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Elias Kipchumba Melly, Dr. Samson Ndege & Dr. Robert Too

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Assessment of Histopathology Patterns of Breast Cancer Managed at Alexandria Cancer Center and Palliative Care Hospital, Eldoret, Uasin Gishu County, Kenya

[*1]Elias Kipchumba Melly, [2]Dr. Samson Ndege & [3]Dr. Robert Too

[1]Student, School of Public Health, Moi University

[2,3]Lecturer, School of Public Health, Moi University

***Email of The Corresponding Author: elimelly11@gmail.com**

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Abstract

Globally approximately 2.3 million cases of breast cancer were reported in 2022. These cases were distributed among different histopathological sub-types. In sub-Saharan Africa 186,598 cancer cases were diagnosed in 2022 and 85,787 deaths occurred annually. In Kenya of the 5985 new cases reported breast cancer contributed 12.5% of all cancer cases. Detailed data on patient characteristics, survival rates, and factors influencing mortality among breast cancer patients at the Alexandria Cancer Center and Palliative Care Hospital (ACCPH) is lacking, hindering effective management and treatment strategies. To determine the characteristics of patients with breast cancer, proportion of different histopathological sub-types of breast cancer and survival. The study was conducted at ACCPH using a cross-sectional study design. Census of all patients who met the inclusion criteria and managed between 2016 and 2019 at ACCPH were included. Data was collected from records using a data abstraction tool. Mean and standard deviation were employed to summarize continuous variables while proportions and frequencies were used for categorical variables. Kaplan-Meier (K-M) survival estimates procedure was used to analyze the 2-year survival time. Cox regression model was fitted to assess predictors of survival time, significance evaluated at p-value <0.05. Fifty-four cases were studied, 52 females and 2 males. Females contributed the highest number and 40 to 49 years (33.3% of the total) was the peak age. Invasive ductal carcinoma accounted for 88.7%, 2-year survival rate was 64.8%. Metastases at diagnosis and disease progression were factors associated with risk of death with a p-value < 0.001. Gender, age and metastasis were also significantly associated with survival time. The most affected age group was 40 to 49 years, invasive ductal carcinoma was the commonest histological sub-type, a significant number of cases presented with metastasis an indicator of late presentation. Majority of the cases were alive 2 years post diagnosis. Those who had metastasis had a higher likelihood of dying. Breast cancer screening among the females above 40 years old. Reduction of risk of metastasis by creating awareness for early diagnosis to further improve the 2-year survival rate.

Keywords: *Histopathology, Breast Cancer, Alexandria Cancer Center, Palliative Care Hospital, Eldoret*

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1.0 Background of The Study

Globally there were 20 million new cases of cancer and 9.7 million deaths from the disease in 2022. The bulk of these instances occurred in countries with low and moderate incomes (Globocan, 2022). A key cause for concern on a global scale is the increasing cancer burden. Cancer is a disease that is characterized by the proliferation of abnormal cells in the affected area of the body, the ability to grow beyond their usual boundaries, and the tendency to invade the surrounding tissues and spread to secondary organs or tissues as metastases (WHO, 2012). Cancer is a disease that occurs when abnormal cells grow in an uncoordinated manner without regard to the normal rules of cell division (Hejmadi, 2013). Within the context of this growth and development continuum, cancer can be prevented or diagnosed at an earlier stage provided the appropriate procedures are followed. Cancer is typically caused by the transformation of normal cells, which occurs over the course of a multistage process. The incidence and mortality rates of cancer continue to rise. Over the next two decades, it was anticipated that the number of newly diagnosed cases of cancer would increase by approximately 70 percent, and the global economic expenditures associated with cancer prevention and treatment were estimated to reach over 1.16 trillion dollars in 2010 (WHO, 2017).

