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A Retrospective analysis for Breast Cancer receptors' prevalence, and HER2 positive Breast Cancer treatment regimens at Palestinian MOH hospitals and Effect of cancer symptoms and treatment on breast cancer patients' daily life activities

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Thesis Approval

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Jerusalem–Palestine
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Dedication:

With profound gratitude and respect, I dedicate this thesis to my family, whose unwavering support, encouragement, and sacrifices have lit my way.

Their belief in me has been my constant strength.

I also extend my sincere thanks to my supervisor, mentors, and lecturers, whose wisdom and guidance have been instrumental in my academic journey and inspired me to achieve my best

Declaration:

I certify that the content of this thesis, submitted in partial fulfillment of the requirements for the degree of Master, represents my own research efforts, with all external sources appropriately acknowledged. I further certify that this study (in its entirety or in part) has not been previously presented for a higher degree at any other university or institution.

Name: Aseel Hisham Salah Erekat

Signature: 

Date: 26/4/2025

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I express profound gratitude to my family and loved ones. Your unwavering love, support, and sacrifices have constituted my foundation throughout this undertaking. This accomplishment belongs to you as much as it does to me.

Abstract:

Background: Breast cancer is the most prevalent cancer among women worldwide, including in Palestine, where it constitutes a significant public health challenge. Identifying hormone receptors, such as ER, PR, and HER2, is critical for customizing therapy approaches and improving patient outcomes. This study aimed to analyze the prevalence of breast cancer receptor subtypes, evaluate treatment regimens for HER2-positive breast cancer patients in Palestinian Ministry of Health (MOH) hospitals, and assess the impact of cancer symptoms and treatments on patients' daily activities using the Arabic version of the MD Anderson Symptom Inventory (MDASI-A).

Methods: A retrospective study was conducted using medical records of breast cancer patients treated in MOH hospitals between 2019 and 2021. The study included demographic data, receptor status (ER, PR, HER2), treatment regimens, and survival outcomes. Additionally, the MDASI-A was administered to assess the severity and interference of cancer-related symptoms in daily life. Data were analyzed using SPSS version 22, employing descriptive statistics and inferential tests to examine associations between variables.

Results: A total of 1,234 breast cancer cases were analyzed, with an average age at diagnosis of 52.76 years. The majority (69%) were ER-positive, 58% were PR-positive, and 21% were HER2-positive. Triple-negative and triple-positive cases accounted for 10% each.

Of the 265 patients with HER2-positive breast cancer registered in the Palestinian Cancer Registry, 220 (83%) were recorded as receiving a first-line treatment protocol. Of those 220 patients, 72 (32.7%) were recorded as receiving a second-line protocol, and 8 (3.6%) received a third-line protocol. Overall, 157 of the 220 patients (71%) were treated in accordance with NCCN guidelines, across all treatment lines.

Results from MDASI indicate that the symptom (Loss of appetite) has the highest reported symptom 86%, followed by Nausea with an average of 78.5% and the symptom (Lack of remembering) at the lowest 16.5%, followed by the symptom Shortness of breath with an average of 36.2%. Most of the patients 52.4% reported the symptoms are moderate. When evaluating symptom interference with life for cancer patients the (Activity) had the highest interference 65.2, followed by (Mood) with an average of 62.1%. and then (Relationship with others) at lowest value of 28.9%, followed by the (Walking) with an average of 30.1%.**Conclusion:** The findings emphasize the need for continued improvements in breast cancer management in Palestine, particularly in adherence to international treatment guidelines and symptom management. The study also highlights the utility of MDASI-A in identifying symptom burden and guiding supportive care strategies. Future research should focus on prospective studies to assess treatment outcomes over time and explore interventions for optimizing the quality of life of breast cancer patients.

List of Abbreviations:

Abbreviation	Full Term or Explanation
AC	Adriamycin and Cyclophosphamide
AC-T	Adriamycin, Cyclophosphamide, and Taxol (Note: Definition for AC-T needs verification)
AC-TH	Adriamycin, Cyclophosphamide, and Trastuzumab Therapy
ACTH	Adriamycin, Cyclophosphamide, Taxol, and Herceptin (Note: Could not verify; assumed based on pattern)
ADC	Antibody-drug conjugates
AUC	Area Under Curve (pharmacokinetics)
BC	Breast Cancer
BRCA1	Breast Cancer 1, early onset (gene)
BRCA2	Breast Cancer 2, early onset (gene)
CMF	Cyclophosphamide, Methotrexate, and Fluorouracil (Note: Definition for CMF needs verification)
DCIS	Ductal Carcinoma In Situ
Docetaxel	Docetaxel, a chemotherapy medication
Doxorubicin	Doxorubicin, a chemotherapy medication
EC	Epirubicin and Cyclophosphamide
EORTC	European Organization for Research and Treatment of Cancer
ER	Estrogen Receptor
FEC	Fluorouracil, Epirubicin, and Cyclophosphamide
FISH	Fluorescence In Situ Hybridization
HER2	Human Epidermal growth factor Receptor 2
HR	Hormone Receptor
IHC	Immunohistochemistry
ILC	Invasive Lobular Carcinoma
IDC	Invasive Ductal Carcinoma
IV	Intravenous
MDASI	MD Anderson Symptom Inventory
MDASI-A	MD Anderson Symptom Inventory - Arabic version
NCCN	National Comprehensive Cancer Network

Abbreviation	Full Term or Explanation
PR	Progesterone Receptor
QoL	Quality of Life
SD	Standard Deviation
SE	Standard Error
SPSS	Statistical Package for the Social Sciences
TC	Taxotere and Cyclophosphamide (Note: Definition for TC needs verification)
TCH	Taxotere, Carboplatin, and Herceptin
TNBC	Triple Negative Breast Cancer
WHO	World Health Organization

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Chapter One:

Introduction:

1.1 What is breast cancer

It is defined by the World Health Organization (WHO) as "a neoplastic intraductal lesion characterized by increased epithelial proliferation, subtle to marked cellular atypia and an inherent but not necessarily obligate tendency for progression to invasive breast cancer" World Health Organization (2022, March 13).

1.2 Types of breast cancer

There are four types of breast cancer:

1.2.1 Ductal carcinoma in situ (DCIS)

DCIS is a non-invasive cancer where abnormal cells have been found in the lining of the breast milk ducts

Ductal carcinoma in situ is also called intraductal carcinoma and is Stage 0 breast cancer. DCIS is early-stage cancer that is highly treatable. Nearly all women with DCIS can be cured

1.2.2 Invasive ductal carcinoma:

Is the most common type of breast cancer, reflecting 80% of all breast cancer types, it is also called infiltrative ductal carcinoma.

Invasive ductal carcinoma (IDC) occurs when cancer cells that began forming in a milk duct of the breast spread beyond the duct into other breast tissue or to other areas of the body. The term "invasive" represents the way the cancerous cells spread to (or invade) the surrounding breast tissue or other body parts.

1.2.3 Inflammatory Breast Cancer (IBC)

Accounting for 1 to 5% of all breast cancer cases, inflammatory breast cancer (IBC) is a rare and aggressive type of breast cancer. IBC occurs when cancer cells infiltrate the skin and lymph vessels of the breast. IBC is harder to diagnose than other types of breast cancer and tends to occur in younger women. It also spreads more quickly than other types of breast cancer

1.2.4 Metastatic breast cancer (MBC):

It is Stage 4 breast cancer that has spread from the original location in the breast to other areas of the body

When breast cancer recurs, or returns, to another part of the body months or years after the initial breast cancer diagnosis and treatment (also referred to as distant recurrence), it is called metastatic breast cancer. When the first diagnosis of breast cancer is metastatic, it is called de novo metastatic breast cancer. This typically means that the cancer has already spread out of the breast and into other areas of the body by the time the initial diagnosis of breast cancer is made" National Breast Cancer (n.d.)

1.3 Breast Cancer Subtypes

"Subtypes are commonly grouped into four categories based on the immunohistochemical expression of hormone receptors:

Estrogen receptor positive (ER+), progesterone receptor positive (PR+), human epidermal growth factor receptor positive (HER2+), and triple-negative (TNBC).

The need for molecular classification is to categorize patients who may benefit from targeted therapy, such as hormone therapy and anti HER2 therapy." National Library of Medicine (National Center of Biotechnology Information chapter 3)

1.3.1 "Estrogen receptor positive. A breast cancer that's estrogen receptor positive, also called ER positive, has receptors for the hormone estrogen. Treatment with hormone therapy can block the growth of the cancer cells. Another term for breast cancer hormone therapy is endocrine therapy.

1.3.2 Progesterone receptor positive. A breast cancer that's progesterone receptor positive, also called PR positive, has receptors for the hormone progesterone. Treatment with endocrine therapy can block the growth of the cancer cells". mayoclinic.org (2024 October 31)

1.3.3 "HER2-positive breast cancer is a breast cancer that tests positive for a protein called human epidermal growth factor receptor 2 (HER2). This protein promotes the growth of cancer cells.

In about 1 of every 5 breast cancers, the cancer cells have extra copies of the gene that makes the HER2 protein. HER2-positive breast cancers tend to be more aggressive than other types of breast cancer" mayoclinic.org (2024 April 9)

1.3.4 “Triple negative breast cancers are cancers whose cells don’t have receptors for nor the hormones estrogen and progesterone neither the HER2 protien.

Some women with triple negative breast cancer also have a fault (mutation) in the BRCA1 or BRCA2 genes. BRCA stands for Breast Cancer gene. Everyone has BRCA1 and BRCA2 genes. They stop cells in our body from growing and dividing out of control. If there is a fault in these genes, it means that cells can grow out of control. This can increase your risk of developing breast cancer”. Cancer Research UK (2023 June 22)

1.4 Her2 positive breast cancer treatment medications

1.4.1 “Monoclonal Antibodies: is a man-made copies of immune system proteins (antibodies) that are intended to bind to a specific target. In this situation, they bind to the HER2 protein on cancer cells, which can help prevent them from developing.

