6(20.0%) experienced this loss of close relative.

Table: 4.13 Respondents experience of some psychosocial factors by Study Site

Variable	Warri				Ibadan			
	Cases N=35 n(%)	Controls N=111 n(%)	OR (95% CI)	p value	Cases N=30 n(%)	Controls N=90 n(%)	OR (95% CI)	p value
How strenuous is your daily activity?								
Stressful	8(22.9)	72(64.9)	0.16	<0.0001*	11(36.7)	38(42.2)	0.79	<0.0001*
Not stressful	27(77.1)	39(35.1)	(0.07-0.39)		19(63.3)	52(57.8)	(0.34-1.86)	
Loss of a close relative								
Yes	16(45.7)	67(60.4)	0.55	0.13	6(20.0)	54(60.0)	0.17	<0.0001*
No	19(54.3)	44(39.6)	(0.26-1.89)		24(80.0)	36(40.0)	(0.06-0.45)	
Ever lost your job								
Yes	0.0	21(18.9)		0.04*	0.0	11(12.2)		0.06
No	35(100.0)	90(81.1)	-	(Fisher's)	30(100.0)	79(87.8)	-	(Fisher's)
Parents ever been divorced								0.20
Yes	2(5.7)	19(17.1)	0.29	0.09	1(3.3)	10(11.1)	0.28	(Fisher's)
No	33(94.3)	92(82.9)	(0.06-1.33)	(Fisher's	29(96.7)	80(88.9)	(0.03-2.25)	

* Significant at 5% level of significance

4.14: Logistic regression to determine predictors of breast cancer

Table 4.14 presents results for the logistic regression to determine possible predictors of breast cancer. The odds of women with high waist hip ratio developing breast cancer was less than women with low waist hip ratio (Odds ratio, OR = 0.24, 95% CI=0.10-0.60). The odds of developing breast cancer was found to be 4.40 (95% CI=1.25-15.57) times more among women who were always exposed to fumes from motorbikes, vehicles, and generators compared to women who were sometimes exposed. Women who were sometimes exposed to effluents from industries showed increased risk of developing breast cancer (OR=6.91, 95% CI=2.87-16.66) compared to those who were never exposed while those who were always exposed showed an increased risk but was not significant (OR=5.07, 95% CI=0.95-26.93). The odds of developing breast cancer was found to be 33.33 (95% CI=<0.0001-0.42) times less likely for women who were always exposed to telecommunication masts.

Table 4.14: Logistic regression to determine predictors of breast cancer

Characteristics	AOR	95% C.I for OR	P Value
WHR			
High abdominal fat	0.24	0.10-0.60	<0.0001*
Low abdominal fat (Ref)	1		
BMI			
Overweight	1.03	0.38-2.78	0.96
Obese	0.38	0.14-1.02	0.05
Normal(Ref)	1		
Do you engage in anything to keep weight low?			
Yes	0.50	0.00-96.85	0.79
No (Ref)	1		
Type of activity			
Exercise	0.50	0.00-96.85	0.79
Diet	1.13	0.00-317.92	0.97
None(Ref)	1		
Do you do any vigorous exercise at least three times a week?			
Yes	0.46	0.10-2.18	0.33
No(Ref)	1		
How frequent are you exposed to fumes from motor bikes, vehicles, generators			
Always	4.40	1.25-15.57	0.02
Sometimes(Ref)	1		
How frequent are you exposed to insecticides or other pesticides			
Always	0.23	0.02-2.62	0.24
Sometimes	0.38	0.09-1.67	0.20
Never(Ref)	1		
How frequent are you exposed to effluents from industries			
Always	5.07	0.95-26 93	0.06
Sometimes	6.91	2.87-16.66	<0.0001
Never(Ref)	1		
How frequent are you exposed to telecommunication mast			
Always	0.03	0.00-0.42	0.01
Sometimes	0.50	0.12-2.19	0.36
Never(Ref)	1		
Have you experienced loss of a close relative?			
Yes	0.20	0.25-1.33	0.05
No(Ref)	1		
Have you experienced loss of a job?			
Yes	0.00	0.00	1.00
No(Ref)	1		
Have you experienced divorce of parents?			
Yes	2.67	0.10-18.08	0.31
No(Ref)	1		
How strenuous is your daily activity?			
Not stressful	1.95	0.88-4.29	0.10
Stressful(Ref)	1		

