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Risk Factors of Breast Cancer among Palestinian Women in North West Bank

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اقرار

أنا الموقع أدناه مقدم الرسالة التي تحمل العنوان:

Risk Factors of Breast Cancer among Palestinian Women in North West Bank

العوامل المساهمة في الاصابة بسرطان الثدي بين النساء الفلسطينيات في شمال الضفة الغربية

اقر بأن ما اشتملت عليه هذه الرسالة إنما هو نتاج جهدي الخاص، باستثناء ما تمت الإشارة إليه حيثما ورد، وان هذه الرسالة ككل، أو أي جزء منها لم يقدم من قبل لنيل أية درجة علمية أو بحث علمي أو بحثي لدى أية مؤسسة تعليمية أو بحثية أخرى.

Declaration

The work provided in this thesis, unless otherwise referenced, is the researcher's own work, and has not been submitted elsewhere for any other degree or qualification.

Student's name: **اسم الطالب:**

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Risk factors of Breast Cancer among Palestinian Women

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Abstract

Registries and research on breast cancer in Palestine are limited. Thus, study of risk factors for breast cancer in Palestinian women is important and might contribute to current knowledge on this important topic. Also it is observable that incidence of this disease among Palestinian women is increasing exponentially in the last few years, with small Age at diagnosis among Palestinians women, so it is recommended to search about the factors that may influence this increase. These factors vary in different parts of the world and that environmental factors are of greater importance than genetic factors. This study will examine environmental and familial risk factors associated with receptors status (estrogen/progesterone) for breast cancer in a woman who have had breast cancer. Studying cases will enhance our ability to understand the interplay of different factors in breast cancer risk and to identify potentially preventable risk factors.

This study is a case-control include 140 women with breast cancer and their aged matched 163 female controls. All cases were recruited to Al-watani hospital in Nablus district from different regions of North West bank. Data on the clinical and epidemiological characteristics will be collected using interviewer questionnaires.

Chapter One

Introduction

1.1 Introduction

Breast cancer is a cancer that starts in the cells of the breast in women and men. Worldwide, breast cancer is the second most common type of cancer after lung cancer (1), and the fifth most common cause of cancer death (2). Generally it refers to a malignancy in women that arises from the terminal ductal-lobular units of epithelial tissue, which in the mature breast represent 10% of the total volume (1).

Latest estimates suggest that more than million new breast cancer cases occur worldwide annually, with nearly 580,000 cases occurring in developed countries and the remainder in developing countries (3). Thus breast cancer now ranks first among cancers affecting women throughout the world and its marked impact is not restricted to Western industrialized societies.

Breast cancer is a multifactorial disease where genetic susceptibility, environment, nutrition and other lifestyle risk factors interact. Better identification of modifiable risk factors and risk reduction of breast cancer may allow implementation of useful strategies for prevention (48).

Geographical variations in incidence and mortality rates of breast cancer suggest that the known risk factors for breast cancer may vary in different parts of the world and that environmental factors are of greater importance than genetic factors (47).

Several studies showed certain risk factors are strongly correlated to development of breast cancer including: early menarche, null parity or late age at first birth, lat menopause, as well as endogenous or exogenous hormonal factors. Other risk factors that may also be mediated through a hormonal pathway include obesity, diet, sedentary lifestyle, and alcohol consumption (6,7). Environmental factors such as xenoestrogens, radiation, pesticides, and radiation have been also to increase risk of breast cancer development (8).

Breast cancer differs from most tumors because of its dependence on female sex hormones for development and growth (38). Estrogen and progesterone help regulate growth and differentiation of normal breast tissue, and they are considered important in the development and progression of breast cancer (39). Evaluations of epidemiologic risk factors in relation to breast cancer classified jointly by estrogen receptor (ER) and progesterone receptor (PR) status have been inconsistent.

Estrogen receptor and progesterone receptor are nuclear receptors; estrogen and progesterone bind specifically to these receptors and affect hormone-dependent organs (40). ER has both an estrogen-binding domain and a DNA-binding domain (41). The estrogen-ER complex binds directly to DNA and influences the expression of estrogen-responsive genes, including the gene for PR (42). Both receptors levels in premalignant or malignant lesions have been reported to be both higher (+) and lower (-) than in adjacent, normal breast tissues (43). Clinically, ER and PR levels in breast cancer tissue have been used as prognostic indicators to predict a patient's course of disease and response to adjuvant hormonal therapy. In general, women whose tumors are positive for both ER and PR survive longer and respond better to endocrine therapy compared with those

whose tumors are negative for both receptors Women whose receptor status is discordant, survival and response are characterized as intermediate (43).

It is not yet clear whether breast cancer of differing hormone receptor status represent etiologically distinct forms of the disease with different risk factor profiles (53,54). Reports that have examined risk factors by estrogen receptor status or by progesterone receptor status have not produced clear and consistent findings (54). The gradient of responsiveness to hormonal therapy leads to the hypothesis that estrogen receptor-positive, progesterone receptor-positive tumors would be most closely related to reproductive risk factors that are probably mediated by endogenous hormones (54, 55), while estrogen receptor-negative, progesterone receptor-negative tumors would be unrelated to these risk factors.

1.2 West Bank, Palestine

The West Bank, Palestinian Territories, is undergoing a transition characterized by rapid urbanization and changing lifestyles (65). According to the Palestinian Central Bureau of Statistics, approximately 40% of West Bank residents lived in rural areas in year 2006 (65,66), compared with 62% in the early 1990s (67). At the same time, the Palestinian Territories have been undergoing an epidemiologic transition characterized by a persistent burden of infectious diseases typical of developing countries and a rise in non-communicable (chronic) diseases such as cancer. Cancer accounted for 10% of total mortality in the West Bank from 1999 through 2003 (table 1) (78).

Table 1: Cause Specific Mortality Rates per 100,000 population, West Bank, Palestinian Territories, 1999-2003 (78).

Cause of Death	Women N.(%)	Men N. (%)	Total N. (%)
Communicable diseases	781 (6.6%)	1,125 (7.5)	1,906 (7.1)
Cancer	1,222 (10.3)	1,515 (10.0)	2,737 (10.2)
Diabetes mellitus	707 (6.0)	601 (4.0)	1,308 (4.9)
Diseases of circulatory system	5,579 (47.2)	6,466 (42.9)	12,045 (44.8)
Unintentional injuries	380 (3.2)	1,520 (10.1)	1,900 (7.1)
Other Causes of death	3,140 (26.6)	3,851 (25.5)	6,991 (26.0)

Lung cancer is the most common cause of cancer deaths among men, followed by cancers of the prostate, colon, liver and bile ducts, and stomach. Breast cancer is the most common cause of cancer deaths among

women, followed by cancer of the liver and bile ducts, colon, lung, and stomach (table 2).

Table 2: Age Standardized Mortality Rates for Cancer per 100,000 population per year, West Bank, Palestinian Territories, 1999-2003 (78).

Type of Cancer	Male	Female
Brain	2.9 (2.2-3.6)	2.2 (1.6-2.7)
Breast	NA*	7.1 (6.1-8.1)
Bladder	2.4 (1.7-3.0)	NA
Lung	14.0 (12.5-15.5)	2.9 (2.3-3.5)
Colon	4.9 (4.0-5.8)	3.7 (3.0-4.5)
Laryngeal	1.3 (0.8-1.8)	NA
Liver and bile duct	3.6 (2.8-4.3)	3.7 (3.0-4.4)
Ovarian	NA	1.3 (0.9-1.8)
Pancreatic	2.0 (1.4-2.5)	1.6 (1.1-2.0)
Prostate	6.8 (5.7-7.8)	NA
Stomach	3.3 (2.5-4.0)	2.3 (1.7-2.8)
Uterine	NA	1.6 (1.1-2.1)

NA*: Not Applicable

Cancer in the West Bank is a public health problem. There's a need to ascertain the risk factors associated with cancer in the Palestinian Territories and to identify possible ways to address these risk factors so that these diseases can be reduced or prevented.

The observed mortality patterns support the hypothesis that the Palestinian Territories have been undergoing a rapid demographic and epidemiologic

transition. Approximately 73% of the population is under the age of 30 years, and approximately 4% of the population is aged
65 years and older (65,68). Whereas 30 years ago major causes of death and disease were communicable diseases, maternal and perinatal conditions, and nutritional deficiencies, today theres a rise in non-communicable diseases without a corresponding decline in communicable diseases (69).

According to the Palestinian Ministry of Health report and based on data from the Palestinian cancer registry in the West Bank, crude cancer incidence in the Palestinian Territories in 1999 was 66.8 per 100,000, which was lower than cancer incidence in neighboring countries such as Jordan and Egypt (70). This figure should be interpreted with caution, as it might underestimate cancer incidence in the West Bank. The observed high proportion of cancer mortality (10%) may support this argument. Therefore, more emphasis should be paid to early detection and increasing awareness of these diseases.

In 2005, the reported number of new cancer cases in the occupied Palestinian territory was 1623 and the crude incidence was 43·1 per 100,000 population: 49·2 per 100 000 in the West Bank and 32·7 per 100 000 in the Gaza Strip (71). Men showed slightly increase rate (55%) than women (45%) (71). Reported age-adjusted cancer incidence for the occupied Palestinian territory for 1998–2001 was lower than that in Jordan, Lebanon, and in Arabs living in Israel (72,74) probably because it was an underestimate since some patients use services outside the territory. In 2005, combined cancer mortality rate was 27·8 per 100 000, which is not much different from that in 2000 (71).