HER2-directed mAbs target the extracellular domains of HER2 and may act through multiple mechanisms, including antibody-dependent cell-mediated cytotoxicity (ADCC) and inhibition of receptor dimerization and downstream signaling

1.4.2 Tyrosine Kinase Inhibitors

TKIs are typically small molecules that target the intracellular kinase domain of receptor tyrosine kinases like HER2 and block downstream antiapoptotic and proliferative signaling pathways”. P Tarantino, E Hamilton, SM Tolaney, *et al*

1.4.3 Antibody Drug Conjugates (ADCs)

“They typically comprise a mAb conjugated to a chemotherapeutic payload by a synthetic linker. The mAb of an ADC targets the chemotherapeutic to specific cells, such as those overexpressing HER2, where the ADCs are internalized”. Jain, SW Smith, S Ghone, B Tomczuk

1.5 Risk Factors for Breast Cancer

History in the family or personal history in breast cancer or in health conditions for the breast, starting the period at younger age, late start of the menopause at older age, alcohol drinking, late first pregnancy after thirty or never being pregnant, dense breast tissue, obesity, radiation exposure, menopausal hormonal therapy, increased age, being female, inherited DNA mutations can increase the risk of having breast cancer. Mayoclinic.org(n.d.)

1.5 Signs and Symptoms

We have to bear in mind that different people may have different symptoms of breast cancer and some people may not have any signs or symptoms at all.

However, according to the centers of disease control and prevention, there are some warning signs of breast cancer that may be well known as symptoms for breast cancer like: “new lump in the breast or underarm (armpit), thickening or swelling of part of the breast, irritation or dimpling of breast skin, redness or flaky skin in the nipple area or the breast,

pulling in of the nipple or pain in the nipple area, nipple discharge other than breast milk, including blood, any change in the size or the shape of the breast and pain in any area of the breast". cdc.gov (2024, September 25)

1.7 Breast cancer facts

According to the world health organization, 2.3 million women were diagnosed with breast cancer in 2022. It was the most common cancer in women in 157 countries in 2022.

50% of all breast cancer cases occur with no specific risk factor except age and sex. World Health Organization (2022, March 13).

Breast cancer is always the most common cancer in Palestine. According to the Palestinian Cancer Registry 2023 which was published in June 2024, the number of new breast cancer cases was 546 cases in the West Bank, with incidence rate 18.6 cases per 100,000 of total population ;(15.2%) of all cancer cases and as top one reported cancer among females' cancers; (37.1%) of all women cancers. moh.ps (2024. June)

1.8 Problem Statement and Significance of the study:

Breast cancer is now the most common cancer and the second leading cause of death in women, making it a serious public health concern.

Novel care of breast cancer rely on exact evaluation of their molecular subtypes, which are recognized by hormone (estrogen and progesterone) receptors and HER2 levels of the initial tumor.

The Palestinian Cancer Registry System is recognized as a leading registry within the Arab world, undergoing regular updates and validation. Its success can be attributed primarily to two key factors: a dedicated and responsible team, and a well-defined strategic plan.

Despite its advanced standing, the system exhibits certain limitations, particularly concerning breast cancer data. While the registry comprehensively captures and records breast cancer cases, it currently lacks detailed information regarding subtypes, histopathology, and receptor status

Numerous studies in Western countries have shown variations in hormonal receptor status, HER2 neu positivity rate, and histology among women of different racial and ethnic backgrounds. However, research on this topic within Palestine is limited. Only two studies have examined the prevalence of ER, PR, and HER-2 receptors in Palestinian breast cancer cases.

One study, conducted at Augusta Victoria Hospital and published in September 2009, included a small sample size of 167 patients. Furthermore, as a private hospital, its patient population may not fully represent the broader Palestinian population, particularly compared to governmental hospitals. A more recent study, published in 2019, included 400 patients from two major governmental hospitals, offering a potentially more representative sample.

So, being sure about the prevalence of one of the most important receptors (HER2 neu) among Palestinians may open another field to be studied on the level of genetics which will help understanding the type of our diseases and so develop and tailor our treatment plans and guidelines.

1.9 Objectives:

The objectives of this study are to:

1. Find out how many Palestinian women having breast cancer had ER, PR, and HER 2/neu receptors at Palestinian MOH hospitals and to compare them with those in the literature in other population.
2. Review prescribing trends in HER2 positive BC patients at our Palestinian Governmental Hospitals.
3. To evaluate the degree of certain breast cancer symptoms and how they affect day-to-day functioning by using MDASI-A

Chapter Two:

Literature Review:

2.1. Breast Cancer in Arab World:

When talking about **epidemiology and prevalence**, we must consider some studies that were conducted in the neighboring countries like:

With the title of "**Prevalence of hormone receptors and HER2/neu in breast cancer cases in Jordan.** A retrospective study for the prevalence of receptors was conducted at Jordan that was published in 2006,

The patient number was 267, and the results were as the following:

68% were ER-positive, 90.9% PR positive and 13.6% HER2/neu-positive" (Sughayer et al., 2006).

Another study called "**Molecular subtypes of breast carcinoma in Saudi Arabia** was published in 2016 which objective was finding out where different molecular subtypes of breast cancer are found in Saudi Arabia and evaluating the relationships between these subtypes and factors such age at diagnosis, tumor size, histopathological type, grade, presence of carcinoma in situ, and lymph node status were the goals.

The results were as the following:

1. Luminous with a frequency of 18.7%, HER2-positive was the least frequent molecular subtype, whereas tumors were the most prevalent.
2. Luminal A tumors accounted for the majority of Lobular carcinomas. Women under 50 years old were more likely to have HER2 positive and triple negative tumors, which also had greater tumor sizes at diagnosis and higher histologic grades. Triple negative tumors had the lowest incidence of carcinoma in situ.

Molecular subtypes and lymph node status did not correlate" (Alnegheimish et al., 2016).

In a different study with the title of "**Epidemiology, Prevention and Management Guidelines for Breast Cancer in Arab Countries**, which was done by performing a literature review pertaining to Arab nations' breast cancer epidemiology, prevention, and therapy.

It concluded that additional primary preventive measures should be made. Early detection and awareness initiatives are examples of secondary prevention. To lower the incidence of locally advanced breast cancer, it is advised to increase awareness and encourage attention to breast symptoms, breast self-examination, and clinical breast inspection.

Additionally, in nations with sufficient resources, screening mammography is advised. Given that half of all incidences of breast cancer in Arab nations occur in women under the age of fifty, they advise beginning screening mammograms at the age of forty, even though this is a contentious issue. Individual doctors treating women with breast cancer need to engage in more interdisciplinary management and group talks".
(https://www.amaac.org/images/files/PAJO/Mar2010_2/PREVENTION_MANAGEMENT_GUIDELINES.pdf)

A study that was published in early 2018 called "**Breast Cancer Subtypes among Iraqi Patients: Identified by Their ER, PR and Her2 Status**, its objective was to determine the prevalence of the various molecular breast cancer subtypes in the tissue samples from female patients with breast cancer in Iraq and compare the results with those found in regional and international literature.

The results of this study were that the registered rates of positive ER, PR and HER2 tumor contents were 67.8%, 65.3% and 29.4% respectively". (Alwan, Nada AS, and Furat N. Tawfeeq)

When comes to comparison; there was a unique study called **"A population-based study of Kurdish breast cancer in northern Iraq: Hormone receptor and HER2 status. A comparison with Arabic women and United States SEER data**

Which was published in June 2012 that compare the Her2 status in Kurdish women and Arabic women to US white women.

The main findings were that most patients were diagnosed at an advanced stage of the disease. However, the prevalence of ER, PR, and HER2 expression in Arabic and Kurdish women's breast cancers was comparable to that of white women in the United States with comparable tumor grades and ages". (Runnak, M. A., Hazha, M. A., Hemin, H. A., Wasan, A. A., Rekawt, R. M., & Michael, H. D. (2012

And when talking about **quality-of-life** studies, we must consider the following studies:

In July 2010, a study called "**Validation and application of the Arabic version of the M. D. Anderson symptom inventory in Moroccan patients with cancer** was published.

It came to the conclusion that the MDASI-A is a legitimate and trustworthy patient-reported outcome tool that can be used to evaluate the various symptoms of cancer patients

who speak Moroccan Arabic". It is necessary to prove its usefulness for application in other Arab nations (Nejmi et al., 2010).

In July 2019, a study called **"Assessment of quality of life (QoL) in breast cancer patients by using EORTC QLQ-C30 and BR-23 questionnaires: A tertiary care center survey in the western region of Saudi Arabia** was published and at the Oncology Department of King Abdulaziz University Hospital (KAUH) in Jeddah, Saudi Arabia, it sought to evaluate the quality of life (QoL) of a cohort of patients with breast cancer and to distinguish QoL between various groups. The survey was filled out by 284 patients, and the following were the findings:

1. 1. Most of the domains had high global health status and functional scales, whereas the majority of the items had moderate-to-low symptom scales, indicating improved quality of life.
2. The two most unsettling symptoms were exhaustion and insomnia.
3. Patients scored better on measures of future perspective and body image.
4. The sexual functioning score is the lowest.
5. The age group ≤50 years had superior global health, physical functioning, and role performance ($p<0.05$).
6. Compared to postmenopausal women, premenopausal and perimenopausal individuals had higher levels of functioning ($p = 0.001$).
7. Compared to perimenopausal and postmenopausal women, premenopausal patients reported higher levels of sexual satisfaction ($p = 0.04$).
8. The group that underwent conservative breast surgery showed greater signs of systemic treatment adverse effects.
9. Eight percent of the variance in physical functioning was explained by predictors (R-squared = 0.08).
10. Menopausal status was a predictor that significantly impacted physical functioning when compared to the other variables in the model ($P = 0.02$)". (Imran M, Al-Wassia R, Alkhayyat SS, Baig M, Al-Saati BA. Assessment of quality of life (QoL) in breast cancer patients by using EORTC QLQ-C30 and BR-23 questionnaires: A tertiary care center survey in the western region of Saudi Arabia. PLoS One. 2019 Jul 10;14(7):e0219093)

2.2 Breast Cancer in Palestine:

A study called "Demographic and clinical predictors of breast cancer among Palestinian women was published in 2015 with the conclusion of that numerous characteristics, including career, marital status, ER, PR, abortion, and psychological distress, have been linked to breast cancer in Palestinian women". Qabaha K, Hassan WA, Bsharat A, Mousa M, Horani Y, 2015. Demographic and clinical predictors of breast cancer among Palestinian women. Int Res J Med Med Sci, 3(2): 35-39.