* Significant at 5% level of significance

CHAPTER FIVE

DISCUSSION, CONCLUSION AND RECOMMENDATIONS

5.1 Discussion

5.1.1 Breast Cancer and Known Risk Factors

Age

Older women are much more likely to get breast cancer than younger women. From 2005-2009, the median age for a breast cancer diagnosis was 61 years of age. Approximately 0.0% were diagnosed under age 20; 1.8% between 20 and 34; 9.9% between 35 and 44; 22.5% between 45 and 54; 24.8% between 55 and 64; 20.2% between 65 and 74; 15.1% between 75 and 84; and 5.7% 85+ years of age (SEER, 2010). In this study age as a risk factor could not be determined because the cases and controls were matched for age. But the mean age of the respondents was 48.7±11.8years.

Familial History

It is documented that all women are at risk for breast cancer but only 5-10% of those with breast cancer have inherited a mutation in the known breast cancer genes (BRCA1 and BRCA2) and 90-95% of breast cancer cases do not involve these inherited mutations (National Cancer Institute, 2006; American Cancer Society, 2012). This study did not show a relationship between breast cancer risk and family history of breast cancer and other types of cancer. This does not support the findings from case control studies (Adebamowo and Ajayi, 2000; Okobia et al, 2006) carried out to identify risk factors for breast cancer among Nigeria women and which found family history to have a positive association with breast cancer. In addition, Malone et al (2006) and Offit, (2006) documented that while there are established breast cancer risk genes, such as BRCA1 and BRCA2 and that these genes are present in only a very small segment of a given population (only about two percent each of breast cancer patients and less than 20% of familial breast cancers). Less than 5% of the total breast cancer incidence is explained by known breast cancer susceptibility genes, mostly those conferring high risks, such as BRCA1 and BRCA2. It is presently not known how many such genes there still are, nor how many will fall into the class of rare high-risk (as BRCA) or common low-risk susceptibility genes, nor if and how these factors interact with each other to cause susceptibility (a polygenic model) according to Oldenburg et al (2007).

Diet, Alcohol Intake and Breast Cancer Risk

In the current study, analysis of reported dietary intake of some food items showed that more of the women with breast cancer (cases) than those without cancer (controls) significantly had higher risk (more than three times a week) consumption of frozen chicken. It was also found that more controls than cases significantly had high risk (more than three times a week) consumption of red meat, egusi/ogbono, and canned foods. Alcohol, smoked fish, fats and oils consumption did not show positive associations for breast cancer. Several studies have looked at possible linkages between single nutrient intake as well as foods or dietary patterns and breast cancer (Wakai et al., 2000; Mattison et al., 2003; Cho et al., 2003; Prentice et al., 2007; Engeset et al., 2009). However, there has been limited evidence suggesting that consumption of total dietary fat and special dietary patterns influence breast cancer risk, but no internationally accepted conclusion was reached (World Cancer Research Fund, 2007; Bosetti et al., 2009; Brennan et al., 2010).