Breast cancer is the most common type in Palestinian women (71). The proportion is similar to that in neighboring countries except Lebanon, where breast cancer accounts for nearly half of all cancers in women (74). This disease causes the highest cancer-related mortality in Palestinian women, 21·1% of all deaths from cancer, and 5·2 deaths per 100 000 women (71). In theory some features of Palestinian society, including a high total fertility rate (4·6%), high rate of breast feeding (95·6%) with a mean duration of 10·9 months, young mean age at first birth (20 years), and low alcohol consumption, should be protective against breast cancer (75). Other features ex, obesity and null parity, might act against these protective factors. About a third of Palestinian women of reproductive age are single and thus mostly childless (75).

Detailed data about human resources and health professionals specializing in cancer are scarce. Information provided by the Medical Association in Jerusalem about registered specialists showed that there are five oncologists in the West Bank (77). The quality of their training and experience varies, and the certification, licensure, and accreditation processes have been suboptimum. Furthermore, no mandatory system exists for continuing medical education. Cardiac surgery, imaging, and anaesthesia, which are specialties relevant to cardiovascular disease and cancer care, also have severe shortages of specialists (76).

1.1 Female Breast Anatomy

The structure of the female breast is remarkable and complex. For the most part, a woman's breasts consist of fat and connective tissue. But there are other, less conspicuous parts in the female breast, including milk ducts, lobes, lobules, arteries and lymph nodes.

Each breast has 15 to 20 sections (lobes). Each lobe is made up of many smaller structures (lobules) that end in tiny bulbs that can produce milk.

Lobes, lobules and bulbs are linked by a network of thin tubes (ducts). Ducts carry milk from the bulbs, where it's produced, toward the dark area of skin in the center of the breast (areola). They join together into larger ducts ending at the nipple, where milk becomes available to the infant.

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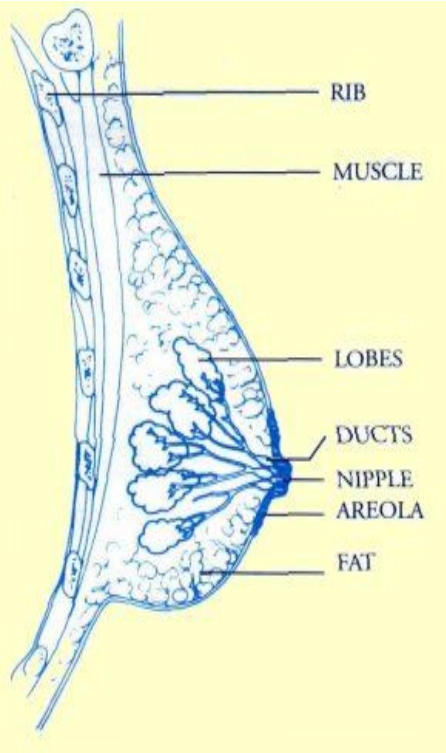

Figure 1: Anatomy o f the breast

Lobes, lobules and bulbs are linked by a network of thin tubes (ducts). Ducts carry milk from the bulbs, where it's produced, toward the dark area

of skin in the center of the breast (areola). They join together into larger ducts ending at the nipple, where milk becomes available to the infant.

Spaces around the lobules and ducts are filled with fatty tissue, ligaments and connective tissue (stroma). The amount of fat in the breasts is largely what determines what size they are. The actual milk-producing structures are nearly the same in all women. The breast has no muscle tissue, but muscles do lie underneath the breasts, separating them from the ribs.

Oxygen, nutrients and other life-sustaining nourishment are delivered to breast tissues by the blood in arteries and capillaries.

The lymphatic system (a network of vessels, lymph ducts and lymph nodes) helps fight off infection. These vessels drain fluid that typically leaks from the capillaries into the lymph nodes under the armpit and behind the breastbone.

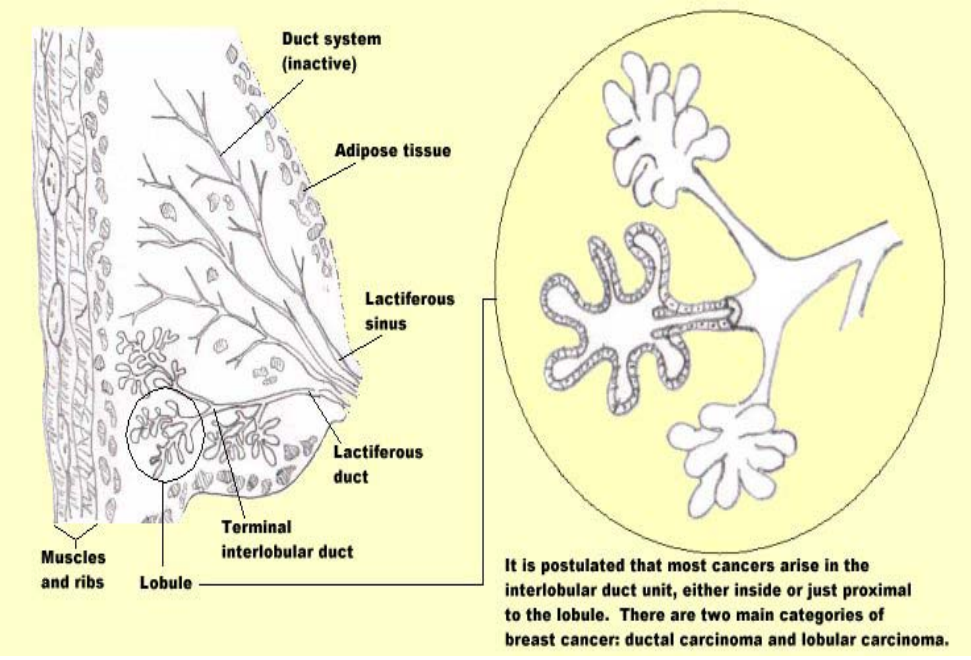

Figure 2: Internal anatomy of women breast.

1.2 Stages of Breast Cancer

There is a system of categorizing cancer into stages, based on three factors. The staging system most widely used is the TNM (Tumor size, Node involvement, Metastasis) system (36).

Stage is based on the size of the primary tumor (T1–4), presence and extent of lymph node involvement (N1–3), and presence or absence of distant metastases (M0–1).
Simplistically stated, these stages may be represented as follows:

1. Early Breast Cancer
- Stage 0: Carcinoma in situ or disease that has not invaded the basement membrane.
- Stage I: Small primary tumor without lymph node involvement.
- Stage II: Involvement of regional lymph nodes.
2. Locally Advanced Breast Cancer
- Stage III: Usually a large tumor with extensive nodal involvement in which node or tumor is fixed to the chest wall; also includes inflammatory breast cancer, which is rapidly progressive.
3. Advanced or Metastatic Breast Cancer
- Stage IV: Metastases in organs distant from the primary tumor.

1.3 Types of Breast Cancer

Most common types of breast cancer are named after the parts of the breast in which they start (37).

- Ductal Carcinoma**:** starts in the cells which line the breast's ducts, beneath the nipple and areola. The ducts supply milk to the nipple. Between 85% and 90% of all breast cancers are ductal. If the cancer is DCIS (ductal carcinoma in situ), it is well contained, not invasive, and can be very successfully treated.

- Lobular Carcinoma**:** begins in the lobes, or glands which produce milk in the breast. The lobes are located deeper inside the breast, under the ducts. About 8% of breast cancers are lobular. If the cancer is LCIS (lobular carcinoma in situ) that means the cancer is limited within the lobe and has not spread.

- Invasive (Infiltrating) Breast Cancer: Invasive, or infiltrating, breast cancer has the potential to spread out of the original tumor site and invade other parts of breast and body. There are several types and subtypes of invasive breast cancer.

- Inflammatory Breast Cancer: is the least common, but most aggressive of breast cancers, taking the form of sheets or nests, instead of lumps. It can start in the soft tissues of the breast, just under the skin, or it can appear in the skin. Unlike ductal and lobular cancers, it is treated first with chemotherapy and then with surgery.

- Paget's disease of the nipple/areola Least common is a cancer of the nipple, often looks like a skin rash, or rough skin. It resembles eczema,

and can be itchy. The itching and scabs (if scratched) are signs that cancer may be under the surface of the skin, and is breaking through.

1.4 Risk Factors of Breast Cancer

1. Age: The strongest risk factor for breast cancer (after gender) is age: the older the woman, the higher her risk.The incidence of breast cancer increases with age, doubling about every 10 years until the menopause, when the rate of increase slows dramatically (11).

2. Geographical Variation: Age adjusted incidence and mortality for breast cancer varies by up to a factor of five between countries. The difference between Far Eastern and Western countries is diminishing but is still about fivefold. Studies of migrants from Japan to Hawaii show that the rates of breast cancer in migrants assume the rate in the host country within one or two generations, indicating that environmental factors are of greater importance than genetic factors (11).