Another study called "**Genomic analysis of inherited breast cancer among Palestinian women: Genetic heterogeneity and a founder mutation in TP53** that was published in 2017 showed that: 875 Palestinian women with invasive breast cancer were included in the research sample overall; 453 of these women were in the discovery series, and 422 were in the older-onset sporadic patient series. For the patients in the discovery series, pathology records were obtained. Of these individuals, 61% (278/453), 36% (161/453), and 49% (220/453) had accessible tumor stage, grade, and hormonal status. The distribution of tumor stage among patients having pathology data was as follows: 9% had stage 1, 45%

had stage 2, 41% had stage 3, and 5% had stage 4. The tumor grade distribution was 51% grade III, 45% grade II, and 4% grade I. According to Lolas Hamameh et al. (2017), 20% of cancers with hormone receptor profiles were triple negative (TNBC)". olas Hamameh, S., Renbaum, P., Kamal, L., Dweik, D., Salahat, M., Jaraysa, T., Abu Rayyan, A., Casadei, S., Mandell, J. B., Gulsuner, S., Lee, M. K., Walsh, T., King, M. C., Levy-Lahad, E., & Kanaan, M. (2017).

Another study was published by a student at Al Quds University in 2017 called **Breast Cancer in Palestine: Expression of the protein Activation Induced Cytidine Deaminase** concluded that aberrant expression of AID protein in Palestinian breast cancer patients. (https://dspace.alquds.edu/handle/20.500.12213/1345)

Most Importantly, there is a study called "**Differences in pathological and clinical features of breast cancer in Arab as compared to Jewish women in Northern Israel** that was published in September 2011 that studied the clinical features of Breast Cancer in Arabs and Jewish women in Israel, and its abstract was as the following:

Ethnic groups are not equally affected by breast cancer (BC). Compared to Israeli Jewish women, Israeli Palestinian Arab women had a greater BC mortality rate. Comparing the clinical, biochemical, and pathological features of breast cancer in the two groups is the goal of this study. The records of 1,140 BC patients—268 Arab and 872 Jewish—who had treatment in Northern Israel between 2002 and 2007 were examined. Estrogen receptor (ER), HER-2 expression, clinical differentiation, tumor stage, and age at diagnosis were assessed. For Arabs and Jews, the primary age at diagnosis was 49.9 and 59.4 years, respectively ($p < 0.0001$). In 53% of Jews and 25% of Arabs.

Among Arab and Jewish women, 78.5% of Jews and 69% of Arabs had positive ER results ($p < 0.001$). HER-2 overexpression was seen in 22% of Jewish women and 35.4% of Arab women ($p < 0.001$)". (Zidan J, Sikorsky N, Basher W, Sharabi A, Friedman E, Steiner M. Differences in pathological and clinical features of breast cancer in Arab as compared to Jewish women in Northern Israel. Int J Cancer. 2012 Aug 15;131(4):924-9. doi: 10.1002/ijc.26431. Epub 2011 Nov 17. PMID: 21918975.)

Related to HER2 receptor status situation, a study called "**Prevalence of hormonal receptors ER,PR and HER-2 new in breast cancer cases in Palestine** was conducted in 2009 to know the prevalence of hormonal receptors ER, PR and HER-2 in breast cancer cases in Palestine.

It concluded that the prevalence of the receptors was as the following: 52.7% ER positive, 47.2% were PR positive and 16.1% were HER 2/neu receptor positive". (Pan Arab Journal of Oncology | vol 2; issue 3 | September 09 <)

A study called "**Evaluation of types and treatment protocols for breast cancer among Palestinian women: a retrospective study** was published in 2019 which aimed to assess the histological types of breast cancer, the stage at diagnosis, and estrogen receptor status of women with breast cancer in the West Bank.

It concluded that:

1. The most prevalent histological type was ductal carcinoma (79%; 317 of 400), which was followed by lobular carcinoma (15%; 60).
2. The most frequent diagnosis for patients was at stage three (27%; 106), followed by stage one (20%; 81), stage two (25%; 100), and stage four (24%; 95).
3. The majority of patients (88%; 353) did not undergo testing for mutations in the BRCA1 and BRCA2 genes. A BRCA1 or BRCA2 gene mutation was found in 5% (21) of the individuals that were screened.
4. Out of the 386 women for whom data were available, 249 (65%) received positive test results for estrogen receptor status.
5. Of the 385 women for whom data were available, 225 (58%) had positive results from the progesterone receptor test.
6. Of the 381 women for whom data were available, 306 (80%) reported negative test findings for HER2 receptor overexpression". Rowa' Al-Ramahi, et al Palestinian Medical and Pharmaceutical Journal (PMPJ). 2020; 5(1): 35-40

In December 2022, a study was published in the Journal of clinical oncology entitled "**Awareness of Palestinian Women About Breast Cancer Risk Factors: A National Cross-Sectional Study.** It evaluated Palestinian women's knowledge of breast cancer (BC) risk factors, age-related and lifetime risks, and variables linked to excellent awareness. It found that the women's knowledge of BC risk factors was below ideal. The results emphasize the necessity of putting in place health education initiatives in addition to regular utilization of ad hoc opportunities by healthcare professionals to increase awareness" (Elshami et al., 2022).

Chapter Three:

Methodology:

3.1 Methodology for Retrospective Study:

3.1 .1 Study Design:

This study employs a retrospective cohort design, by going back to medical records concentrating on individuals diagnosed with or treated for breast cancer between January 2019 and December 2021.

3.1.2 Study Setting:

The study will use a non-probability purposive sampling method for the hospital's selection. This sampling method is chosen because it allows for the selection of specific hospitals strategically positioned throughout the West Bank and can provide a diverse view of the region's healthcare system. The selected hospitals represent several geographical regions (North, Middle, and South) and have been chosen to ensure the West Bank's heterogeneous healthcare landscape.

Palestine Medical Complex: was chosen since it is the only central government hospital serving the entire Ramallah area in the middle region of the West Bank. The complex is divided into several departments, such as pediatric cardiology, intensive care, high-dependency care, obstetrics and gynecology, NICU.

Al Hussein Governmental Hospital at Bet Jala: Al Hussein Hospital, also referred to as Beit Jala Hospital, is located next to the Grand Park Hotel in Bab Al-Zqaq, Bethlehem. It has been serving the community for several years and provides various medical services as a governmental hospital. The hospital has been actively involved in community outreach and healthcare initiatives, including programs like Smiles of Hope which support children diagnosed with cancer.

Al Watany Governmental Hospital: is located in Nablus, a major city in the northern West Bank, Palestine. It serves as one of the key healthcare facilities in the region, providing medical services to the local population.

Like other governmental hospitals in Palestine, Al Watany Hospital offers a variety of services, including as emergency care, and general medicine. It also offers specialized services such as oncology, cardiology, and diagnostic imaging, depending on the resources available.

3.1.3 Study Population:

The population comprised all patients diagnosed with breast cancer who were admitted throughout the designated study period. Patients lacking definitive histological proof of breast cancer or those who were discharged at their own request were eliminated.

3.1.4 Inclusion criteria:

1. Breast cancer patients were diagnosed or treated during the period between Jan. 2019 and Dec. 2021.
2. Breast cancer patients whose medical records have sufficient data on their health status.

3.1.5 Exclusion criteria:

1. The patients who had a benign tumor.
2. Patients who had missing data on their files.
3. Patients who had cancer outside of the research period between (January 2019 and December 2021).

3.1.6 Data Collection:

After getting all the required approvals by the ethical committee of Al Quds University and after the completion of two training courses on medical research which were requested by Al-Quds research ethics committee, also formal written permission was obtained from the Palestinian Ministry of Health to give their approval to conduct this study. Following the approval, the data collection process included a comprehensive review of hospital records for all cases that occurred between January 2019 and December 2021 at the selected hospitals.

Data Extraction: Trained staff from the Ministry of Health extracted data from the Health Information System, the central electronic health records system utilized by hospitals. The staff was trained in data extraction processes and monitored by the lead investigator to ensure consistency and accuracy.

3.1.7 Data analysis:

- The pathology reports were reviewed for receptors' status (HER2, ER, PR) and treatment regimens for HER2 positive patients if available.
- The percentages of the HER2, ER, PR receptors positivity were calculated.
- The treatment regimens for Her2 positive BC used at Palestinian MOH hospitals were stated if it was available in the registered files.

3.1.8 Ethical Considerations:

In this retrospective cohort study, ethical approval was obtained from the Ministry of Health and the Ethical Committee at Al-Quds University before data collection. To ensure confidentially, the data was stored safely and only the research team will have access to it. The study was only utilized the data for scientific reasons, with no commercial use. The study followed ethical principles such as transparency in reporting and harm minimization.

3.2 MDASI Methodology:

The M.D. Anderson Symptom Inventory (MDASI) is a patient-reported outcome (PRO) instrument intended to evaluate the intensity of cancer-related symptoms and their effects on everyday activities. The MDASI, created by researchers at the University of Texas M.D. Anderson Cancer Center, is a concise, multidimensional questionnaire that has undergone extensive validation and is utilized in clinical and research environments.

The MDASI consists of two main components: symptom severity and symptom interference. These sections aim to document both the physical and psychological toll of cancer symptoms and their effect on patients' daily lives.

Symptom Severity: This section encompasses a fundamental array of symptoms frequently seen by cancer patients, including pain, exhaustion, nausea, disrupted sleep, discomfort, dyspnea, memory impairment, anorexia, somnolence, xerostomia, melancholy, and emesis (Cleeland et al., 2000).

Patients are requested to evaluate the intensity of each symptom experienced in the preceding 24 hours on a number scale from 0 to 10, with 0 signifying "not present" and 10 denoting "as severe as conceivable." This scale facilitates a quantitative evaluation of symptom load.

The interference section assesses the extent to which reported symptoms disrupt many facets of daily living, including general activity, mood, work, interpersonal connections, mobility, and overall enjoyment of life (Cleeland et al., 2000). Patients assess interference using a 0–10 scale, with 0 indicating "no interference" and 10 signifying "total interference." This section elucidates the functional ramifications of symptoms, which is essential for comprehending the overall quality of life of cancer patients.

The MDASI has been translated and validated in other languages, including Arabic, Chinese, Spanish, and Japanese, rendering it a universally usable instrument for symptom evaluation. This versatility increases its efficacy in global clinical trials and cross-cultural studies.

3.2.1 Study Population:

The study population comprised adult breast cancer patients who attended oncology clinics at three Palestinian hospitals: Al Hussein Governmental Hospital in Bet Jala, Al Watany Governmental Hospital in Nablus, and Palestine Medical Complex in Ramallah. The patients were undergoing routine care visits, representing a typical sample of breast cancer patients receiving conventional oncology treatment in the area.