Anthropometric Indices and Breast Cancer Risk

The influence of anthropometric measures on breast cancer risk has been the subject of many studies (Adebamowo et al., 2003; Lahmann et al., 2004; Ogundiran et al., 2010). In this study, no significant relationship was found between BMI and breast cancer. Although this study used a fewer sample size, the findings are consistent with that of Ogundiran et al. (2010) who conducted a case control study in Ibadan using 1,000 cases and 1,000 controls. Their study did not find a significant relationship between body weight and breast cancer risk but rather found an inverse relation between high BMI and breast cancer risk. The inverse association between BMI and breast cancer in Nigerian women was consistent with many previous studies, but not all. A cohort study in African Americans also showed that high BMI was associated with reduced risk of breast cancer (Palmer et al., 2007). However, several studies of African Americans also found inconsistent results, with high BMI being associated with an increased risk of postmenopausal breast cancer (Zhu et al., 2005), and no association (McCullough et al., 2005). Further observed in this study was that high abdominal fat when adjusted for confounders showed an inverse relationship with breast cancer risk. This finding is in contrast to that of Adebamowo et al. (2003) who found a positive relationship between waist-hip ratio (WHR) and breast cancer risk among postmenopausal women. However, it is important to note that majority of the women in the present study are in their premenopausal stage thus probably the reason for the inverse relationship found between WHR and breast cancer risk. In addition the inverse relationship found in this study between WHR and breast

cancer could probably be due to the fact that most of the cases had lost weight as a result of their ill health.

Physical Inactivity and Breast Cancer Risk

There is convincing evidence for a decreased risk of breast cancer with increased physical activity. Uncertainties remain, however, about the role of different types of physical activity on breast cancer risk and the potential effect modification of these associations (Petra et al., 2007). In this study, it was found that higher proportion of the women with breast cancer reported that they had little or no exercise both when younger and currently. The distribution on physical activity in this study showed that a significant higher proportion of controls than cases reported that they exercise currently for at least three times a week. It can be deduced that the reason why more controls than cases currently exercise for at least three times a week in this study was because the cases are already sick with breast cancer therefore lack energy and motivation to exercise unlike the controls. Physical activity is associated with reduced risks of breast cancer. Steindorf, et al. (2013) documented that physical activity is associated with reduced risks of breast cancer based on their study findings. The results of this prospective study on the protective effects of physical activity indicated that moderate and high physical activity is associated with modest decreased breast cancer risk.

5.1.2 Breast cancer risk associated with some environmental pollutants

This study suggested significant association between some environmental factors and breast cancer risk after adjusting for confounding. In 2010, Ana et al carried out an ecologic study which assessed disparities between environmental risk factors and cancers in two Nigerian cities. Environmental data were obtained for Port Harcourt and Ibadan cities respectively. Ten- year cancer records were also obtained from the University of Port Harcourt Teaching Hospital (UPTH), Port Harcourt and the University College Hospital (UCH), Ibadan. They found environmental risk factors particularly levels of polycyclic aromatic hydrocarbons was in air though it was higher in Port Harcourt than Ibadan locality ($p < 0.05$) and further concluded that people living in industrialized communities with increased environmental risk factors are likely to have a higher probability to develop cancers but however suggested that in-depth studies are required to establish empirical links between the identified environmental risk factors and the prevalence of cancers.

Polycyclic aromatic hydrocarbons are very common in the environment and are largely present in the atmosphere, rivers and oceans, soil and processed foods (Adebamowo and Ajayi, 2000). The study sites Warri and Ibadan are industrialised cities thus women who must

have lived there for more than five years could be exposed to carcinogens which leads to the risk of developing breast cancer. This supports the findings of this study which identified increased breast cancer risk for exposures to effluents. Epidemiological studies of environmental exposures are extremely challenging to conduct, because of difficulties in exposure assessment and for many pollutants, finding women who are unexposed. To investigate the possible role of pollutants classified as carcinogenic, or potentially carcinogenic, it is necessary to conduct large, well-designed studies with longer follow-up of existing cohorts of women exposed to high doses of environmental pollutants.

5.2 Conclusion

This study aimed at identifying risk factors for breast cancer among women in Warri, Delta and Ibadan, Oyo state. The study design was analytical and a total of 65 breast cancer cases and 201 community controls were recruited from June 2011 to January 2012. This study assessed a number of both established and suspected risk factors for breast cancer of which some environmental risk factors were identified. There is need for more research on the relationship between environmental factors and breast cancer risk. Breast cancer risk factors from findings are obviously more of modifiable factors like lifestyles, diet and environmental exposures than age and family history. In conclusion, preventive strategies could help reduce the burden of breast cancer if new studies confirm the present results. In addition, health education, awareness campaign to improve the adoption of a healthy dietary habit and lifestyle may reduce the risk and burden of breast cancer among Nigerian women and globally.