According to Siu (2016), breast cancer is a disease that poses a significant risk to the lives of both men and women. According to Laishram and Singh (2015), it is a disease that is believed to be complicated and heterogeneous in terms of histology, cellular origin, mutations, metastatic potential, progression, therapeutic response, and clinical outcome. It accounts for sixteen percent of all cancers (Taheri et al., 2019) and one-quarter of all female cancers worldwide (Bray et al., 2018); (Makki, 2015). It is the most common form of cancer, with 2.2 million cases, and it is a substantial cause of cancer fatalities, with 626,679 deaths in females worldwide (Bray et al., 2018). In industrialized countries, the incidence of breast cancer is significantly higher than in developing countries; yet, according to Ahmedin Jemal (2011), around sixty percent of breast cancer deaths and fifty percent of new cases of occur in developing countries. According to Jemal, Centre, DeSantis, and Ward (2010), the greater rates in developing nations are a result of disparities in reproductive and hormonal factors, as well as the availability of early diagnosis services in industrialized countries.

As of the year 2020, the World Health Organization (WHO) reported that cancer was the greatest cause of illness and mortality across the globe. According to the report, around 18.1 million new instances of cancer were reported as having occurred over the world in 2018. According to the World Health Organization's (WHO) estimation models of the evolution of cancer, the number of deaths caused by cancer is expected to increase by forty-five percent by the year 2030. It was estimated in the paper that the increase in the burden of the disease could be five times bigger in nations with intermediate to low income in comparison to those with developed income countries. The projection also indicated that the economic burden of the disease would increase, with the cost of cancer prevention and treatment estimated to be $1.6 trillion as of 2018. This would pose a threat to the budgets of individuals with varying levels of income, and it would cause individuals who have developed cancers and their families to experience unimaginable suffering and financial distress (WHO, 2020).

Cancer accounts for 7% of overall mortality in Kenya, with 42,116 new cases and 27,092 deaths in 2020 (GLOBOCAN, 2020). In Kenya, infectious and cardiovascular diseases are the primary causes of death, but cancer is the third highest. The majority of cancers are identified at advanced stage, which is a time when the prognosis is not favourable and there are few therapeutic choices

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available that can cure the disease. In contrast to many developing countries, where the number of newly diagnosed cases of breast cancer has rapidly increased over the past few decades, the number of new cases of breast cancer has slowed down in developed countries (Nematolahi & Ayatollahi, 2017). This is probably due to the rise in life expectancy, the expansion of urban areas, and the acceptance of the western way of lifestyle (Tazhibi & Feizi, 2014). More than two hundred and fifty thousand new cases of breast cancer were reported in the United States of America (USA) in the year 2017. It is estimated that twelve percent of all women in the United States will be diagnosed with it at some point in their lives (Waks & Winer, 2019).

When compared to other types of cancer, breast cancer has the greatest incidence rate, with over 2.2 million cases being reported worldwide in the year 2020. On the other hand, it is extremely uncommon in males, accounting for fewer than one percent of all occurrences of breast cancer. In high income countries, breast cancer is common among postmenopausal women compared to those from LMICs where it is common in postmenopausal. Countries with low and moderate incomes are the ones that experience the majority of breast cancer incidences and fatalities. According to the American Cancer Society (2018), breast cancer is one of the most common cancers that affect women and is responsible for the majority of cancer fatalities that occur among women of all races when compared to other malignancies. Furthermore, according to the American Cancer Society, each year in the United States, there are approximately 200,000 women who are diagnosed with breast cancer, and at least 40,000 women pass away as a result of the same condition. In LMICs, metastasis and lack of access to timely quality management are the leading causes of morbidity and mortality.