3.2.2 Criteria for Eligibility:

Inclusion Criteria for Breast Cancer: Only individuals with a verified pathologic diagnosis of breast cancer were considered.

Age: Participants have to be at least 18 years old.

Language Proficiency: Patients were required to possess the ability to speak and read to ensure comprehension and completion of the questionnaire.

Physical and Cognitive Competence: Participants were required to possess the physical and cognitive abilities necessary for involvement in the study, as assessed by the researcher during recruiting.

Implementation of the MDASI

The M.D. Anderson Symptom Inventory (MDASI) was employed to evaluate the intensity of cancer-related symptoms and their effect on everyday activities. The administrative procedure was as follows:

Approach and Recruitment: The researcher engaged eligible patients during their standard healthcare appointments. The study's goal was elucidated, and informed verbal consent was secured from participants who agreed to participate.

The MDASI was administered in person. The researcher aided patients by examining the questionnaire's contents to guarantee clarity and comprehension. Patients were instructed to evaluate the intensity of their symptoms and the extent to which these symptoms disrupted their everyday activities on the MDASI’s 0–10 scale.

The researcher documented the current treatment regimen (e.g., chemotherapy, radiation therapy, or hormonal therapy) for each patient on the upper section of the hard copy of the questionnaire. This further information facilitated the investigation of symptom burden concerning various treatments.

3.2.3 Data collection Procedure:

The MDASI was administered during the patients' clinical appointments, guaranteeing that the results accurately represented their present symptomatology.

The researcher guaranteed the precise documentation of all responses and swiftly answered any queries or concerns made by participants.

3.2.4 Validity and Reliability:

The MDASI has undergone extensive psychometric evaluation to confirm its validity and reliability. Research has shown its capacity to consistently assess symptom severity and interference across various cancer types and treatment stages. The internal consistency of the MDASI, assessed by Cronbach's alpha, has been reported to exceed 0.80, signifying strong reliability (Cleeland et al., 2000). Furthermore, test-retest reliability has been validated, affirming the tool's temporal stability. **3.2.5 Statistical Treatment**

After collecting the questionnaires and verifying their validity for the analysis, they were encoded (giving them two specific numbers), in preparation for entering their data into the computer for performing the appropriate statistical treatments and analyzing the data according to the study's questions. The study data. Statistical processing of the data was done by extracting the arithmetic averages and the standard deviations for each of the paragraphs. Resolution, t-test, one way ANOVA, leaner regression, Pearson correlation coefficient, and Cronbach Alpha, using SPSS (Statistical Package For Social Sciences).

Chapter Four:

Analysis Results:

4.1 The retrospective analysis results:

This dataset includes 1234 breast cancer cases with an average patient age at diagnosis of 52.76 years. Most cases, **69%** (n=850) were **ER positive**, **65%** (n=797) were **Her2 negative**, **58%** (n=714) **PR positive**, **45%** (n=555) **Her2 negative/HR positive**, **28%** (n=342) **PR negative**, **21%** (n=265) **Her2 positive**, **19%** (n=233) **ER negative**, **Triple-positive and triple-negative** cases each comprised **10%** of the total (n=120 and n=118, respectively), while **Her2-positive/HR-negative** cases represented **8%** (n=96).

The same patient file could be counted and included in more than one category; for example: file number 812205 was counted in the Her2 positive category, in the ER positive category, in the PR positive category and in the triple positive category.

Table (4.1-A) Percentages of the characteristics of patients' files in the retrospective analysis

characteristic		%
Years of filing	2019-2021	
Total Number of files	1234	
Average Age of Diagnosis	52.76	
HER2 positive	265	21%
HER2 negative	797	65%
HER2 not available	172	14%
ER positive	850	69%
ER negative	233	19%

(4.1-B) Percentages of the characteristics of patients' files in the retrospective analysis

characteristic		%
ER not available	151	12%
PR positive	714	58%
PR negative	342	28%
PR not available	178	14%
Triple Positive	120	10%
Triple Negative	118	10%
HER2 positive HR negative	96	8%
HER2 negative HR positive	555	45%
Dead Patients	100	8%

4.2 Treatment Protocol used for Her2 positive Breast Cancer Patients:

Of the 265 patients with HER2-positive breast cancer registered in the Palestinian Cancer Registry, 220 (83%) were recorded as receiving a first-line treatment protocol. Of those 220 patients, 72 (32.7%) were recorded as receiving a second-line protocol, and 8 (3.6%) received a third-line protocol. Overall, 157 of the 220 patients (71%) were treated in accordance with NCCN guidelines, across all treatment lines.

Detailed as the following tables:

Table (4.2-A) First regimen treatment protocol

1st regimen treatment protocol number	No. of patients used this protocol
14	5
61	1
63	1
109	1
129	2
132	4
145	38
146	93
147	14
153	4
221	2

Table (4.2-B) First regimen treatment protocol

1st regimen treatment protocol number	No. of patients used this protocol
225	3
262	12
282	4
284	3
317	4
330	4
376	1
379	1
383	1
385	1
389	2
402	3
411	1
416	1
425	7
426	4
466	3

Table (4.3.-A) Second regimen treatment protocol

2nd regimen treatment protocol number	No. of patients used this protocol
330	10
195	1
216	1
262	7
317	6
201	16
281	7
284	2
409	1
225	4

Table (4.3 -B) Second regimen treatment protocol

2nd regimen treatment protocol number	No. of patients used this protocol
376	6
411	2
354	3
379	1
283	1
145	1
426	1
153	1
132	1

Table (4.4) Third regimen treatment protocol

3rd regimen treatment protocol number	No. of patients used this protocol
61	1
354	2
221	1
201	1
330	1
411	1
265	1

(Table 4.5-A) Treatment Protocol Key Table

14	5-Fluorouracil, Epirubicin 50-100 and Cyclophosphamide (FEC 50-100) Therapy (014)
61	Capecitabine 500- 825mg/m2 (061)
63	Carboplatin and Paclitaxel (063)
64	Carboplatin (AUC 4-6) Monotherapy- 21-28 day (064)
72	Doxorubicin, Cyclophosphamide Therapy-Triple Negative Breast Cancer Therapy (072)
85	Cetuximab Therapy (085)
109	Cyclophosphamide (IV) or Oral Methotrexate and 5-Fluorouracil (CMF) Therapy 21-28 day (109)
129	Docetaxel Monotherapy 50mg, 75mg,100mg/m2 14-21 day cycle (129)
132	Docetaxel, Carboplatin and Trastuzumab (TCH)-21 days (132)
134	Docetaxel/Cyclophosphamide (TC) Therapy-21 day (134)

(Table 4.5-B) Treatment Protocol Key Table

138	Gemcitabine (1000mg/m2) and Carboplatin (AUC 2-5) Therapy-21 day (183)
139	Doxorubicin (25mg/m2/day and Cisplatin (100mg/m2) Therapy-21 day cycle (139)
145	Doxorubicin and Cyclophosphamide (AC) Therapy 14- 21 day (145)
146	Doxorubicin, Cyclophosphamide (AC 60/600) day followed by PACLitaxel and Trastuzumab Therapy (AC-TH) oR (DD AC-TH) (146)
147	Doxorubicin, Cyclophosphamide followed by weekly PACLitaxel Therapy (AC-T) OR (DD AC-T
153	Epirubicin 75,90 + Cyclophosphamide (EC75, 90) Therapy (153)
166	Exemestane Monotherapy (166)
178	Fulvestrant Monotherapy (178)
184	Gemcitabine (1000mg-1250mg/m2) and Cisplatin (25mg- 80mg /m2)Therapy-21 - 28 day (184)
195	Gemcitabine 400- 1000mg/m2 Monotherapy- 7-56 day (195)
201	Goserelin 3.6mg Therapy -28 day (201)
216	Vinorelbine Therapy-Oral or intravenous 7-21 days (216)
221	Lapatinib and Capecitabine (221)
225	Letrozole
243	Nab-Paclitaxel (Abraxane?) Monotherapy ? 21 day cycle (243)
262	Paclitaxel (80) and Trastuzumab Therapy ? 7 day (12 weeks) (262)
265	Palbociclib Therapy-28 day (265)
281	Pertuzumab and Trastuzumab therapy (281)
282	Pertuzumab and Trastuzumab and DOCEtaxel?Therapy-21 day cycle (282)
283	Pertuzumab Trastuzumab and Vinorelbine (283)
284	Pertuzumab Trastuzumab and weekly PACLitaxelTherapy-21 day cycle (284)
297	Ribociclib Therapy-28 day (297)
317	Tamoxifen Monotherapy (317)
330	Trastuzumab (IV or subcutaneous) - 7-21 days (330)
354	Zoledronic Acid (354)
376	Goserelim, Tamoxifen (376)
379	Docetaxel, Adriamycin, Cyclophosphamide TAC (379)
383	Paclitaxel Therapy (383)
385	Cyclophosphamide, Doxorubicin, Fluouracil CAF (385)
389	Epirubicin and Cyclophosphamide, Paclitaxel (389)
402	Trastuzumab, Vinorelbine (402)
409	Goserelin, Exemestance (409)
411	Goserelin, letrozole (411)
416	Megestrol acetate 40mg tab (416)
425	5-Fluorouracil, Epirubicin, Cyclophosphamide – Docetaxel FEC-T protocol
426	Docetaxel, Trastuzumab (426)
430	Denosumab (Xgeva) (430)
446	Doxorubicin, Cyclophosphamide, Docetaxel, Trastuzumab (446)

Source: (The mentioned table was taken as it is from the Palestinian MoH Data Center)

4.3 The MDASI questionnaire results:

- A sample consisting of 105 forms was filled.

The following table shows the distribution of the study sample individuals according to:

1. **The type of disease variable**, shows that 67.7% for Hormonal Positive (HR +ve), 8.6% for HER2 Positive and 23.8 % for Triple Positive (HER2 positive and PR positive).
2. **The treatment variable**, shows that 19% for (AC), 16.2% for (AC-T), 5.7% for (AC-TH), 3.8% for (FEC), 2.9% for (ACTH/Goserelin, Letrozole), and the percentage ranged from 2-1% for the remaining answers.
3. **The age variable,** shows the rate of 31.4% for less than 50 years old, 33.3% from 50-59, and 35.2% for 60 years old and more.