3. Reproductive History: Women in developed countries are at increased risk of breast cancer compared with women from less developed countries. Much of this variation can be explained by the fact that women in developed countries have fewer children and a limited duration of breastfeeding (11).

It is estimated that the cumulative incidence of breast cancer in developed countries would be reduced by more than half, from 6.3 to 2.7 per 100, if the average number of births (6.5 instead of 2.5 births) and lifetime duration of breastfeeding (breastfeed each child, on average, for 24 months instead of a lifetime mean of 8.7 months) (11).

Reproductive Factors That Influence Breast Cancer Risk

-Age at menarche: Early age at menarche has been consistently associated with an increased risk of breast cancer. Average age of menarche in developed countries fell from around 16-17 years in the mid 19th century to 12-13 today (12) . Relative risk for premenopausal breast cancer is reduced by an estimated 7% for each year that menarche is delayed after age 12 years, and by 3% for postmenopausal breast cancer (13). Low risk countries such as China have a later average age at menarche (16-17 years).

-Age at first birth: The younger the woman is when she begins childbearing, the lower her risk of breast cancer. The relative risk of developing breast cancer increases by 3% for each year of delay (11). For example, a woman who has her first baby at age 28 would have a 3% lower risk of breast cancer than a woman who had her first baby at 29, all other factors being equal.

- Parity: The effect of parity on reducing the risk of breast cancer has long been recognized. In the 18th century Bernado Ramazzini (1633-1714) reported the high rate of breast cancer in nuns compared with married women and speculated that this might be associated with their lack of children. In one meta-analysis nulliparity was associated with a 30% increase in risk compared with parous women. The higher the number of full-term pregnancies, the greater the protection. There is a reduction in risk of 7% for each birth after the first, in the absence of breast feeding (11).

- Breastfeeding: Women who breastfeed reduce their risk compared with women who do not breastfeed. The longer a woman breastfeeds, the greater the protection: risk is reduced by 4.3% for each year a woman breastfeeds (11).
- Age at menopause: Late menopause increases the risk of breast cancer (14). For each year menopause is delayed, there is an approximate 3% increase in breast cancer risk (15). Postmenopausal women have a lower risk of breast cancer compared to premenopausal women of the same age. This is true for both natural menopause or menopause induced through surgery (15).

4. Exogenous Hormones

-The Pill: The use of oral contraceptives (OCs) slightly increases the risk of breast cancer in current and recent users, but there is no significant excess risk ten or more years after stopping use (16). These estimates are based on a collaborative analysis of 54 studies in 25 countries, with data on over 50,000 women with breast cancer. Cancers diagnosed in women who have used OC tend to be less clinically advanced than those detected in never-users. OC users are generally younger women whose breast cancer risk is comparatively low, so the small excess risk in current users will result in a relatively small number of additional cases.

The formulation of OCs has changed considerably since use became widespread in the 1960s but current evidence suggests that this does not affect risk (16). The risk of oral contraceptive use in women is similar regardless of a woman's family history, ethnic origin, years of education, age at menarche, height, weight, menopausal status and alcohol consumption (16).

-Hormone Replacement Therapy (HRT) HRT use increases the risk of breast cancer and reduces the sensitivity of mammography (17). The risk of breast cancer for current or recent users of HRT increases by 2% per year of use. For women who had used it for at least five years (average 11 years) the risk increase was 35%. (18).

The effect is substantially greater for estrogen-progestagen combinations than for estrogen only HRT. Risk increases with duration of use: the risk for current users of estrogen-progestagen combinations for 10 or more years was 2.31 compared to 1.74 for 1-4 years of use (19).

5. Endogenous Hormones

Higher levels of endogenous hormones have long been hypothesized to increase breast cancer risk. A pooled analysis of nine prospective cohort studies found a statistically significant increased risk of breast cancer in postmenopausal women with higher levels of sex hormones (20). The risk was approximately double for women whose oestradiol levels were in the top quintile compared with women whose oestradiol levels were in the bottom quintile. Evidence for premenopausal women is inconclusive.

6. Bodyweight: Overweight and obesity, as measured by high body mass index (BMI), moderately increases the risk of postmenopausal breast cancer and is one of the few modifiable risk factors for breast cancer (21).

After the menopause, when the ovaries stop producing oestrogen, adipose tissue is the primary source of endogenous oestrogen so obese and overweight women are exposed to higher levels of oestrogen. Obesity is also associated with lower levels of sex hormone-binding globulin (SHBG) which increases the amount of bio-available oestradiol (23).

7. Physical Activity: A recent report from the International Agency for Research on Cancer concluded that physical activity has a preventive effect on breast cancer (24). This may be an indirect effect with exercise lowering BMI, or a direct effect on hormonal and growth factor levels.

8. Alcohol Intake: A significant association between alcohol intake and breast cancer has been found, with an increase of risk of 7% for each additional 10 grams of alcohol consumed on a daily basis (25). Around 4% of breast cancers in women in developed countries may be attributable to alcohol. Although alcohol and tobacco smoking are closely related social habits, there is no direct association between tobacco and breast cancer.

9. Diet: A diet high in fat has been positively associated with breast cancer in international correlation studies (26). Overall, the evidence suggests fat intake, particularly animal fat, may cause a small increased risk of breast cancer but probably does not play as large a role as was once thought.

10. Height: Taller women have an increased risk of breast cancer (27). There was an approximate increase in relative risk of 7% for each additional 5 cm in height for postmenopausal women and 2% for premenopausal women (21).

The underlying mechanism for the association between height and breast cancer risk is unclear, and it is likely that height may be a marker for other exposures that influence breast cancer risk (28).

11. Ionizing Radiation: Ionizing radiation is an established risk factor for breast cancer and excessive exposure to radiation should be avoided. The effect of radiation on the breast is strongly related to age at exposure, the younger the woman is exposed the greater the excess risk.

12. Breast Density: Mammographic density is related to the risk of breast cancer. (Density relates to the relative amounts of fat, connective tissue and epithelial tissue in the breast. Breasts with a higher proportion of fatty tissue are less dense. Cancer is less easily detected in denser breasts.) Women with denser breasts have 2-6 times the risk of breast cancer compared to women with less dense breasts (29).

13. Benign Breast Disease: Benign breast disease is a generic term describing all non-malignant breast conditions. As such it encompasses diseases associated with an increased risk of breast cancer and others that do not have a raised risk (30).

14. Personal History of Breast Cancer: If a woman has had breast cancer, her risk of developing a second primary breast cancer is 2-6 times the risk seen in the general population of developing a primary breast cancer (31).

15. Family History of Breast Cancer: A woman with one affected first degree relative (mother or sister) has approximately double the risk of breast cancer of a woman with no family history of the disease; if two (or more) relatives are affected, her risk increases further (32).

However, over 85% of women who have a close relative with breast cancer will never develop the disease, and more than 85% of women with

breast cancer have no family history of it (32). In developed countries it is estimated that hereditary factors contribute around a quarter of inter-individual differences in susceptibility to breast cancer, while environmental and lifestyle factors contribute the remaining three-quarters (33).

A small proportion of women has a particularly strong family history of breast cancer and are at very high risk. Mutations in the breast cancer susceptibility genes BRCA1 and BRCA2 account for the majority of families with four or more affected members and 2-5% of all breast cancers (34). Women carrying such a mutation have a 50-80% chance of developing the disease.

Since breast cancer affects one woman in nine there will be many women who have a mother or sister with the disease. But only if there are several family members with early onset breast cancer is there a likelihood of a significant inherited predisposition to the disease (35).

1.5 Objectives

Reports from ministry of health and other studies concerning the Palestinian community have shown an increase incidence of breast cancer. The current study aims thus to explore various risk factors associated with the development of breast cancer in women in the north of West Bank.

Evaluations of epidemiologic risk factors in relation to breast cancer classified jointly by estrogen receptor (ER) and progesterone receptor (PR) status have been inconsistent. To address this issue, this study conducted an evaluation of risk factors for breast cancer classified according to receptor status among Palestinian women. The study will help to understand the interaction of these factors and receptors (ER/PR) status among Palestinian women, where there's a limited researches and insufficient knowledge about this disease. The finding of the study might help set guidelines for prevention strategies of breast cancer in Palestine.

1.6 Literature Review

The incidence rate in the USA is estimated at 91.4 per 100,000. Such high rates are also observed in Europe, Australia and New Zealand, and in some parts of South America, especially Uruguay and Argentina (4). In contrast, low rates are found among African and Asian populations. Amongst population-based cancer registries (as distinct from national estimates), the 30 recording the highest rates include 20 registries from North America, one from South America (Montevideo), two from Israel and five from Europe. Amongst this group, the only one from Africa is for Europeans in Harare. By contrast, among population-based registries with the 30 lowest rates, five are from Africa, 18 from Asia and Israel, three from South America, two from Eastern Europe and two from the United States of America (American Indians in New Mexico and Koreans in Los Angeles, California) (4).These large geographical differences are potentially explicable on the basis of genetics or the influences of lifestyle and environment. Studies of migrant populations have revealed that when women migrate from low-risk to high-risk regions, the migrant populations acquire the rates of the host country after two or three generations, indicating lifestyle as primarily determining the geographic variations in risk. The absolute number of new breast cancer cases worldwide has doubled from 1980 to the most recent period (5).