5.3 Recommendations

1. There is need for government, health institutions and non governmental organizations to prioritize and implement breast prevention strategies such as advocacy programs to educate people on breast cancer risk factors and the need for a healthy lifestyle and dietary intake.
2. There is also need for strategic plan across federal agencies — coordination and collaboration that can accelerate the pace of research.
3. There is need for public stakeholders to be engaged at every stage from research planning through disseminating findings.

5.8 Future Directions

Future studies in Nigeria could further explore analytically environmental factors and breast cancer risk using well-designed studies with longer follow-up of existing cohorts of women exposed to high doses of environmental pollutants.

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APPENDIX 1

RISK FACTORS ASSOCIATED WITH BREAST CANCER AMONG WOMEN IN TWO REFERRAL CENTRES IN NIGERIA

Consent Form

My name is Emeji, Elizabeth Kelechi, a Master's student of the Department Epidemiology and Medical Statistics, Faculty of Public Health, University of Ibadan. I am carrying out a study on "Breast cancer". The purpose of the study is to evaluate some potential risk factors. I will be taking some measurements for weight and height and also asking some questions relevant to each risk factor.

You will be given a number and your name will not be required. The answers will be kept very confidential or secret. The information given me will be helpful to the Ministry of Health in future to know the peculiarity of these risk factors. There may be no direct benefit to you but I do know that the information you provide will help health practionners learn more about breast cancer and the best way to prevent it. This information could help cancer patients further in the future.

Taking part is voluntary, you are free to decline consent to take part and also have the right to withdraw at any given time you choose. I will appreciate your consent to take part in this study.

Consent:

Now that the study has been well explained to me and I fully understand the content of the study process, I hereby voluntarily consent to take part in the study.

_____

Participants Signature / Date

_____

Witness / Date

APPENDIX 2

A QUESTIONNAIRE ON RISK FACTORS ASSOCIATED WITH BREAST CANCER AMONG WOMEN IN TWO REFERRAL CENTRES IN NIGERIA

INSTRUCTION

To be completed by the interviewer. The questions are to find out general exposures associated with breast cancer risk.

Name of Interviewer_____

SECTION A: SOCIODEMOGRAPHIC CHARACTERISTICS

1. Serial number: _____ 2. Date enrolled into the study: _____

3. Residential address (site)_____

4. Duration residing in site of Residence _____

5. Age (at last birthday) _____ Years

6. Ethnicity/ Tribe: 1. Urhobo [ ] 2. Itsekiri [ ] 3. Ijaw 4. Isoko [ ] 5. Delta Ibo [ ] 4. Ibo [ ]
7. Yoruba [ ] 8. Others (please specify) _____

7. Religious group? 1. Christianity [ ]2.[ ]Islam[ ]3.Traditional [ ]4.Others(please specify)

8. Highest educational qualification

1. No formal education [ ] 2. Primary six certificate [ ] 3.SSCE [ ]

4. Tertiary [ ] 5. Postgraduate

9. Occupation: _____

10. Marital status: 1. Married [ ] 2. Single [ ] 3.Separated [ ] 4. Widowed [ ]

SECTION B: FAMILY HISTORY OF BREAST CANCER

11. Any family history of breast cancer? 1. Yes [ ] 2. No [ ]

12. Side of the family where relatives of breast cancer from? 1.Mother's 2.Father's 3.Both 4.Nil

13. Any family history of other types of cancer? 1. Yes [ ] 2. No [ ]

SECTION C: FOOD FREQUENCY QUESTIONNAIRE

Below is a table showing a list of food items. Please tick how often you eat each of the following food items in the past one years:

Food items	More than once a day	3-6 times per week	1-2 times per week	Twice per month	Never
Groundnut/Cashew nut					
Egusi/ Ogbono					
Palm oil/ Vegetable oil					
Butter/Margarine/					

Mayonnaise					
Red Meat					
Frozen Chicken					
Smoked fish or meat (tiko)					
Suya meat					
Beer					
Ogogoro or Dry Gin					
Canned foods e.g tin tomatoes, canned peas, sweet corn, canned beef and fish products etc					

Section D: ANTHROPOMETRY

Parameter	Reading 1	Reading 2	Average	BMI(kg/m^2)	WHR
Weight (kg)					
Height (cm)					
Waist circumference (cm)					
Hip circumference (cm)					

SECTION G: LIFESTYLE

28. Do you do any form of exercise vigorously for at least 3 times per week?1.Yes [ ] 2.No [ ]

29. When you were younger did you engage in any activity to keep physically fit?

1. Yes [ ] 2. No [ ] 3. Don't know 4. Can't recall.

30. If yes, please state the type of activity:_____

31. Do you take alcohol? 1. Yes [ ] 2. No [ ]

32. Have you ever smoked cigarettes? 1. Yes [ ] 2. No [ ]

SECTION H: ENVIRONMENTAL EXPOSURES

33. Are you usually exposed to?

	Exposures	Daily	sometimes	Never
1.	Fumes from exhaust of cars and motorbike, generators			
2.	Smoke from cooking with firewood			
3.	Insecticides, pesticides			
4.	Effluents from industries			
6.	Telecommunication mast			

34. What are your water sources for domestic uses? _____

SECTION I: PSYCHOSOCIAL FACTORS FOR BREAST CANCER

35. How strenuous is your daily activities? .....

36. Give an estimate of time you relax in a day?.....

37. Have you ever lived with someone who had breast cancer? 1) No 2) Yes 3) don't know

38. If yes, when _____

39. Duration of illness _____

40. Have you ever experienced any of the following life events?

1. loss of a relative 1. No 2. Yes	If yes, at what age?
2. loss of a spouse 1. No 2. Yes	If yes, at what age?
3. divorce of parents before age 20 1. No 2. Yes	If yes, at what age?
4. separation from spouse 1. No 2. Yes	If yes, at what age?
5. loss of a job 1. No 2. Yes	If yes, at what age?
6. A personal economic crisis	If yes, at what age?

41. Do worrying thoughts about getting breast cancer go through your mind always?

1. Yes [ ] 2. No [ ]

APPPENDIX 3

IBERE LORI AWON OHUN TIO JE OKUNFAFUN AARUN JEJERE OMU (BREAST CANCER) LAARIN AWON OBINRIN NI IPIN MEJI NI NIGERIA FUN OLUBERE

Awon ibere yi wa lati mo ijinle ewu inu aarun jejere.

Oruko Olubere:_____

APA KINNIN:

1. Nomba: _____ 2. Ojo igbani sinu eko: _____

3. Kini adiresi ibi ti ongbe (iboni pato)_____

4. Nje iti lo to odun melo ni be? _____

5. Omo odun melo loje _____

6. Ede wo loje? 1. Urhobo [ ] 2. Itsekiri [ ] 3. Ijaw 4. Isoko [ ] 5. Delta Ibo [ ] 6. Ibo [ ]
   7. Yoruba [ ] 8. Ede mii (ko sile) _____