Table (4.6-A) Distribution of study samples according to the study variables

Variables	Levels	N	%
Type of disease	Hormonal Positive	71	67.6
	HER2 +ve	9	8.6
	Triple +ve	25	23.8
Treatment Regimens	AC	20	19.0
	AC- Goserelin	1	1.0
	AC-T	17	16.2
	AC-T/Letrozole	1	1.0
	AC-TH	6	5.7
	AC/Tamoxifen	1	1.0
	AC + Letrozole	1	1.0
	ACTH/Goserelin	3	2.9
	ACTH/TCH	1	1.0
	Carboplatin + Paclitaxel	1	1.0
	CMF	1	1.0
	CMF/Tamoxifen	1	1.0
	Docetaxel Zoledronic Acid	2	1.9
	Docetaxel/Adriamycin/ Cyclophosphamide	1	1.0
	EC/ Paclitaxel + Trastuzumab	1	1.0
	ECP/ Gosereline + Letrozole	1	1.0
	ECP + Capcitabine	1	1.0
	FEC	4	3.8
	FEC/Trastuzumab	2	1.9
	Goserelin/ FEC-T	1	1.0
	Goserelin+Letrozole/ Paclitaxel+Trastuzumab	1	1.0
	Goserelin+Letrozole/ Zoledronic acid	1	1.0

Table (4.6-B) Distribution of study samples according to the study variables

Variables	Levels	N	%
	Gosereline/AC-T	1	1.0
	Gosereline+Letrozole	1	1.0
	Gosereline+Letrozole/ Zoledronic Acid	1	1.0
	Gosereline+Tamoxifen/ Trastuzumab	1	1.0
	Letrozole	3	2.9
	Letrozole/TC	1	1.0
	Letrozole/trastuzumab	1	1.0
	Letrozole/zoledronic Acid	1	1.0
	Paclitaxel/Trastuzumab	1	1.0
	Paclitaxel/Trastuzumab/Tamoxifen	1	1.0
	Paclitaxel/Zoledronic Acid	1	1.0
	Palbociclib + Letrozole	1	1.0
	Pertuzumab/ Trastuzumab/Paclitaxel	1	1.0
	Pertuzumab/ Trastuzumab/ Paclitaxel/ Zoledronic Acid	1	1.0
	Ribociclib/Docetaxel/ Gosereline+letrozole	1	1.0
	Ribociclib /Zoledronic acid	1	1.0
	TAC	2	1.9
	TAC+ Zoledronic Acid	1	1.0
	Tamoxifen	2	1.9
	Tamoxifen + ECP	1	1.0
	Tamoxifen + Letrozole	1	1.0
	TC	3	2.9
	TC + Letrozole	1	1.0
	TCH	2	1.9
	Trastuzumab	1	1.0
	unavailable	3	2.9
	Zoledronic Acid + Letrozole	1	1.0
Age	Less than 50 years old	33	31.4
	From 50-59	35	33.3
	Above 60 years old	37	35.2

4.4 Results related to the *first question:*

(What is the level of the severity of symptoms for cancer patients?)

To answer this question, we calculated the arithmetic averages and the standard deviations of the responses of the study sample individuals on the questionnaire fields that express the level of the severity of symptoms for cancer patients.

Table 4.7: Means and standard deviations for the level of the severity of symptoms for cancer patients

N	Sentences	Mean	SD	%
1	Pain	4.51	2.450	45.1
2	Fatigue (tiredness)	7.42	2.009	74.2
3	Nausea	7.85	1.910	78.5
4	Disturbed sleep	7.60	2.064	76.0
5	Being Distressed	6.25	2.187	62.5
6	Shortness of breath	3.62	2.864	36.2
7	Difficulty remembering	1.65	2.000	16.5
8	Lack of appetite	8.60	1.724	86.0
9	Feeling drowsy	6.64	2.189	66.4
10	Dry mouth	5.58	2.766	55.8
11	Feeling sad	4.37	2.185	43.7
12	Vomiting	7.28	1.894	72.8
13	Numbness or tingling	5.00	2.249	50.0
Average		5.874	1.3807	58.7

It is noted from table 7 that expresses the arithmetic averages and the standard deviations of the responses of the study sample individuals on the level of the severity of symptoms for cancer patients that the arithmetic mean for the total score was (5.874) and the standard deviation was (1.3807), this indicates that the level of the severity of symptoms for cancer patients came with 58.7%.

The results in table 7 indicate that the symptom (Loss of appetite) at the highest arithmetic average (8.60), followed by the symptom (Nausea) with an average of (7.85) and the symptom (Lack of remembering) at the lowest arithmetic average (1.65), followed by the symptom (Shortness of breath) with an average of (3.62).

Then we calculated the frequencies and percentages of the responses of the study sample individuals on the questionnaire fields that express the level of the Severity of symptoms for cancer patients.

Table (4.8) The level of the severity of symptoms for cancer patients

Levels	N	%
Low	26	24.8
Moderate	55	52.4
Severe	24	22.9

The previous table shows that 24.8% of patients have lower symptoms' severity, and 52.4% of them have moderate severity of the symptoms, and 22.9% of the patients' symptoms were severe.

4.5 Results related to the *second question:*

(What is the level of the symptom interference with life for cancer patients)?

To answer this question, we calculated the arithmetic averages and the standard deviations of the responses of the study sample individuals on the questionnaire fields that express the level of the symptom interference with life for cancer patients.

Table (4.9) Means and standard deviations for the level of the symptom interference with life for cancer patients

N	Fields	Mean	SD	%
1	Activity	6.52	1.618	65.2
2	Mood	6.21	1.989	62.1
3	Working (including housework)	5.06	1.936	50.6
4	Relationship with others	2.89	2.194	28.9
5	Walking	3.01	2.359	30.1
6	Enjoyment of life	6.02	2.210	60.2
Average		4.951	1.5643	49.5

It is noted from table 9 that expresses the arithmetic averages and the standard deviations of the responses of the study sample individuals on the level of the symptom interference with life for cancer patients that the arithmetic mean for the total score was (4.951) and standard deviation was (1.564) and this indicates that the level of the symptom interference with life for cancer patients came with 49.5%.

The results also indicate in Table 9 that the (Activity) was at the highest arithmetic average of interference (6.52), followed by the (Mood) with an average of (6.21). and then (Relationship with others) at the lowest arithmetic average (2.89), followed by the (Walking) with an average of (3.01).

4.6 Results related to the third question:

(Is there any difference in level of the Severity of symptoms for cancer patients according to the variable (type of disease)?

To answer this question, it was converted to the following hypotheses:

Results of the first hypothesis: "There are no statistically significant differences at the level of significance ($0.05 \geq \alpha$) in Level of the Severity of symptoms for cancer patients due to the type variable"

The first hypothesis was examined. The arithmetic averages were calculated for the response of the study sample individuals on Level of the Severity of symptoms for cancer patients due to the type of disease variable.

Table (4.10) Means and standard deviation for level of the Severity of symptoms for cancer patients due to the disease type variable

Type	N	Mean	SD
Hormonal Positive	71	5.8635	1.28659
HER2+ve	9	5.9487	1.59604
HER2+ve /PR+ve	2	6.5000	1.90375
Triple+ve	23	5.8227	1.61646

Based on data shown in table 10 a statistical analysis was done to evaluate if the level of the Severity of symptoms for cancer patients correlates with disease type variable. To know the significance of the differences, one way ANOVA was used as shown in the following table

Table (4.11) One way ANOVA test for Level of the Severity of symptoms for cancer patients Depending on the disease type variable

	Mean Square	d.f	Sum of Squares	Value of "F"	Sig
Between Groups	0.902	3	0.301	0.154	0.927
Within Groups	197.360	101	1.954		
Total	198.262	104			

It is noted that the value of P for the total score was (0.154) and the level of significance was (0.927) is greater than the level of significance ($\alpha \geq 0.05$), meaning that there are no statistically significant differences in Level of the Severity of symptoms for cancer patients due to the disease type variable, Thus the first hypothesis was accepted.

Results of the Second hypothesis: "There are no statistically significant differences at the level of significance ($0.05 \geq \alpha$) in Level of the Severity of symptoms for cancer patients due to the Age variable**"**

The Second hypothesis was examined. The arithmetic averages were calculated for the response of the study sample individuals on Level of the Severity of symptoms for cancer patients due to the Age variable.

Table (4.12) Means and standard deviation for level of the Severity of symptoms for cancer patients due to the Age variable

Age	N	Mean	SD
less than 50	33	5.8951	1.14368
from 50-59	35	5.7890	1.55056
60 and more	37	5.9356	1.43619

It is noted from the previous table that there are apparent differences in Level of the Severity of symptoms for cancer patients due to the Age variable, and to know the significance of the differences, one way ANOVA was used as shown in the next table:

Table (4.13) one way ANOVA test for Level of the Severity of symptoms for cancer patients Depending on the Age variable

	Mean Square	d.f	Sum of Squares	Value of "F"	Sig
Between Groups	0.408	2	0.204	0.105	0.900
Within Groups	197.854	102	1.940		
Total	198.262	104			

It is noted that the value of P for the total score (0.105) and the level of significance (0.900) is greater than the level of significance ($\alpha \geq 0.05$), meaning that there are no statistically significant differences in Level of the Severity of symptoms for cancer patients due to the Age variable, Thus the second hypothesis was accepted.

4.7 Results related to the fourth question:

(Are there any differences in level of the Symptom interference with life for cancer patients according to the variables (type of disease, Age))?

To answer this question, it was converted to the following hypotheses:

Results of the first hypothesis: "There are no statistically significant differences at the level of significance ($0.05 \geq \alpha$) in Level of the Symptom interference with life for cancer patients due to the type variable"

The first hypothesis was examined. The arithmetic averages were calculated for the response of the study sample individuals on Level of the Symptom interference with life for cancer patients due to the disease type variable.

Table (4.14) Means and standard deviation for level of the Symptom interference with life for cancer patients due to the type variable

Type	N	Mean	SD
Hormonal Positive	71	4.8897	1.53477
HER2+ve	9	5.5741	1.48864
HER2+ve /PR+ve	2	4.5833	1.29636
Triple+ve	23	4.9275	1.73411

It is noted from the previous table that there are apparent differences in Level of the Symptom interference with life for cancer patients due to the type variable, and to know the significance of the differences, one way ANOVA was used as shown in the following table:

Table (4.15) One way ANOVA test for Level of the Symptom interference with life for cancer patients Depending on the disease type variable

	Mean Square	d.f	Sum of Squares	Value of "F"	Sig
Between Groups	4.044	3	1.348	0.544	0.654
Within Groups	250.452	101	2.480		
Total	254.496	104			

It is noted that the value of P for the total score (0.544) and the level of significance (0.654) is greater than the level of significance ($\alpha \geq 0.05$), meaning that there are no statistically significant differences in Level of the Symptom interference with life for cancer patients due to the type variable, Thus the first hypothesis was accepted.