In the UK over the past ten years, it is estimated that 20,000 extra breast cancer cases have occurred among women aged 50-64 as a result of HRT use and three quarters (15,000) of these additional breast cancers are due to the use of estrogen-progesterone HRT (19).

About 8% of breast cancer cases in the UK may be attributable to overweight and obesity (22). In one pooled analysis the risk of developing breast cancer was increased by around 30% in postmenopausal women with a BMI >28kg/m2 compared to a BMI of less than 21kg/m2 (21).

Epidemiologic studies that have examined breast cancer risk factors by either ER or PR status separately have shown inconsistent results (44).
By using data from a prospective cohort study, Potter et al. (45) found that several risk factors related to endogenous hormone exposure, including age at menarche, parity, age at first live birth, body mass index, and waist-hip ratio, showed expected patterns of association with ER+PR+ but not with ER+PR- or ER-PR- breast cancers. Similarly,
Giuffrida et al. (46) reported that breast cancer patients with a higher body mass index, in comparison to patients with a lower body mass index, were significantly more likely to have ER+PR+ tumors.
A substantial proportion of primary breast cancers contain estrogen receptors and/or progesterone receptors (49-52). The hormone receptor status of breast tumors and their responsiveness to endocrine therapy are highly correlated, with receptor-positive tumors responding favorably (49-52). Patients with receptor-positive tumors have a somewhat better prognosis than patients with receptor-negative tumors, and receptor-positive cancers tend to have less aggressive biologic properties than receptor-negative cancers (49-52).

In a large population-based case-control study of breast cancer conducted in China, 534 histologically confirmed incident cases of breast cancer in Chinese women of Shanghai and an equal number of age and sex-matched

population controls were interviewed to determine the risk factors of breast cancer among this population.

Early age at menarche was positively associated with breast cancer risk whereas early age at first full term pregnancy, high parity, and long duration of nursing were each negatively associated. They found high average body weight to be a risk factor, especially among women over age 60. Use of oral contraceptives after age 45 was also a risk factor, but use in general was not. Personal history of benign breast disease and history of breast cancer in first degree female relatives both increased risk (56).

The Nurses' Health Study follow up 66 145 women participating from 1980 through 2000, of whom 2096 incident cases of breast cancer identified, and their ER/PR status was available: 1281 were ER+/PR+, 318 were ER+/PR-, 80 were ER-/PR+, and 417 were ER-/PR-. They conclude that Incidence rates and risk factors for breast cancer differ according to ER and PR status. In this prospective study, they observed that the number of ER+/PR+ breast tumors increased at a faster rate than the number of ER-/PR- tumors both before and after menopause. Parity and timing of births (i.e., early versus late) were inversely associated with ER+/PR+ tumors but not with ER-/PR- tumors, whereas the one-time adverse association of first pregnancy with incidence was evident only among ER-/PR- and ER+/PR- tumors. Women who used postmenopausal hormones had a substantially reduced risk for developing ER-/PR- tumors after stopping use of the hormones. BMI after menopause was statistically significantly more strongly associated with ER+/PR+ tumors than with ER-/PR- tumors. Overall, the four categories of tumors based on ER/PR status showed different associations with age, pregnancy history, postmenopausal hormone use, and BMI after menopause (57).

A large case-control analysis of 1,154 breast cancer cases and 21,714 cancer-free controls at the Aichi Cancer Center Hospital, Nagoya, Japan between 1988 and 1992, found that age at diagnosis/interview, occupation, age at menarche, menstrual regularity at ages 20-29 years, and cigarette smoking differed significantly in effect according to progesterone receptor status (58).

A Swedish population-based study include Postmenopausal women ages 50 to 74 years, diagnosed with invasive breast cancer during 1993 to 1995, were compared with 3,065 age frequency-matched controls, conclude that high age at first birth, substantial weight gain in adult age, and use of menopausal estrogen-progestin therapy were more strongly related to receptor-positive breast cancer than receptor-negative breast cancer. They found that Women ages >or=30 years, compared with those ages 20 to 24 years at first birth, were at an increased risk of ER+PR+ tumors but not ER-PR- tumors. Also Women who gained >or=30 kg in weight during adulthood had an approximately 3-fold increased relative risk of ER+PR+ tumors, but no risk increase of ER-PR- tumors, compared with women who gained <10 kg. Compared with never users, women who used menopausal estrogen-progestin therapy for at least 5 years were at increased risk of ER+PR+ tumors but not ER-PR- tumors (59).

Another reported data on alcohol consumption were collected in 1987 and 1997 from 51,847 postmenopausal women in the population-based Swedish Mammography Cohort. 1188 invasive breast cancer case patients with known ER and PR status were identified during an average 8.3-year follow-up. Alcohol consumption was associated with an increased risk for the development of ER-positive (+) tumors, irrespective of PR status .No association was observed between alcohol intake and the risk of developing ER-tumors. They observed a statistically significant

interaction between alcohol intake and the use of postmenopausal hormones on the risk for ER+PR+ tumors (60).

In the same study, they observed a positive association between obesity and risk for the development of ER+ PR+ tumors and an inverse association for the development of all PR- tumors. The positive association of obesity with the development of ER+ PR+ tumors was confined to never-users of postmenopausal hormones and to those without a family history of breast cancer. Their results support the hypothesis that excess endogenous estrogen due to obesity contributes to an increased risk of ER+ PR+ postmenopausal breast cancer (61).

A hospital-based case-control study, among 317 cases and 401 controls, They found significant heterogeneity across the four tumor receptor subtypes for older age at first full-term pregnancy and post-menopausal status. For older age at first full-term pregnancy, an elevated risk was found for the $ER_{+}PR_{-}$ subtype. For post-menopausal status, elevated risks were found for both the $ER_{+}PR_{+}$ and $ER_{+}PR_{-}$ subtypes. Also they observed that cases, who had consumed alcohol for more than 1 year were 3.4 times more likely to have $ER_{+}PR_{+}$ tumors than $ER_{-}PR_{-}$ tumors (62).

A comparison of ER/PR status in a case-control study include 1,725 case patients and 440 control subjects aged 20 to 49 years, found that number of full-term pregnancies was inversely associated with the risk of $ER^{+}PR^{+}$ breast cancer, whereas recent average alcohol consumption was associated with an increased risk of $ER^{+}PR^{+}$ breast cancer. Neither of these two factors was associated with the risk of ER^{-} PR^{-} breast cancer. Late age at menarche and a longer duration of breastfeeding were both associated with decreased breast cancer risk, irrespective of receptor status. These

Results suggest that the number of full-term pregnancies and recent alcohol consumption affect breast cancer risk in younger women predominantly through estrogen and progesterone mediated by their respective receptors. Late age at menarche and breastfeeding may act through different hormonal mechanisms (63).

A meta-analysis of results from epidemiological studies that have investigated risk factors of breast cancer shows that parity and early age at first birth protect only against ER^+PR^+ breast cancer whereas breastfeeding and late age at menarche protect against both ER^+PR^+ and ER^-PR^- breast cancer. Their findings suggest that breastfeeding (and age at menarche) may act through different hormonal mechanisms than do parity and age at first birth (64).

Chapter Two

Methodology

2. Methodology

2.1 Study Design

This case-control study was conducted in the period of Feb.-May 2009.Women aged 25-70 years old of either having breast cancer confirmed histologically (cases) or healthy women (controls) were selected from those attending Al-watani hospital in Nablus, Notrh of the West Bank. Women who attended this hospital are residents of cities of North of West Bank including Nablus, Jenin, Tulkarim, and Qalqilya. Residence of North of West bank is about a million according to the Palestenian Central Bureau of Statistics in the year 2006 form 2.480.762 of the total population in West Bank. Nablus is the largest city in the North which nearly occupies the third population of this area.
Women (cases) attending the oncology department, which is the oldest and biggest department of its kind in the Northern region of West Bank, were interviewed by author in order to collect data of risk factors. Alongside, data about the ER/PR test has been taken from the case files. Controls were selected from the general population and they were matched the cases with respect to age and geographical characteristics with no history of breast problems or neoplastic disease.
Al-Watani hospital which considered as a central hospital in North West bank, established before hundred years ago, it has oncology department that contains one unit for treating patients who are in need of chemotherapy. Capacity of this department is 14 bed for both males and females. Patients can review this department three days per week (Monday, Tuesday, Wednesday), thus collecting data was done in these days each week through the study period.

Controls were chosen from the general population of the North West bank, they were matched with cases by age group and geographical area without any history of breast problems or neoplastic disease and not had any other cancers.