One of the most significant contributors to death and morbidity in the region is cancer, as is the case in other nations in the sub-Saharan region. It was estimated that the proportion of cancer burden would increase by more than 85 percent by the year 2030 over the entirety of sub-Saharan Africa alone (Bello et al., 2013). Additionally, it was projected that there would be a significant global increase of 19.3 million new cancer cases per year by the year 2025 (Globocan, 2012). Breast cancer was responsible for 28% of all cancers and 20% of all cancer deaths among women in Africa in 2012 (Clegg-Lamptey, 2016). Among both sexes, it accounted for 16% of all cases and 11% of total fatalities. Breast cancer was specifically responsible for the deaths of women. According to the American Cancer Association (2018), it was placed second next to cervical cancer among women in East Africa in terms of the number of deaths and the prevalence of the disease.

According to the Globocan report for 2018, the International Agency for Research on Cancer (IARC) estimated that there were 47,887 new instances of cancer diagnosed per year in Kenya, with 32,987 deaths resulting from the disease. According to the information provided by the Kenya National Cancer Control Strategy 2017-2022, around 37,000 new infections were reported in the year 2012. According to the Ministry of Health (2017), during the same period, a total of 28,500 people lost their lives due to cancer. There were 47,887 new cases of cancer diagnosed in 2018, according to the National Cancer Institute's most recent figures, and 32,987 people lost their lives to the disease. It is the most prevalent form of cancer in Kenya, with 6,799 new cases expected to take place in the year 2020 and an age-standardized prevalence of 41 per 100,000 people. It has been determined using preliminary data from the Kenya National Cancer Registry 2014-2019 (KNCR) that seven out of ten cases of cancer are identified at late stages, specifically stage III and stage IV. Kenya tends to experience it at a relatively younger age (35-50 years), in contrast to western countries, where it typically occurs between the ages of 50 to 55. In the United States of America, around 90 percent of breast cancer cases are random, whereas only 5 to 10 percent may

be related to a genetic predisposition. The invasive ductal carcinoma (IDC), is the most prevalent histological form of breast cancer that is identified, accounting for up to 75% of all breast cancers. One of the most significant obstacles in the fight against breast cancer is the restricted availability of prevention, diagnostic, treatment, and rehabilitation services for cancer patients.

Breast and cervical cancer screening rates in the country continue to be low, a fact that may be related to a lack of understanding regarding these malignancies as well as inadequate and rare access to sexual reproductive healthcare services (KNBS & Macro, 2014). The low uptake of these screening services necessitates the implementation of novel approaches to improve information about these diseases and as a result to encourage screening, which ultimately results in the early diagnosis of these cancers.

1.1 Problem statement

In 2022, breast cancer remained the most common cancer among women globally, with estimated 2.3 million new cases and 666,000 deaths. In sub-Saharan Africa, most patients present with advanced disease due to delayed diagnosis. The patients diagnosed with breast cancer have different histologic sub-types and characteristics which influence morbidity and mortality. General statistics compiled by the Alexandria Cancer Centre and Palliative Care Hospital, breast cancer was the most prevalent form of cancer in the years 2016 and 2019, accounting for 13.5% and 12.7% of all malignancies, respectively. This illustrates that breast cancer is a significant burden on the government's health system. According to the Eldoret Cancer Population Based Registry, which is based at Moi Teaching and Referral Hospital, the results of cancer in general and breast cancer in particular, continue to be dismal in the western region of Kenya. Patients who come with advanced disease have diseases that has spread to numerous organs, including the brain, bones, lung, and regional lymph nodes. A very unfavorable prognosis is associated with breast tumours that are in stages 3 and 4. The various genetic compositions shed light on the behaviour of the histological patterns and molecular characterization of breast cancer, both of which have the potential to influence the aggressiveness of the disease progression. Cancer and patient characteristics, such as age, gender, histological sub-type, molecular characterizations, and so on, are diverse and present a significant challenge in terms of the physical, social, financial, and emotional costs that are associated with living with the disease.

1.2 General Objective

To assess characteristics, histopathological sub-types, and survival of breast cancer treated at Alexandria Cancer Center and Palliative Care Hospital.