Results of the Second hypothesis:

"There are no statistically significant differences at the level of significance ($0.05 \geq \alpha$) in Level of the Symptom interference with life for cancer patients due to the Age variable"

The Second hypothesis was examined. The arithmetic averages were calculated for the response of the study sample individuals on Level of the Symptom interference with life for cancer patients due to the Age variable.

Table (4.16) means and standard deviation for level of the Symptom interference with life for cancer patients due to the Age variable

Age	N	Mean	SD
less than 50	33	4.7374	1.29437
from 50-59	35	5.0952	1.67707
60 and more	37	5.0045	1.69079

It is noted from the previous table that there are apparent differences in Level of the Symptom interference with life for cancer patients due to the Age variable, and to know the significance of the differences, one way ANOVA was used as shown in the following table:

Table (4.17) one way ANOVA test for Level of the Symptom interference with life for cancer patients Depending on the Age variable

	Mean Square	d.f	Sum of Squares	Value of "F"	Sig
Between Groups	2.340	2	1.170	0.473	0.624
Within Groups	252.156	102	2.472		
Total	254.496	104			

It is noted that the value of P for the total score (0.473) and the level of significance (0.624) is greater than the level of significance ($\alpha \geq 0.05$), meaning that there are no statistically significant differences in Level of the Symptom interference with life for cancer patients due to the Age variable, Thus the second hypothesis was accepted.

Chapter Five:

Discussion:

5.1 Discussion:

The study indicated that 69% of breast cancer patients were estrogen receptor-positive, 58% were progesterone receptor-positive, and 21% were human epidermal growth factor receptor 2-positive. These results align with another study in Palestine that is published in 2019 which indicated comparable receptor positive rates: 64.5% for ER, 58.4% for PR, and 19.7% for HER2. The strong correlation between the two studies indicates that the receptor status distribution among Palestinian women is similar to that of other groups, especially in the Middle East (Al-Ramahi et al., 2019).

The study revealed that 83% of HER2-positive breast cancer patients underwent a first-line therapy regimen, with 71% of these individuals receiving treatment aligned with the National Comprehensive Cancer Network (NCCN) guidelines since most HER2 positive patients were administered monoclonal antibodies and kinase inhibitors. This treatment method is substantiated by research that illustrates the effectiveness of such regimens in extending disease-free life and diminishing recurrence rates. The strong compliance with treatment criteria is praiseworthy and demonstrates the commitment of Palestinian healthcare providers to adhere to international standards in breast cancer therapy.

The remaining 17% of patients who did not receive guideline-concordant treatment may have had specific health problems or performance statuses that prevented routine therapy. This underscores the significance of individualized treatment strategies, especially in resource-constrained environments where patients may exhibit advanced disease or concomitant conditions.

In comparison to studies from neighboring countries, receptor positivity rates in Palestine are analogous to those documented in Jordan (68% ER-positive, 90.9% PR-positive, and 13.6% HER2-positive)(Sughayer et al., 2006) and Saudi Arabia (18.7% HER2-positive) (Alnegheimish et al., 2016). Conversely, the HER2 positivity rate in Iraq (29.4%) exceeds

that reported in Palestine (21%). These discrepancies may stem from variations in genetic, environmental, and lifestyle factors among populations, as well as differences in diagnostic and screening methodologies. The results also correspond with global data, particularly from the United States, where HER2 positivity rates range from 15% to 20%. This indicates that while regional variations in breast cancer subtypes exist, the overall distribution of hormone receptors remains relatively uniform across diverse populations.

Results from MDASI indicate that the symptom (Loss of appetite) has the highest reported symptom 86%, followed by Nausea with an average of 78.5% and the symptom (Lack of remembering) at the lowest 16.5%, followed by the symptom Shortness of breath with an average of 36.2%. Most of the patients 52.4% reported the symptoms are moderate. When evaluating symptom interference with life for cancer patients the (Activity) had the highest interference 65.2, followed by (Mood) with an average of 62.1%. and then (Relationship with others) at lowest value of 28.9%, followed by the (Walking) with an average of 30.1%.

These findings align with prior research that has recognized fatigue, nausea, and anorexia as prevalent and debilitating symptoms in breast cancer patients receiving treatment . The significant incidence of these symptoms highlights the necessity for appropriate management options to enhance patients' quality of life.

The significant intensity of these symptoms highlights the necessity for thorough symptom management measures, encompassing nutritional support, antiemetic drugs, and interventions to mitigate fatigue, such as exercise programs or pharmaceutical treatments.

Notably, the difficulty in remembering had the lowest mean score (1.65), indicating that cognitive impairment may not pose a considerable concern for the majority of patients in this study. This finding must be interpreted cautiously, as cognitive symptoms may be underreported or neglected in therapeutic environments.

The study revealed that cancer symptoms substantially disrupted patients' daily activities, especially general activity (mean score: 6.52) and mood (mean score: 6.21). These findings align with prior studies indicating that breast cancer symptoms significantly affect patients' capacity to execute everyday activities and sustain mental health. The disruption of interpersonal ties was very minimal (mean score: 2.89), potentially indicative of the robust social support networks within Palestinian culture.

This suggests that while breast cancer symptoms significantly impair patients' ability to perform daily tasks and maintain emotional well-being, they may have a lesser impact on social interactions. This could be attributed to the strong social support networks within Palestinian culture, which may help mitigate the impact of cancer on interpersonal relationships.

A majority of patients (52.4%) indicated moderate symptom severity, consistent with other research that has recognized moderate symptom load as a prevalent experience among cancer patients.

The moderate severity of symptoms noted in this study may be ascribed to the adverse effects of cancer therapies, including chemotherapy and radiation, which are recognized to induce fatigue, nausea, and pain. Moreover, the psychological strain associated with a

cancer diagnosis and its treatment might intensify physical symptoms, resulting in a moderate degree of total symptom intensity.

The research revealed no statistically significant variations in symptom severity or interference related to the type of breast cancer (hormone receptor-positive, HER2-positive, or triple-positive) or age. This indicates that the symptom load is rather uniform across various breast cancer subtypes and age demographics. It is crucial to acknowledge that the sample size for some subgroups (e.g., HER2-positive patients) was comparatively small, potentially constraining the capacity to identify meaningful changes.

The MDASI outcomes from this study correspond with findings from other areas, particularly the Middle East and North Africa (MENA) region. A study in Saudi Arabia utilizing the EORTC QLQ-C30 and BR-23 questionnaires identified fatigue and sleeplessness as the most disturbing symptoms for breast cancer patients, paralleling the findings of our study. A study conducted in Morocco confirmed the reliability of the Arabic version of the MDASI as an effective instrument for evaluating cancer-related symptoms in Arabic-speaking populations(Nejmi et al., 2010). The observed commonalities indicate that the symptom burden faced by breast cancer patients in Palestine aligns with that of patients in other Arab nations, underscoring the necessity for region-specific symptom management approaches.

5.2 Implications for Clinical Practice and Policy:

This study's findings hold significant implications for clinical treatment and policy in Palestine.

The significant prevalence of HER2-positive breast cancer (21%) underscores the necessity for improved access to targeted medicines.. The study revealed that 71% of HER2-positive patients received treatment in accordance with guidelines; nonetheless, initiatives must be implemented to guarantee that all eligible patients may get these life-saving medications.

The significant intensity of symptoms, including fatigue, nausea, and anorexia, highlights the necessity for comprehensive symptom treatment strategies. Healthcare practitioners must prioritize the establishment of supportive care services, encompassing nutritional assistance, psychological counseling, and palliative care, to alleviate the physical and emotional burdens associated with breast cancer.

The research underscores the need of public awareness initiatives and early detection programs to enhance breast cancer outcomes in Palestine. Timely diagnosis and intervention can markedly enhance survival rates and alleviate the impact of advanced disease.

5.3 Limitations:

This study offers significant insights into breast cancer in Palestine, although it possesses multiple limitations:

The retrospective design of the study constrains the capacity to determine causal correlations among variables. Future research should use a prospective strategy to enhance comprehension of the effects of treatment and symptom management on patient outcomes.

The study encompassed a substantial sample size (1234 individuals); nevertheless, some subgroups (e.g., HER2-positive patients) were inadequately represented. This may have constrained the capacity to identify substantial variations in symptom severity and interference.

The study depended on medical records, which may have been inadequate or inconsistent. Subsequent research should focus on gathering more extensive data, encompassing patient comorbidities, treatment compliance, and long-term outcomes.

Chapter Six:

Conclusion:

This study elucidates the incidence of hormone receptors, treatment regimen in Her2 positive breast cancer patients and symptomatology among breast cancer patients in Palestine. The results underscore the necessity for enhanced access to targeted medicines, thorough symptom management, and public awareness initiatives to alleviate the impact of breast cancer in the area. Subsequent research ought to concentrate on mitigating the limitations of this study and investigating the influence of genetic and environmental factors on breast cancer outcomes in Palestine.

By actively participating in the oncology team, our pharmacists can significantly contribute to successful cancer treatment. Their expertise allows them to directly influence patient satisfaction by implementing key strategies. This includes educating patients to improve their understanding of medication side effects, how to mitigate them, and what to do if they occur. Pharmacists can also foster treatment adherence by clearly explaining its importance. Moreover, their involvement in formulating cancer treatment policies would be a valuable asset

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Appendices:
Appendix 1: Questionnaire:

التاريخ: _____ المؤسسة: _____

الحروف الأولى من اسم المشارك: _____ رقم ملف المريض بالمستشفى: _____

رقم المشارك: _____

البنود الرئيسية لقائمة أعراض مركز إم دي أندرسون (MDASI)

الجزء الأول – ما مدى شدة أعراضك؟

كثيراً ما تحدث لدى المصابين بالسرطان أعراض سببها المرض أو العلاج. نودُّ منك أن تُقدِّر شدّة الأعراض التالية **خلال الأربع والعشرين ساعة الماضية**. من فضلك، اختر رقم من سفر (يشير إلى عدم وجود العرض المذكور) إلى 10 (يشير إلى وجود العرض في أسوأ ما يمكن أن تتصور من الشدّة) لكلّ عرض من الأعراض المذكورة.