2.2 Sampling

303 women participate in this study: 140 case and 160 control, data were collected by interview with cases and control, medical data were collected using patients files, the receptor status was available for 100 case from 140 breast cancer case. All samples are residents in North West Bank distributed as follow in table 3

Table 3: Distribution of Cases According to Their Residence

District	Cases No.	Cases %
Nablus	78	55.7
Qalqilya	22	15.7
Tulkarim	22	15.7
Jenin	9	6.4
Salfit	9	6.4

2.3 Inclusion Criteria

1- Resident of North West bank

2- Cases should have pathological breast cancer

2.4 Exclusion Criteria

1-Women who are not residents in North West Bank

2- Controls should not have any history of breast problems or neoplastic disease

2.5 Questionnaire

A structured questionnaire containing both open-ended and close-ended questions was developed for this study. The questionnaire contained four sections. The first was the demographic section which contained questions regarding age, education level, residence, career, marital status, body mass index (<30 or ≥30), and age at marriage (≤20 or more than 20, since the mean age at marriage in Palestine is 19.1 years). The second section contained reproductive data that used to asses the effect of reproductive factors such as age at menarche which is divided into less than 13 years and more than 13 years, the average age of menarche in our region is 13.7 so this cut point was chosen, menopause status, age at menopause (< 50 or ≥50) women are classified as menopausal if they had not menstruated during the 12 months before the date of data collection. Hormone replacement therapy, number of deliveries (1-3,or ≥4 deliviries) , age at first birth (≤20, 21-29, and ≥20), breast feeding (1-3 years, ≥4 years), oral contraceptive use, anti-miss carriage use, and abortion. The third section is the medical one that contained medical data recorded in patients files,

include age at diagnosis (<50 years or ≥50 years), breast cancer type (ductal, lobular, invasive, inflammatory, or others), estrogen and progesterone receptor status (+ve or –ve). The final section was the family history that search about cancer in family through first and second male, female, relative degree. Medical data as cancer type, site, node metastasis, age at diagnosis and receptor status (estrogen and progesterone) were recorded from patients files in hospital. The questionnaire has been validated by distributing to 20 person in the same hospital, after analysis using SPSS, some questionnaire were changed into another form in order to make it relevant.

The mean time interval between diagnosis and interview of cases was 1.6 years, and 81% of cases were interviewed within 3 years of diagnosis. The distributions of selected demographic characteristics and major risk factors for breast cancer of whole cases and controls are shown in table 4.

Table 4: The distribution of selected demographic characteristics and major risk factors for breast cancer of whole study population: breast cancer versus control groups

characteristic	Case No. (%)	Control No. (%)
Residence		
City	73 (52.1)	104 (63.8)
Out city	67 (47.9	59 (36.2)
Body mass Index		
<30	95 (67.9)	122 (74.8)
≥30	45 (32.1)	41 (25.2)
Age at Marriage		
≤20	62 (44.3)	69 (42.3)
>20	58 (41.4)	73 (44.8)
Not Married	20 (14.3)	21 (12.9)
Education		
High	22 (15.7)	67 (41.1)
Low	118 (84.3)	96 (58.9)
Profession		
Housewife	106 (75.7)	109 (66.9)
Employee	34 (24.3)	54 (33.1)
Age at menarche		

≤13 years	93 (66.4)	40 (24.5)
>13 years	47 (33.6)	123 (75.5)
Menopause		
Yes	75 (53.6)	89 (54.6)
No	65 (46.4)	74 (45.4)
Age at menopause		
<50 years	41 (29.3)	60 (36.8)
≥50 years	35 (25)	29 (17.8)
Not Menopause	64 (45.7)	74 (45.4)
Hormone Replacement Therapy		
Yes	32 (22.90	30 (18.4)
No	108 (77.1)	133 (81.6)
No. of Deliveries		
1-3	20 (14.3)	38 (23.3)
≥4	92 (65.7)	100 (61.3)
0	28 (20)	25 (15.3)
Age at 1st delivery		
<30 years	104 (74.3)	134 (82.2)
≥30 years	9 (6.4)	4 (2.5)
Not Married	27 (19.3)	25 (15.3)
Lactation		
<4 years	36 (25.7)	22 (13.5)
≥4 years	75 (53.6)	114 (69.9)
Not BF.	29 (20.7)	27 (16.6)
Oral Contraceptive Pills		
Yes	61 (43.6)	38 (23.3)
No	79 (56.4)	125 (76.7)
Abortion		
Yes	77 (55)	30 (18.4)
No	43 (30.7	112 (68.7)
Not Married	20 (14.3)	21 (12.9)
Smoking		
Yes	21 (15)	22 (13.5)
No	119 (85)	141 (86.5)
Anti-misscarriage		
Yes	36 (25.7)	15 (9.2)
No	84 (59.9)	129 (79.1)
Not Married	20 (14.3)	21 (12.9)
Environment		
Yes	59 (42.1)	48 (29.4)
No	81 (57.9)	115 (70.6)
Family History		
First Degree Affected	55 (39.2)	14 (8.5)
Not affected	85 (60.7)	149 (91.4)
Second degree Affected	82 (58.5)	28 (17.1)
Not Affected	58 (41.4)	135 (82.8)

2.6 Data Analysis

Statistical Package for Social Science (SPSS) version 15 was used for data analysis. Calculated Values included means, frequencies, chi-square, and odds ratio were used to determine variation significance.

Chapter Three

Results and Discussion

3.1 Results

The majority of the participant cases (60.7%) in this case-control study are aged less than 50 years at the time of diagnosis. Their mean age was 48.7. Table 5 summarize the demographic characteristics and major risk factors among cases and controls. Statistical analysis of the study variables showed that there were significant difference between cases and controls, with respect to education level, family history, (either of 1st and 2nd female or male-degree) (figure 3). However, there were no significance difference between both groups with respect to body mass index, marital status, and profession. The following table shows the results of Chi-square and Relative risk test at confidence interval = 95%. Residence distribution showed that 63.8% of controls are resident primarily in city. Moreover controls participants have more education level where 41.1% of them have attended university compared to 15.7 5 of cases. Our results showed no difference in profession between cases and controls. Both groups were mostly housewives without significance difference between them (p =0.118). Few difference but not significant between two groups in body mass index (32.1% of cases was obese compared to 25.2% of controls). Marital status showed no association with breast cancer risk (P-value =.85), Just 14.3% of cases was not married with nearly equal percent (12.9%) in controls. Also age at marriage showed no association among cases and controls. There was no association between risk of breast cancer and smoking, only 15% of cases and 13.5% of controls had ever smoking. The environmental factors have shown a significance difference between cases and controls (P =0.029) with relative risk =1.74. Family history (figure 3) indicates a strong

association with risk of developing breast cancer. This association was significant among all degree of relative between cases and controls.

Table 5: Frequencies distribution of demographic characteristics and major risk factors among cases and controls.

	Case		Control		Total		Test Result (CI 95%)	
Characteristic	**Freq.**	**%**	**Freq.**	**%**	**Freq.**	**%**	**OR***	**P-value**
Residence								
Urban	73	52.1	104	63.8	177	58.4	0.618	0.053
Rural	67	47.9	59	36.2	126	41.6		
Body mass Index								
<30	95	67.9	122	74.8	217	71.6	0.709	0.223
≥30	45	32.1	41	25.2	86	28.4		
Marital status								
Married	120	85.7	142	87.1	262	86.5	0.887	0.851
Single	20	14.3	21	12.9	41	13.5		
Age at Marriage								
≤20	62	44.3	69	42.3	131	43.2	1.1	0.545
>20	58	41.4	73	44.8	131	43.2		
Not Married	20	14.3	21	12.9	41	13.5		
Education								
High	22	15.7	67	41.1	89	29.4	0.267	0.000
Low	118	84.3	96	58.9	214	70.6		
Profession								
Housewife	106	75.7	109	66.9	215	71.0	1.545	0.118
Employee	34	24.3	54	33.1	88	29.0		
Environment								
Yes	59	42.1	48	29.4	107	35.3	1.745	0.029
No	81	57.9	115	70.6	196	64.7		
Family History								
-1st female affected	31	22.1	9	5.5	40	13.2	4.866	0.000
-Not Affected	109	77.9	154	94.5	263	86.8		
-1st male -affected	24	17.1	5	3.1	29	9.6	6.538	0.000
-Not Affected	116	82.9	158	96.9	273	90.1		
-2nd female -affected	45	32.1	11	6.7	11	6.7	6.545	0.000
-Not Affected	95	67.9	152	93.3	152	93.3		
-2nd male								

-affected	37	26.4	17	10.4	54	17.8	3.085	0.001
-Not Affected	103	73.6	146	89.6	249	82.2		

*OR: Odds Ratio

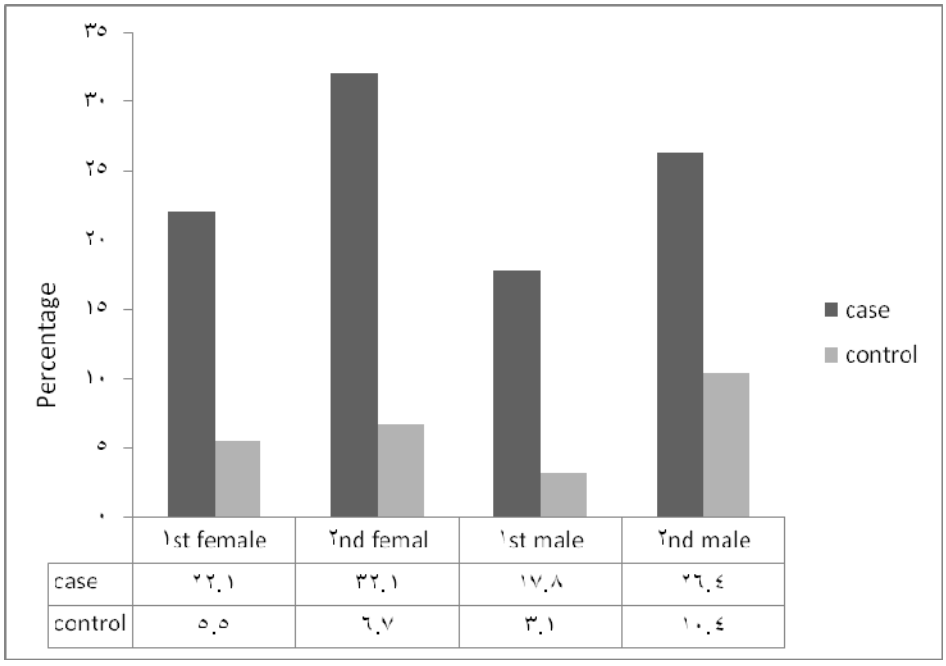

Figure 3: Family history of cancer among cases and controls.