7. Esin wo loje? 1. Onigbagbo [ ] 2. Musulumi [ ] 3. Esin iblile [ ] 4. Esin mii (Ko sile)

8. Eko wo loni? 1. Kosi ile iwe eko [ ] 2. Eko ibere [ ] 3. Eko girama [ ] 4. Eko giga [ ]
   5. Eko giga agba [ ]

9. Kini ise re: _____

10. Eto idile eni: 1. Moti se igbeyawo [ ] 2. Omoge/mi oto gbeyawo [ ] 3. Moti pinya [ ]
    4. Oko mi tiku [ ]

APA KEJI: ITAN AARUN JEJERE OMU NINU IDILE

11. Itan aarun omu nimu idile? 1. Beeni [ ] 2. Beeko [ ]

12. Lati idile tani aarun jejere mi wa? 1. Iya [ ] 2. Baba [ ] 3. Idile mejeji [ ] 4. Kosi [ ]

13. Nje itan idile aaurun jejere ni wa? 1. Beeni [ ] 2. Beeko [ ]

APA KETA: IBEERE LORI OUNJE

Tabili orisirisi/oniruru ounje iowa ni sale yi. Bawo ni ose nje awon ounje si laarin osu kan seyin:

Aon ounje	Ju ekan lo ni ose	Emeta si emefa ni ose	Ekan si emeji ni ose	Emeji losu	Lailai
Epa /Eso kashu					
Egusi/ Ogbono					
Epo pupa/ Ororo					
Bota/Majirin/Mayonisi					
Eran malu, ewure/ogufe					
Eran adiye					

Eja gbigbe abi eran gbigbe (tiko)					
Eran suja					
Eran igbe					
Ogogoro/oti lile					
Awon ounje inu agolo bi tomato alagolo, geisha, agbado inu agolo, eran inu agolo					

APA KERIN: IWON ARA

Parameter	Iwon ikinnin	Iwon ikeji	Average	BMI(kg/m^2)	WHR
Orisi iwon (kg)					
Iwon titobi ara (cm)					
Iwon giga re (cm)					
Hip circumference (cm)					

APA IKARUN: IGBE AIYE

28. Nje onse ere idaraya okere ju emeta laarin ose? 1. Beeni [ ] 2. Beeko [ ]

29. Nje ose ere idaraya karakara nigba? 1.Beeni [ ] 2.Beeko [ ] 3.Mi omo [ ] 4.Mi ole ranti [ ].

30. Toba je beeni, iru ere iadaraya wo ni?_____

31. Nje omu oti? 1. Beeni [ ] 2. Beeko [ ]

32. Nje oti mu siga ri? 1. Beeni [ ] 2. Beeko [ ]

APA KEFA: IRIRI AYIKA

33. Nje onfi ara awon nkan wonyi bi?

	Exposures	Ojojumo	Ni gba mii	Kosi
1.	Eefi ara moto, mashini, ero engine amuna wa			
2.	Eefi igi idana			
3.	Oorun ogun eku ati kokoro			
4.	Oorun ati eefi awon ile ise			
6.	Irinse ero ibani soro			

34. Kini orisiri awon omi elo yin? _____

APA KEJE: AWON EERO ATI ISE AARUN JEJERE OMU

35. bawo ni awon eero ati ise oojo re seni agbara to? .....

36. Iye akoko melo ni isinmi re loojo?.....

37. Nje oti gbe pelu eni to ni aisan aarun jejere omu ri? 1. Beeni [ ] 2. Beeko [ ] 3. Mi omo

38. Ti obaje bee ni, igbawo ni _____

39. Bawo ni aisan naa se peto? _____

40. Nje oti ni iriri okan lara awon isele yi ri?

1. Adanu ebi 1. Beeni [ ] 2. Beeko [ ] T'oba je beeni, omo odun melo ni?___
2. Adanu oko abi iyawo1.Beeni [ ] 2.Beeko [ ] T'oba je beeni, omo odun melo ni?___
3. Ipinya obi ki oto di omo ogun odun 1. Beeni [ ] 2. Beeko [ ] T'oba je beeni, omo odun melo ni?___
4. Ipinya oko pelu aya? 1.Beeni [ ] 2.Beeko [ ] T'oba je beeni, omo odun melo ni?___
5. Ipadanu ise 1. Beeni [ ] 2. Beeko [ ] T'oba je beeni, omo odun melo ni?___
6. Ogun eto pelu inawo ara eni 1.Beeni [ ] 2.Beeko [ ] T'oba je beeni, omo odun melo ni?___