	غير موجود 0	1	2	3	4	5	6	7	8	9	أسوأ ما تتصور 10
1. **الألم** في أسوأ حالاته؟	○	○	○	○	○	○	○	○	○	○	○
2. **الإرهاق (التعب)** في أسوأ حالاته؟	○	○	○	○	○	○	○	○	○	○	○
3. **الغثيان** في أسوأ حالاته؟	○	○	○	○	○	○	○	○	○	○	○
4. **اضطراب النوم** في أسوأ حالاته؟	○	○	○	○	○	○	○	○	○	○	○
5. إحساسك **بأنك مُستاء (متزعج)** في أسوأ الحالات؟	○	○	○	○	○	○	○	○	○	○	○
6. **ضيق التنفس** في أسوأ حالاته؟	○	○	○	○	○	○	○	○	○	○	○
7. صعوبة **تذكر الأشياء** في أسوأ حالاتها؟	○	○	○	○	○	○	○	○	○	○	○
8. **فقدان الشهية** في أسوأ حالاتها؟	○	○	○	○	○	○	○	○	○	○	○
9. شعورك **بالدوخة (التعاس)** في أسوأ حالاتها؟	○	○	○	○	○	○	○	○	○	○	○
10. **جفاف الفم** في أسوأ حالاته؟	○	○	○	○	○	○	○	○	○	○	○

التاريخ: _____ المؤسسة: _____

الحروف الأولى من اسم المشارك: _____ رقم ملف المريض بالمستشفى: _____

رقم المشارك: _____

	غير موجود 0	1	2	3	4	5	6	7	8	9	أسوأ ما تتصور 10
11. الشعور **بالحزن** في **أسوأ** حالاته؟	○	○	○	○	○	○	○	○	○	○	○
12. **القيء** في **أسوأ** حالاته؟	○	○	○	○	○	○	○	○	○	○	○
13. **التململ أو النخز (الوخز)** في **أسوأ** حالاته؟	○	○	○	○	○	○	○	○	○	○	○

الجزء الثاني: كيف تداخلت أعراضك مع مُجريات حياتك؟

كثيراً ما تؤثّرُ الأعراض على مشاعرنا وأداءنا لنشاطاتنا. إلى أيّ مدى تداخلت أعراضك مع الأشياء التالية ***خلال الأربع والعشرين ساعة الماضية؟*** اختر رقم من صفر (يشير إلى عدم وجود العرض المذكور) إلى 10 (يشير إلى وجود العرض في أسوأ ما يمكن أن تتصور من الشدّة) لكلّ عرض من الأعراض المذكورة.

	لا تداخل 0	1	2	3	4	5	6	7	8	9	تداخل كامل 10
14. **النشاط العامة؟**	○	○	○	○	○	○	○	○	○	○	○
15. **المزاج؟**	○	○	○	○	○	○	○	○	○	○	○
16. **العمل (بما في ذلك الأعمال المنزلية)؟**	○	○	○	○	○	○	○	○	○	○	○
17. **العلاقة مع الأشخاص الآخرين؟**	○	○	○	○	○	○	○	○	○	○	○
18. **المشي؟**	○	○	○	○	○	○	○	○	○	○	○
19. **التمتع بالحياة**	○	○	○	○	○	○	○	○	○	○	○

Appendix 2 :

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SYMPTOM ASSESSMENT TOOL LICENSE AGREEMENT

This Symptom Assessment Tool License Agreement (the "Agreement," including both Part I License Information and Part II Terms & Conditions) is entered into as of the Effective Date by and between The University of Texas M. D. Anderson Cancer Center ("MD Anderson") and the Licensee identified below. MD Anderson and Licensee may each hereinafter be individually referred to as a "Party" and collectively as the "Parties."

Under certain license agreements with Symptom Assessment Systems, LLC, MD Anderson has obtained the exclusive right to grant a license to use, reproduce, and/or distribute copies of, the Symptom Assessment Tool. Licensee desires to obtain the right to use, reproduce, and/or distribute copies of, the Symptom Assessment Tool for the Permitted Use described herein.

NOW, THEREFORE, in consideration of the promises, conditions, covenants and warranties herein contained, the Parties agree as follows:

PART I LICENSE INFORMATION

1.	**Licensee**	Name:	Al Quds University
		ATTN:	Aseel Erekat
		Address Line 1:	AbuDess University Street
		Address Line 2:	Jerusalem, 0000 00972
		Address Line 3:	Jerusalem
		Address Line 4:	N/A
		Email Address:	aerekat6@gmail.com
2.	**Permitted Use**	Student research -) MDASI ONLY in the chapter which is the qualitative part of my research.	
3.	**Symptom Assessment Tool**	MDASI-CORE ARABIC	
4.	**License Fee:**	$ 200.00	

IN WITNESS WHEREOF, the parties hereto have caused their duly authorized representatives to execute this Agreement.

Licensee *(see Item 1, above)*		**The University of Texas M.D. Anderson Cancer Center**	
Signed:	(signature of representative)	Signed:	(signature of representative)
Name: Aseel Erekat	(printed name of representative)	Name: Andrew Dennis	(printed name of representative)
Title: MRS.	(position within Licensee organization)	Title: Managing Director	(position within MD Anderson)
Date: 8. Feb. 2023	(date signed by representative)	Date: 2/16/2023 | 4:21 PM CST	(date signed by representative)

Part II Terms & Conditions are available at the following URL:
https://www.mdanderson.org/content/dam/mdanderson/documents/about-md-anderson/about-us/Office-of-Technology-Commercialization/Terms-Conditions-BPI.MDASI.v11.NMD951.pdf

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Appendix 3: Approval Letter

State of Palestine
Ministry of Health
Education in Health and Scientific Research Unit

دولة فلسطين
وزارة الصحة
وحدة التعليم الصحي والبحث العلمي

Ref.: .....
Date:.....

الرقم: ٢٠٢٢/٤٣/١٦٤
التاريخ: ٢٠٢٢/١١/٢٥

الأخ مدير عام الادارة العامة للمستشفيات المحترم ،،،
عطوفة الوكيل المساعد المدير التنفيذي لمجمع فلسطين الطبي المحترم،،،
تحية واحترام،،

الموضـــوع: تسهيل مهمة بحث

مرفق طلب تسهيل مهمة الطالبة: أسيل هشام عريقات– ماجستير العلوم الصيدلانية/ جامعة القدس، وباشراف د. حسين الحلاق، في عمل بحث علمي بعنوان:

"A Retrospective analysis for :HER2 receptor prevalence AND HER2 positive Breast Cancer Treatment Regimens at Palestinian MOH Hospitals"

من خلال السماح للطالبة بجمع معلومات ملفات المرضى في قسم الاورام (بعد موافقة رئيس القسم) ودون التعرض للمعلومات الشخصية للمرضى، وذلك في:

- مستشفى الوطني– – مستشف بيت جالا – مجمع فلسطين الطبي

على ان يتم الالتزام باساليب واخلاقيات البحث العلمي.
على ان يتم الالتزام بجميع تعليمات واجراءات الوقاية والسلامة الصادرة عن وزارة الصحة بخصوص جائحة كورونا، وتحت طائلة المسؤولية. وابراز شهادة التطعيم قبل دخول مرافق وزارة الصحة.
على ان يتم تزويد الوزارة بنسخة PDF من نتائج البحث، التعهد بعدم النشر لحين الحصول على موافقة الوزارة على نتائج البحث.

مع الاحترام،،

State of Palestine Ministry Of Health مدير التعليم الصحي والبحث العلمي Health Education and Scientific Research Unit

نسخة: مشرف الدراسة المحترم/ جامعة القدس

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State of Palestine
Ministry of Health
Education in Health and Scientific
Research Unit

دولة فلسطين
وزارة الصحة
وحدة التعليم الصحي
والبحث العلمي

Ref: .....
Date:.....

الرقـــم: .....
التـاريخ: .....

الأخ علي الحلو المحترم ،،،
مدير عام الادارة العامة لتكنولوجيا المعلومات،،،
تحية واحترام،،

S-HESRU / Sent:23/02/2022 / 102

الموضـــوع: تسهيل مهمة بحث

مرفق طلب تسهيل مهمة **الطالبة: أسيل هشام عريقات– ماجستير العلوم الصيدلانية/ جامعة القدس**، وباشراف د. حسين الحلاق، في عمل بحث علمي بعنوان:

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- **مستشفى الوطني- - مستشف بيت جالا – مجمع فلسطين الطبي**

على ان يتم الالتزام باساليب واخلاقيات البحث العلمي.
على ان يتم الالتزام بجميع تعليمات واجراءات الوقاية والسلامة الصادرة عن وزارة الصحة بخصوص جائحة كورونا، وتحت طائلة المسؤولية. وابراز شهادة التطعيم قبل دخول مرافق وزارة الصحة.
على ان يتم تزويد الوزارة بنسخة PDF من نتائج البحث، التعهد بعدم النشر لحين الحصول على موافقة الوزارة على نتائج البحث.

مع الاحترام،،

دولة فلسطين
وزارة الصحة
وحدة التعليم الصحي والبحث العلمي
صادر رقم HESRU/823
التاريخ 23.02.2022

دولة فلسطين وزارة الصحة
د. عبد [illegible]
مدير التعليم الصحي والبحث العلمي

نسخة: مشرف الدراسة المحترم/ جامعة القدس

P.O .Box: 14
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Appendix 4: Ethical Approval:

Al-Quds University – Research Ethics Committee

RESEARCH ETHICS CHECKLIST

Instructions for applicants:

This checklist should be completed for every research project which involves human participants and including personal, medical or otherwise sensitive data or methodologically controversial approaches. ***This checklist must be completed before potential participants are approached to take part in any research.*** The research ethics review process is not designed to assess the merits of the research project in question, but is merely a tool to ensure that ethical considerations have been fully considered and ethical issues have been properly dealt with when arise.

Before completing this form, please read the Code of Good Practice in Research of Al-Quds University and the Ethical principles for medical research involving Human subjects (the most recent version of the Helsinki Declaration). The principal investigator and, where the principal investigator is a student, the **supervisor**, are responsible for exercising appropriate professional judgment in this review.