Family history indicates a strong association with risk of developing breast cancer (p-value <0.001). 2nd female and male relative degree showed the highest percent of cancer among patient's families.

Menstrual and reproductive factors varies among cases and controls. Among these factors; age at menarche was inversely related to risk of breast cancer. Women who began menstruation at age 13 or younger had a relative risk of 6.5 (95% CI) compared to those who began menstruation after age 13. (table 6). Abortion among cases (6.7%) was significantly associated with breast cancer risk (p-value <0.001) (figure 4).

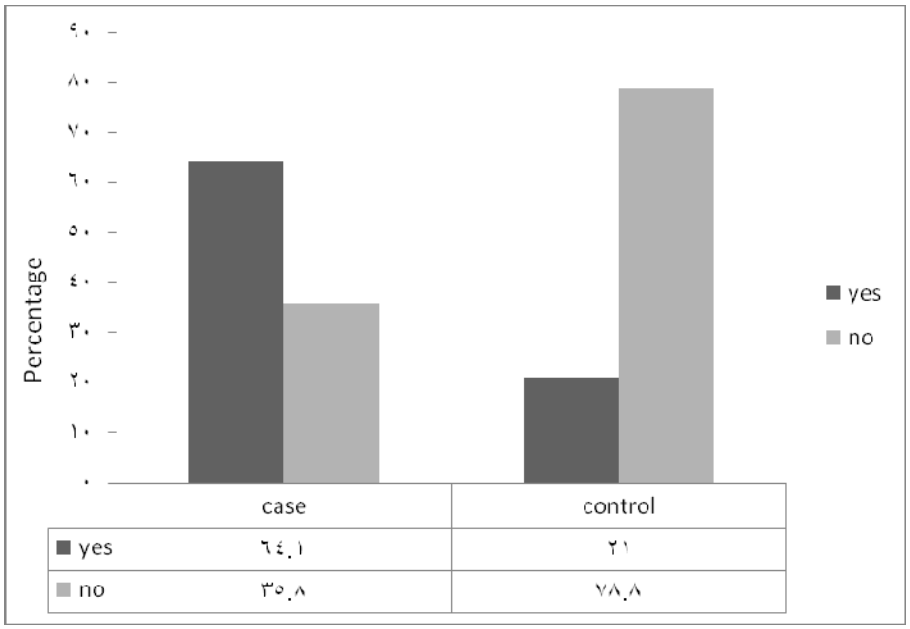

Figure 4: Abortion frequencies among cases and controls

Abortion history among cases was nearly 3 times higher than controls. A strong association between abortion and risk of breast cancer (p-value <0.001, CI 95%).

Age at menopause (50 years), breast feeding (4 years), oral contraceptive pills, abortion, and anti-miscarriage use show a significance difference between cases and controls ($p<0.05$) (table 6). Other factors showed no significance difference among the two groups as shown in table 6.

Table 6: Menstrual and reproductive characteristics in cases versus controls.

	Case		Control		Total		Test Result (CI 95%)	
Characteristic	**Freq.**	**%**	**Freq.**	**%**	**Freq.**	**%**	**OR**	**P**
Age at menarche								
≤13 years	93	66.4	40	24.5	96	31.7	6.5	.000
>13 years	47	33.6	123	75.5	207	68.3		
Menopause								
Yes	75	53.6	89	54.6	164	54.1	0.959	0.949
No	65	46.4	74	45.4	139	45.9		
Age at menopause								
<50 years	31	22.1	60	36.8	91	30	3.3	.001
≥50 years	45	32.1	29	17.8	74	24.4		
Not Menopause	64	45.7	74	45.4	138	45.5		
Hormone Replacement Therapy								
Yes	32	22.9	30	18.4	62	20.5	1.314	0.415
No	108	77.1	133	81.6	241	79.5		
No. of Deliveries								
1-3	20	14.3	38	23.3	58	19.1	.57	.098
≥4	92	65.7	100	61.3	192	63.4		
0	28	20	25	15.3	53	17.5		
Age at 1st delivery								
<30 years	104	74.3	134	82.2	238	78.5	.313	.919
≥30 years	9	6.4	4	2.5	13	4.3		
No Delivery	27	19.3	25	15.3	52	17.2		
Breast Feeding	36	25.7	22	13.5	58	19.1	2.4	.004
<4 years	75	53.6	114	69.9	189	62.4		
≥4 years	29	20.7	27	16.6	56	18.5		
Not BF.								
Oral Contraceptive Pills								
Yes	61	43.6	38	23.3	99	32.7	2.54	.000
No	79	56.4	125	76.7	204	67.3		

Abortion								
Yes	77	55	30	18.4	107	35.3	6.685	.000
No	43	30.7	112	68.7	155	51.2		
Not Married	20	14.3	21	12.9	41	13.5		
Anti-miscarriage								
Yes	36	25.7	15	9.2	50	16.5	3.7	.000
No	84	59.9	129	79.1	217	71.6		
Not Married	20	14.3	21	12.9	36	11.9		

Clinical characteristics of the 140 breast cancer patients in the study are shown in the table 7. About the majority (60.7%) of cases was below 50 years old at the time of diagnosis with breast cancer (figure 5).

Table 7: Clinical characteristics of the breast cancer cases

Clinical Characteristic	Number	Percent
Age at Diagnosis		
20-29	5	3.6
30-39	27	19.3
40-49	53	37.9
50 or more	55	39.3
Type of Breast Cancer		
Ductal	12	8.6
Lobular	2	1.4
Invasive	115	82.1
Inflammatory	11	7.9
Lymph node Metastasis		
Yes	85	60.7
No	55	39.3
Site of Breast Cancer		
Right	76	54.2
Left	64	45.7
ER Expression		
+ve	45	32.1
-ve	55	39.3
Not available	40	28.6
PR Expression		
+ve	49	35.0
-ve	51	36.4
Not available	40	28.6

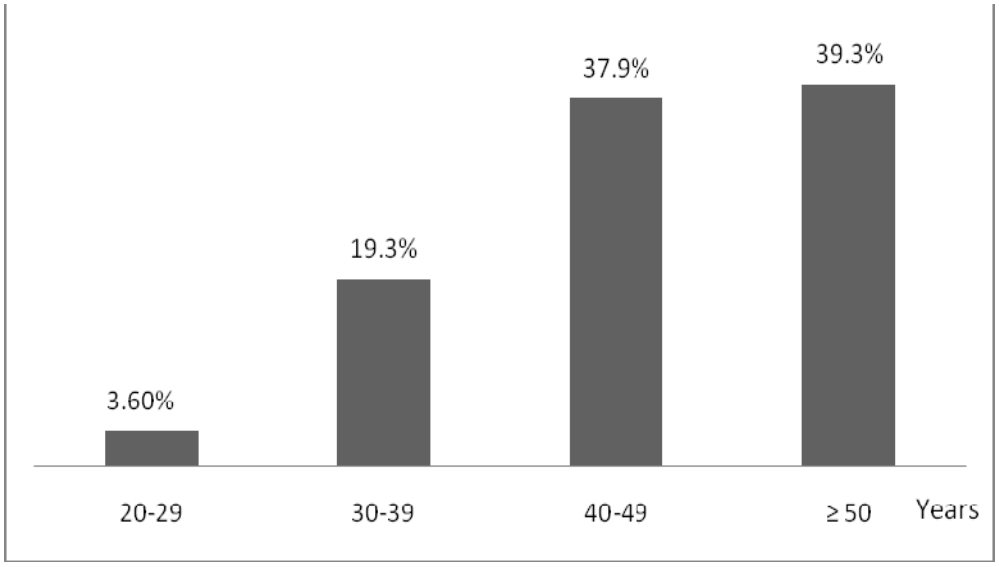

Figure 5: Age at diagnosis of breast cancer among cases

About 61% of cases was below 50 years old at diagnosis. Of which, most of these cases were aged 40-49 years.

Figure 6 demonstrate the distribution of Breast cancer types among cases, the results showed that the majority of cases have invasive type (82.1%). About 10% have ductal or lobular type of cancer. Invasiveness results in the metastasis of cancer cells, the high percent of metastasis correlates with high percent of invasiveness. About 60.7% of patients had metastasis in lymph nodes (table 7). Cancer in right breast was more common (45.2%) than cancer in left breast (figure 7).