41. Nje eero iberu ati ni aarun jejere omu nwa si okan re bi? 1. Beeni [ ] 2. Beeko [ ]

legram PERMHEALTH

Telephone

DELTA STATE

MINISTRY OF HEALTH

P. M. B. 5012
ASABA
DELTA STATE OF NIGERIA

Your Ref:

Our Ref: HM.520/T/5

20th Jan. 2012

Miss Kelechi Elizabeth Emeji,
Department of Epidemiology,
Medical Statistics Environmental Health,
Faculty of Public Health,
University of Ibadan, Nigeria.

RE: ETHICAL APPROVAL TO CONDUCT A RESEARCH ON "RISK FACTORS ASSOCIATED WITH BREAST CANCER".

I wish to acknowledge the receipt of your letter and proposal to conduct a research on the above subject dated 14th October, 2011.

2. I further wish to convey approval to you to conduct this research in Delta State Hospitals.

3. With kind regards.

Dr. Mrs. Gloria Patrick- Ferife
for: Hon. Commissioner

INSTITUTE FOR ADVANCED MEDICAL RESEARCH AND TRAINING (IAMRAT)

COLLEGE OF MEDICINE, UNIVERSITY OF IBADAN. IBADAN, NIGERIA.

Director: Prof. A. Ogunniyi, B.Sc(Hons), MBChB, FMCP, FWACP, FRCP (Edin), FRCP (Lond)

Tel: 08023038583, 08038094173

E-mail: aogunniyi@comui.edu.ng

UI/UCH EC Registration Number: **NHREC/05/01/2008a**

NOTICE OF FULL APPROVAL AFTER FULL COMMITTEE REVIEW

Re: Risk Factors Associated with Breast Cancer Among Women in Two Nigerian Cities

UI/UCH Ethics Committee assigned number: UI/EC/11/0262

Name of Principal Investigator: **Kelechi E. Emeji**

Address of Principal Investigator: Department of EMSEH,
College of Medicine,
University of Ibadan, Ibadan

Date of receipt of valid application: 26/10/2011

Date of meeting when final determination on ethical approval was made: **N/A**

This is to inform you that the research described in the submitted protocol, the consent forms, and other participant information materials have been reviewed and given *full approval by the UI/UCH Ethics Committee.*

This approval dates from 23/03/2012 to 22/03/2013. If there is delay in starting the research, please inform the UI/UCH Ethics Committee so that the dates of approval can be adjusted accordingly. Note that no participant accrual or activity related to this research may be conducted outside of these dates. *All informed consent forms used in this study must carry the* UI/UCH EC *assigned number and duration of* UI/UCH EC *approval of the study.* It is expected that you submit your annual report as well as an annual request for the project renewal to the UI/UCH EC early in order to obtain renewal of your approval to avoid disruption of your research.

The National Code for Health Research Ethics requires you to comply with all institutional guidelines, rules and regulations and with the tenets of the Code including ensuring that all adverse events are reported promptly to the UI/UCH EC. *No changes are permitted in the research without prior approval by the* UI/UCH EC *except in circumstances outlined in the Code. The* UI/UCH EC *reserves the right to conduct compliance visit to your research site without previous notification.*

UI/UCH EC
23 MAR 2012
APPROVED
COLLEGE OF MEDICINE, U

Prof. A. Ogunniyi
Director, IAMRAT
Chairman, UI/UCH Ethics Committee
E-mail: uiuchirc@yahoo.com

INSTITUTE FOR ADVANCED MEDICAL RESEARCH AND TRAINING (IAMRAT)

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UI/UCH EC
23 MAR 2012
APPROVED
COLLEGE OF MEDICINE, U

Prof. A. Ogunniyi
Director, IAMRAT
Chairman, UI/UCH Ethics Committee
E-mail: uiuchirc@yahoo.com