Complete all sections of this checklist as accurate as possible. After completing sections I to IV, check the following: If all items in the Declaration in section III are ticked AND if you have answered NO to all questions in section IV (questions 1-14), send the completed & signed copy of this form to the Head of your faculty/center/institute and a copy to the REC office for information. You may proceed with the research project but you should follow any subsequent guidance or requests from the faculty/centre/institute or your supervisor where appropriate. Undergraduate and postgraduate students should retain a copy of this form and submit it with their research report or thesis (bound in the appendix). Also graduate students should submit a copy of this form to the Deanship of Graduate Studies (DGS) when seeking registration for thesis' defense (Forms 5 & 6 of DGS). **Work which is submitted without the fully completed copy of this form will be returned unassessed or cannot complete the defense of their thesis.**

If ANY of the items in the Declaration in section III are not ticked AND / OR if you have answered YES to ANY of the questions (1-13) in Section IV, you will need to describe more fully in Section V of this form below how you plan to deal with the ethical issues raised by your research. This does not mean that you cannot do the research project, only that your proposal will need to be approved by the faculty/centre/institute or REC. After completing section V as described in the above paragraph, submit a copy of this form with properly filled section V to the faculty/centre/institute and REC office along with the Application form.

If you answered YES to ***question 14***, you will also have to submit an application to the appropriate external health authority ethics committee, after you have received approval from the faculty/centre/institute or REC office.

Section I: Applicant details

1. Name of principal investigator (applicant): 1a. Associated investigators:	Aseel Erekat
2. Status (please click to select):	Staff, *GRADUATE STUDENT*, undergraduate student
3. Email address:	aerekat6@gmail.com
4a. Contact address:	Jerusalem/ AbuDees/ Al Quds University Street
4b. Telephone number:	00972 569944386

Section II: Project details

5. Project title:	**A Retrospective analysis for** **HER2 receptor prevalence AND HER2 positive Breast Cancer Treatment Regimens at Palestinian MOH Hospitals**

Section III: For Students only:

6.	Course title and module name and number where appropriate faculty/centre/institute:	Three Governmental Hospitals at Ramallah / Nablus / Bethlehem – Retrospective Analysis
7.	**Supervisor's** or module leader's name:	Dr. Hussein Hallak
8.	Email address:	husseinhallak@hotmail.com
9.	Telephone extension::	00972 548886310

Declaration by researcher (please tick the appropriate boxes)

✓	I have read the Code of Good Practice in Research of Al-Quds University
✓	The topic merits further research
✓	I have the skills to carry out the research
✓	The participant information sheet, if needed, is appropriate
✓	The procedures for recruitment and obtaining informed consent, if needed, are appropriate
✓	The research is exempt from further ethics review according to current University guidelines

Comments from researcher, and/or from postgraduate student:

Section IV: Research

Please answer each question by ticking the appropriate box:

		YES	**NO**
1.	Will the study involve participants who are particularly vulnerable or who may be unable to give informed consent (e.g. children, people with learning disabilities, emotional difficulties, problems with understanding		✓

	and/or communication, your own students)?		
2.	Will the study require the co-operation of a gatekeeper for initial access to the groups or individuals to be recruited (e.g. students at school, members of self-help group, and residents of nursing home)?		✓
3.	Will deception be necessary, i.e. will participants take part without knowing the true purpose of the study or without their knowledge/consent at the time (e.g. covert observation of people in non-public places)?		✓
4.	Will the study involve discussion of topics which the participants may find sensitive (e.g. sexual activity, own drug use)?		✓
5.	Will drugs, placebos or other substances (e.g. food substances, alcohol, nicotine and vitamins) be administered or ingested by participants or will the study involve invasive, intrusive or potentially harmful procedures of any kind?		✓
6.	Will blood or tissue samples be obtained from participants?		✓
7.	Will pain or more than mild discomfort be likely to result from the study?		✓
8.	Could the study induce psychological stress or anxiety or cause harm or negative consequences beyond the risks encountered in normal life?		✓
9.	Will the study involve prolonged or repetitive testing?		✓
10.	Will financial inducements (other than reasonable expenses and compensation for time) be offered to participants?		✓
11.	Will participants' right to withdraw from the study at any time be withheld?		✓
12.	Will participants' anonymity be compromised or their right to anonymity be withheld or information they give be identifiable as theirs?		✓
13.	Might permission for the study need to be sought from the researcher's or from participants' employer?		✓
14.	Will the study involve recruitment of patients or staff through the National Health Information System, (NHIS)?		✓

Section V: Addressing ethical problems

If you have answered YES to any of questions 1-13 please complete below and submit this form to your faculty/centre/institute or REC.

Project title

Principal investigator/student

Supervisor (if principal investigator)

Summary of issues and action to be taken to address the ethics problem(s)

Please note that it is your responsibility to follow the Code of Good Practice in Research of Al-Quds University and any relevant academic or professional guidelines in the conduct of your research project. **This includes providing appropriate information sheets and consent forms, and ensuring confidentiality in the storage and use of data.** Any significant change to the design or conduct of the research should be notified to the faculty/centre/institute or REC office and may require a new application for ethics approval.

Signed: _____ Principal Investigator

Approved: _____ Supervisor or module leader (where appropriate)

Date: _____

For use by faculty/centre/institute or REC office:

- No ethical problems are raised by this proposed research - **Retain this form on record**

- Appropriate action was taken to maintain ethical standards

- The research protocol should be revised to eliminate the ethical concerns or reduce them to an acceptable level, using the attached suggestions.

- Please submit faculty/centre/institute application for Ethics Approval

- Please submit REC Application for Ethics Approval

Signed: Aseel Erekat Abed

Date: 8 January 2022

Retain this form on record and return a copy of section V to Researcher

Al-Quds University
Jerusalem
Deanship of Scientific Research

بسم الله الرحمن الرحيم

جامعة القدس
القدس
عمادة البحث العلمي

Research Ethics Committee
Committee's Decision Letter

Date: February 9, 2022
Ref No: 218/REC/2022

Dears Dr. Hussein Hallak, MS. Aseel Erekat,

Thank you for submitting your application for research ethics approval. After reviewing your application entitled "A Retrospective analysis for HER2 receptor prevalence AND HER2 positive Breast Cancer Treatment Regimens at Palestinian MOH Hospitals", the Research Ethics Committee confirms that your application is in accordance with the research ethics guidelines at Al-Quds University.

We would appreciate receiving a copy of your final research report/ publication.

Thank you again and wish you a productive research that serves the best interests of your subjects.

PS: This letter will be valid for two years.

Sincerely,

Suheir Ereqat, PhD
Associate Professor of Molecular Biology

Suhair Ereqat

Research Ethics Committee Chair

Cc. Prof. Imad Abu Kishek - President
Cc. Members of the committee
Cc. file

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تحليل استعادي لانتشار مستقبلات سرطان الثدي وأنظمة علاج سرطان الثدي الإيجابي لـــ HER2 في مستشفيات وزارة الصحة الفلسطينية ودراسة تأثير أعراض السرطان والعلاج على أنشطة الحياة اليومية لمرضى سرطان الثدي باستخدام النسخة العربية من مخزون أعراض مؤسسة أندرسون للسرطان.(MDASI-A)

اعداد الطالبة: أسيل هشام صلاح عريقات

المشرف الدكتور: حسين الحلاق

الملخص

الاهداف: سرطان الثدي هو الأكثر شيوعًا بين النساء في جميع أنحاء العالم، بما في ذلك فلسطين، حيث يشكل تحديًا كبيرًا للصحة العامة. تعد تحديد مستقبلات الهرمونات، بما في ذلك مستقبلات الإستروجين (ER)، ومستقبلات البروجسترون(PR) ، ومستقبلات عامل نمو البشرة البشري 2(HER2) ، أمرًا حاسمًا لتفصيل خطط العلاج وتحسين نتائج المرضى. هدفت هذه الدراسة إلى تحليل انتشار أنواع مستقبلات سرطان الثدي، وتقييم أنظمة العلاج لمرضى سرطان الثدي الإيجابيين لـــ HER2 في مستشفيات وزارة الصحة الفلسطينية، وتقييم تأثير أعراض السرطان والعلاجات على الأنشطة اليومية للمرضى باستخدام النسخة العربية من مخزون أعراض أندرسون.(MDASI-A)

المنهجية: أُجريت دراسة استعادية باستخدام سجلات طبية لمرضى سرطان الثدي الذين تم علاجهم في مستشفيات وزارة الصحة بين عامي 2019 و2021. شملت الدراسة البيانات الديموغرافية، وحالة المستقبلاتER) ، PR، (HER2، وأنظمة العلاج، ونتائج البقاء على قيد الحياة. بالإضافة إلى ذلك، تم إعطاء MDASI-A لتقييم شدة وتداخل الأعراض المتعلقة بالسرطان في الحياة اليومية. تم تحليل البيانات باستخدام الإصدار 22 منSPSS ، باستخدام الإحصائيات الوصفية والاختبارات الاستدلالية لفحص العلاقات بين المتغيرات.

النتائج: تم تحليل ما مجموعه 1234 حالة من سرطان الثدي، بمتوسط عمر عند التشخيص 52.76 سنة. كانت الأغلبية (69٪) إيجابية لـــER ، و58٪ إيجابية لـــPR ، و21٪ إيجابية لـــ .HER2 شكلت الحالات السلبية الثلاثية والإيجابية الثلاثية 10٪ لكل منهما. بين المرضى الإيجابيين لـــ(n=265) HER2 ، تلقى 83٪ علاجًا أوليًا، بينما التزم 71٪ ببروتوكولات NCCN الموصى بها. كشفت نتائج MDASI-A أن الأعراض الأكثر إزعاجًا كانت الإرهاق والألم والغثيان، مما أثر بشكل كبير على الوظائف اليومية، خاصة العمل والنشاط العام.

النتائج: تؤكد النتائج على الحاجة إلى تحسينات مستمرة في إدارة سرطان الثدي في فلسطين، خاصة في الالتزام بالمبادئ التوجيهية العلاجية الدولية وإدارة الأعراض. تبرز الدراسة أيضًا فائدة MDASI-A في تحديد عبء الأعراض وتوجيه استراتيجيات الرعاية الداعمة. ينبغي أن تركز الأبحاث المستقبلية على الدراسات الاستشرافية لتقييم نتائج العلاج بمرور الوقت.