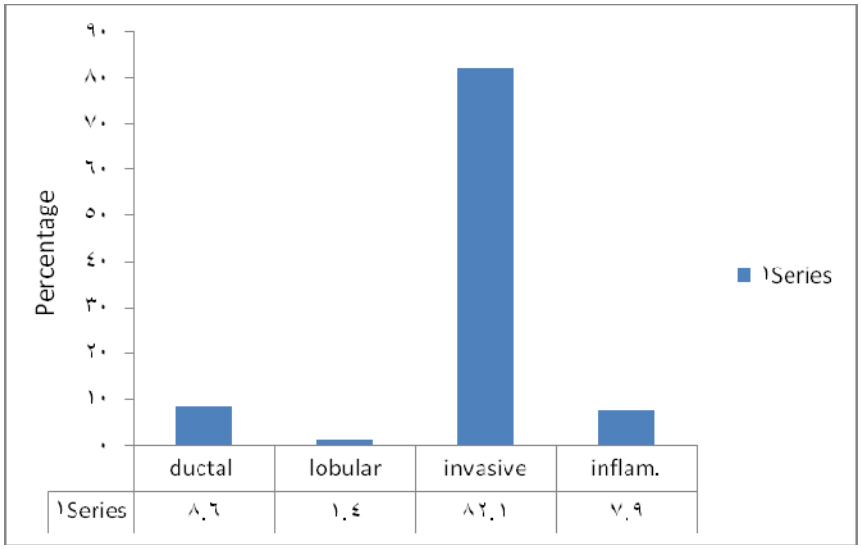

Figure 6: Distribution of breast cancer type among cases

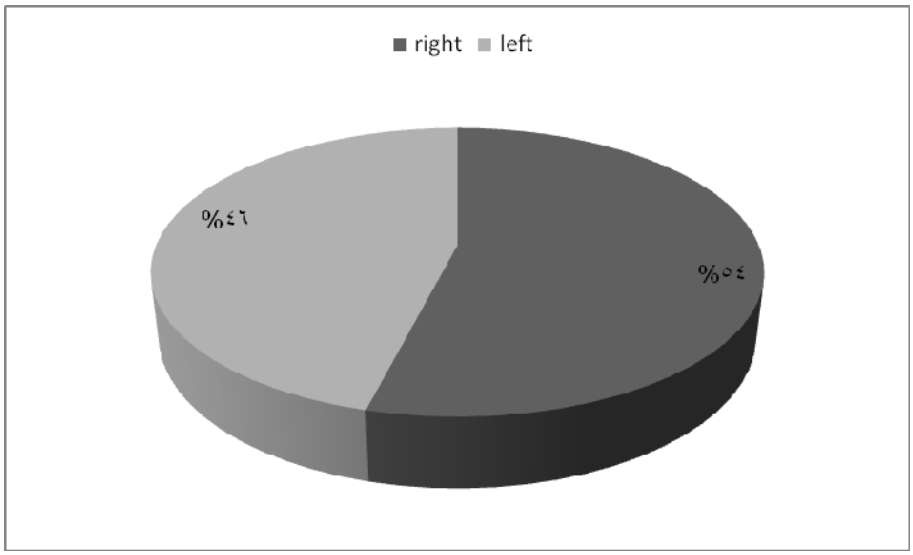

Figure 7: Site of Breast Cancer among cases

The results regarding receptors status among breast cancer cases were only from 100 patients since the other 40 did not have receptors status in their pathology reports. The distribution of estrogen receptors among cases is shown in figure 8. The results showed that more than 50% of cases are negative to either ER or PR.

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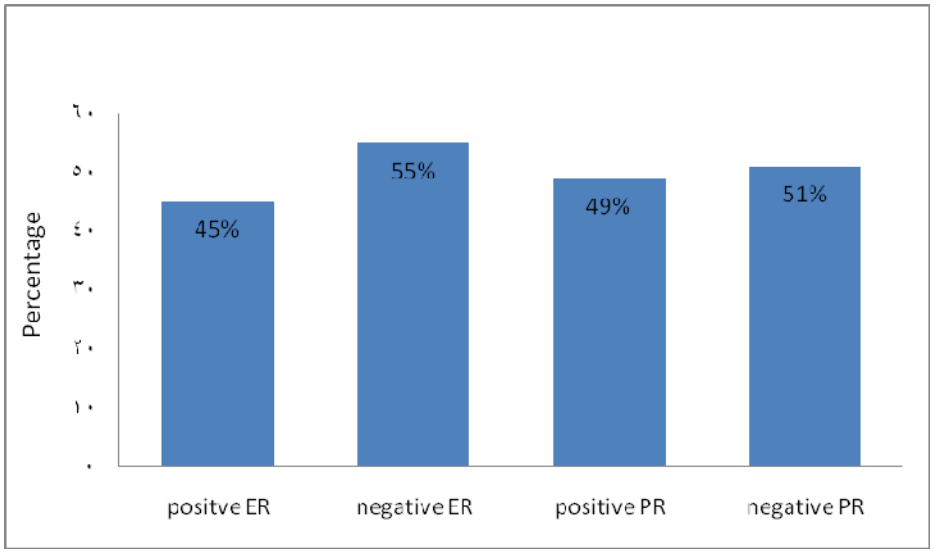

Figure 8: Distribution of receptors among breast cancer cases

Reproductive variables (menopause, age at menarche, abortion, etc) have different association and correlation to breast cancer regarding both tumor receptors 55% of estrogen receptors was –ve, and 45% was +ve. Progesterone receptor was 49% +ve and 51% -ve. The status of ER and reproductive variables associated with breast cancer cases was studied. For example, age at menarche had a strong association with receptors status (p-value = 0.007) (figure 9). As demonstrated from figure 6, most cases where age at menarche ≤ 13 years showed negative ER (78.9%), compared to cases of age at menarche > 13 years that showed only 21.1%.

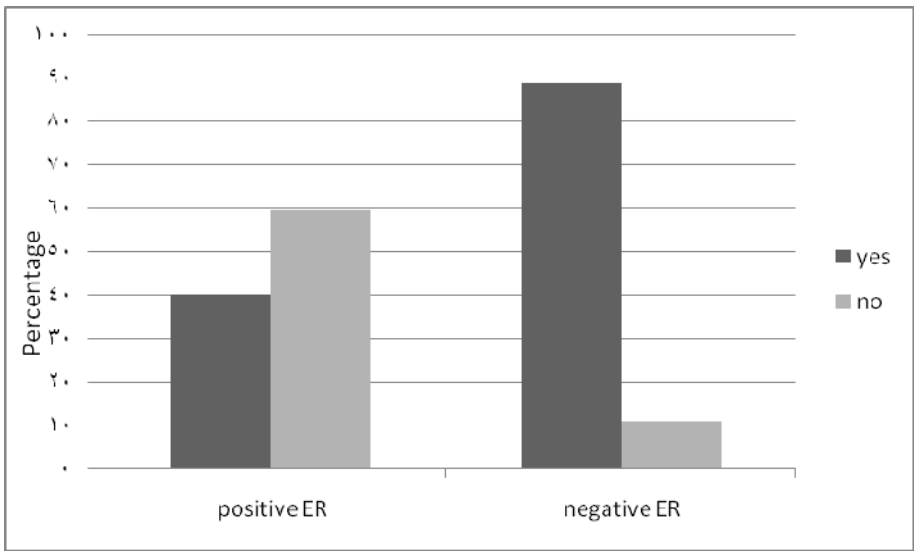

Figure 9: Distribution of Estrogen Receptors among Cases at menarche age.

Also the results showed that about 90% of cases that expressed at least one abortion were negative to ER ($p < 0.001$) (figure 10).

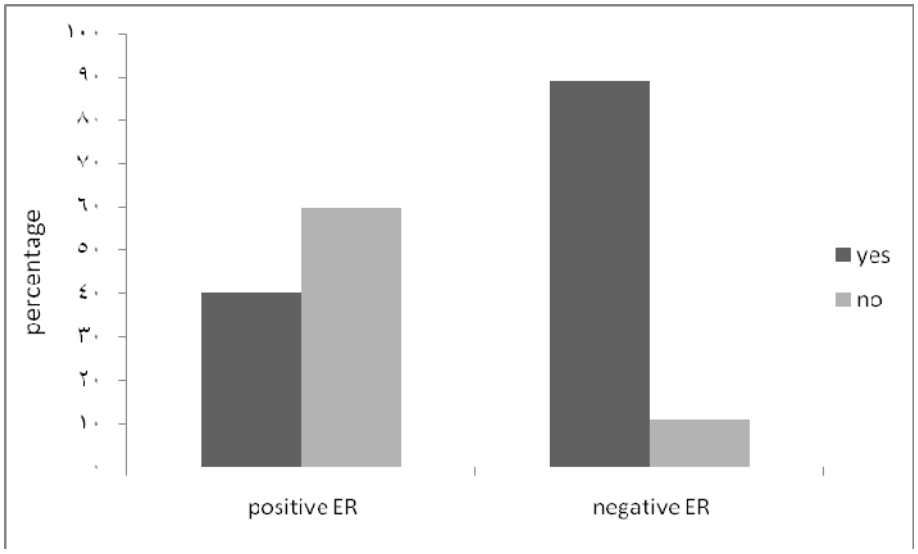

Figure 10: Abortion frequencies among cases regarding estrogen receptors

Clinical Characteristics varies among cases in relation to ER status and not to PR status. A shown in figure 11, 74.4% of –ve ER cases had node metastasis compared to 49.1% in +ve ER with metastasis (p =.019, CI 95%). Type of breast cancer, cancer site and age at diagnosis showed no association with receptors status.

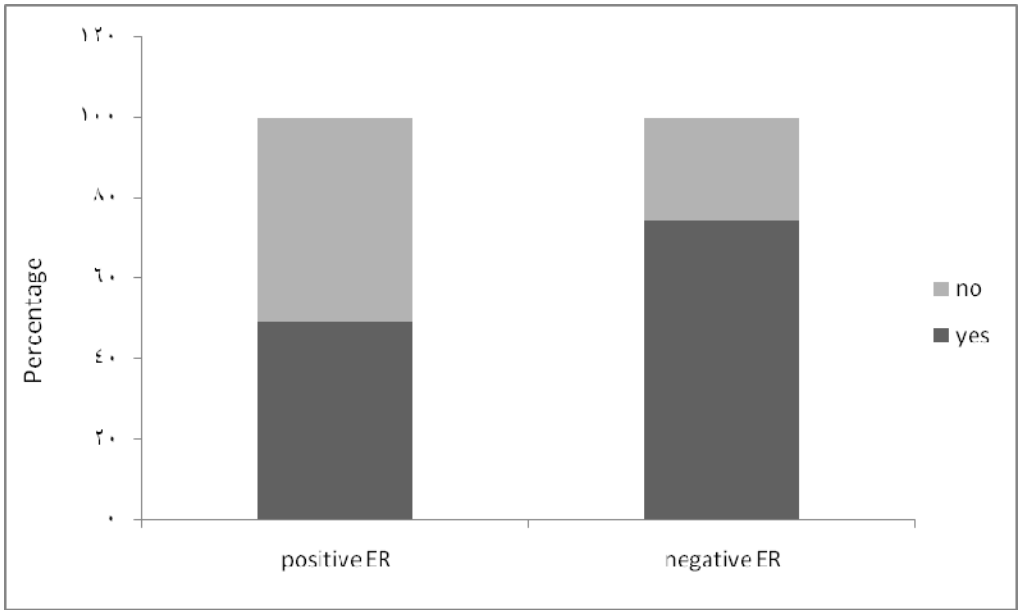

Figure 11: Distribution of node metastasis among cases regarding estrogen receptors

3.2 Discussion

In this case-control study among 140 cancer patients participants 60.7% were below 50 years old and among 163 controls group 57.3% were below 50 years old. The mean age at diagnosis was 48.7 which is considered as a young age compared to neighboring countries, such as Israel, in which the mean age among Jewish women is 55.9 years (Abu-Khalaf, personal communication), 12% of patients were aged <35 at the time of diagnosis, among Jewish women just 5% of patients were below 35 years at the time of diagnosis. Among women in Arab world, half of breast cancer cases are below 50 and median age is 49-52 years as compared to 63 in industrialized nations. These results may be attributed to: genetic predisposition, environmental and Revolution in life style, and hormonal risk factors.

Type of breast cancer at the time of diagnosis was shown to be at advanced stage, this may explain the high percent of metastasis among cases (60.7%). Marital status was not a risk for breast cancer in contracts to other studies which shows that unmarried women were at higher risk for breast cancer (31). In most studies single and nulliparous married women were found to have a similar increased risk for breast cancer as compared with parous women of the same age (79). Thus, one may argue that marital status by itself is not a determining factor for increased or reduced breast cancer risk and rather the main protective effect is from early first full-term pregnancy. However, in the present study no association with parity. Evidence suggests that there is an interaction between marital status and parity (81), supporting a dual effect of parity on breast cancer risk with pregnancy.

Family history of cancer is risk factors for breast cancer. This is in accordance with other research findings indicating that a positive family history of breast cancer is a strong risk factor for breast cancer at young age (82), although this has a comparatively small effect on the absolute lifetime incidence of and mortality from breast cancer (87). In this study, family history as a strong factor in developing breast cancer in the life time, was statistically significant differences ($p < .001$ CI 95%) between cancer patients and the control.

However, with regard to the findings from the present study, one may argue that the relatively high proportion of young breast cancer cases in Palestine is most likely due to a young population structure and to a combination of high age at menarche and low age at first pregnancy, which are protective in later life. Evidence from the USA (80) also suggests that, in some Asian subgroups such as the Vietnamese, women diagnosed with breast cancer tend to be younger than those from other racial or ethnic groups, with half of the diagnoses occurring in women younger than 50 years; this needs further exploration.

Our results suggest that Breast cancer patients in Palestine are relatively young, and the findings presented here suggest that age at menarche, abortion and a positive family history of cancer are risk factors for breast cancer in Palestine.. the associations between some known risk factors for breast cancer may differ in Palestine as compared with Western countries and that familial breast cancer in young Palestinians breast cancer patients deserves further investigation.

ER-/PR- tumors were more common than the +ve tumor. Reproductive variables appeared to show differing associations with breast cancer

among the two tumor receptor categories. There was a strong association between positive ER and age at menarche below 13 years. Abortion showed a strong significance in cases with negative ER. Also –ER showed a strong association with lymph node metastasis (74.4% of metastasis cases had -ER)

Similar to the findings of Potter et al. (83), our findings show that epidemiologic risk factors vary by the hormone receptor expression of the breast cancer, supporting the hypothesis that these receptor expression categories represent distinct stable phenotypes in human breast cancer (85) rather than a single disease with a single biologic pathway. Anderson et al. (86) showed that among lymph node-negative women, each of the ER/PR tumor subtypes was associated with separate age frequency-density plots, again suggesting that breast cancer does not represent a single disease. Treatment of breast cancer has already been divided by hormone receptor status in that hormonal agents are only used in receptor-positive cancers, and the same division of cancer cases according to receptor status should be considered.

Our data indicate that some risk factors for breast cancer differ according to ER status. These data support the hypothesis that different patterns of receptor expression correspond to different types of breast tumor. Thus, we suggest that it would be prudent to divide breast cancer cases according to both the ER status of the tumor.

3.3 Study Limitation

Because of limited medical information in patients files, some data were missing as receptor status and cancer type and unfortunately an important test was not available that detect the breast density, the technique necessary for this test is not available in our region. Also some patient didn’t respond to questionnaire and reject to participate in the study.

Chapter Four

Recommendation

Recommendations

-Alert policy makers to design governmental control programs against breast cancer to minimize prevalence in Palestine, and ensure effective protection for women at risk of having the disease.

-Health education to general public using various methods, namely TV, and teaching posters.

-Raise the need for early detection and defining of high risk groups.

-Developing preventive, diagnostic, treatment guidelines and Palliative care.

-Developing a breast cancer screening program.

-Implementing research activities.

-Genetic testing

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جامعة النجاح الوطنية
كلية الدراسات العليا

العوامل المساهمة في الاصابة بسرطان الثدي بين النساء الفلسطينيات في شمال الضفة الغربية

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قدمت هذه الاطروحة استكمالا لمتطلبات درجة الماجستير في الصحة العامة بكلية الدراسات العليا في جامعة النجاح الوطنية- نابلس- فلسطين

2009

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الملخص

يعد سرطان الثدي من أخطر أنواع السرطانات التي تصيب المرأة خلال فترة حياتها. وهو ثاني أهم أنواع السرطانات انتشارا في العالم بعد سرطان الرئة. المعلومات والأبحاث المتعلق بهذا المرض في فلسطين محدودة و غير متوفرة، لذا فأن دراسة هذ المرض والعوامل المؤثرة فيه تعد مهمة وقد تساعد في اعطاء صورة أوضح عنه. وقد لوحظ في خلال السنوات الأخيرة زيادة في نسبة الأصابة بالمرض بين النساء الفلسطينيات وخاصة في عمر صغير مقارنة بالدول الأخرى، لذا فمن الضروري البحث عن العوامل التي قد تساهم في الأصابة بهذ المرض في فلسطين. و يتفاوت تأثير هذه العوامل من منطقة الى أخرى ولا يوجد مقياس محدد لها، مع العلم بأن العوامل البيئية لها تأثير أكبر من العوامل الوراثية.

هذه الدراسةهي محاولة لفهم العوامل المؤثرة بالأصابة بسرطان الثدي بين النساء الفلسطينيات و علاقة هذه العوامل مع مستقبلات الهرمونات (الأستروجين والبروجستيرون). ذراسة الحالات المصابة ستوضح التداخل بين مختلف الهوامل وتأثير حالة المستقبلات الهرمونية مع هذه العوامل، وهذا سيساعد في وضع استراتيجيات تساعد في منع هذا المرض والسيطرة عليه. تتضمن هذه الدراسة 140 امرأة مصابة بسرطان الثدي و 163 امرأة غير مصابة. كل الحالات مسجلة في مستشفى الوطني في نابلس في شمال الضفة الغربية. تم جمع المعلومات الديمغرافية والطبية بواسطة استبيان واجراء مقابلة مباشرة مع السيدات المصابة.