1.2.1 Specific Objectives

i. To determine characteristics of breast cancer sub-types among patients being managed for breast cancer at ACC&PCH
ii. To evaluate the percentage of different sub-types of breast cancer among patients being managed for breast cancer at ACC&PCH
iii. To determine the relationship between histopathological sub-types and metastasis among patients being managed for breast cancer at ACC&PCH
iv. To determine the two-year survival rate of different histopathological sub-types among patients being managed for breast cancer at ACC&PCH

1.3 Research Questions

i. What are the characteristics of breast cancer sub-types among patients being managed for breast cancer at ACC & PCH?
ii. What is the percentage distribution of the different sub-types of breast cancer among patients being managed for breast cancer at ACC & PCH?
iii. What is the relationship between histopathological sub-types and metastasis among patients being managed for breast cancer at ACC & PCH?
iv. What is the two-year survival rate for the different histopathological sub-types among patients being managed for breast cancer at ACC & PCH?

2.0 Literature Review

The literature review examines existing research on breast cancer characteristics, histopathological subtypes, metastasis patterns, and survival outcomes. This chapter synthesizes evidence from global and regional studies to contextualize the research objectives. The review highlights knowledge gaps in breast cancer epidemiology within sub-Saharan Africa. It provides a theoretical framework for understanding breast cancer patterns in low-resource settings.

2.1 Characteristics of Patients with Breast Cancer

Breast cancer predominantly affects females worldwide, with males accounting for less than 1% of all cases (American Cancer Society, 2016a). In the United States, approximately 2,670 new male breast cancer cases were diagnosed in 2019, representing 0.7% of all breast cancers (Ravi et al., 2012). Studies in East Africa reported male breast cancer rates between 3-4%, consistent with global patterns (Bird et al., 2008; Roy & Othieno, 2011). Anderson et al. (2010) noted that male breast cancer occurs 100 times less frequently than female breast cancer, with similar histological patterns including ductal carcinoma in situ and invasive ductal carcinoma. Age represents the most significant risk factor for breast cancer development, with incidence increasing sharply among premenopausal women (Ma & Jemal, 2012). Sripan et al. (2017) demonstrated that breast cancer risk increases with age, influenced by hormonal changes throughout the aging process. In high-risk populations, peak incidence occurs after age 60, while low-risk populations experience maximum incidence around age 50 (Hemminki et al., 2011). Youlden et al. (2014) reported that in the Asia-Pacific region, 42% of breast cancer diagnoses occurred in women under 50 years. Rao et al. (2013) found that 67% of Indian breast cancer patients were younger than 50 years by 2013.

Socioeconomic status significantly influences breast cancer screening participation and disease presentation, with lower uptake observed in deprived populations (Moser et al., 2009; Bouchardy et al., 2006). Cuthbertson et al. (2009) demonstrated that deprived populations in London presented with later-stage breast cancer compared to affluent populations. Maheswarab et al. (2006) found strong associations between socioeconomic deprivation and reduced breast screening uptake, with significantly lower participation from deprived areas. Cultural beliefs create substantial barriers to breast cancer screening, particularly in Africa where cancer remains taboo and stigmatized (WHO, 2006; Gulshan et al., 2007). Psychosocial factors including fear, embarrassment, and denial significantly impede breast cancer screening uptake across diverse populations (Lamyian et al., 2007; Magai et al., 2007). Magai et al. (2007) found that women with higher embarrassment levels were 29% less likely to undergo screening after adjusting for other factors. Rural residence negatively correlates with mammography utilization, with adjusted odds ratio of 0.75 (Schueler et al., 2008). Cohen (2010) demonstrated that nurses positively impact patient compliance with breast

screening and educate women on recognizing breast changes. Meissner et al. (2007) identified nurse intervention as the most significant factor motivating breast screening attendance.

2.2 Histological Subtypes of Breast Cancer

In situ breast carcinomas represent abnormal epithelial cells that have not invaded neighboring tissues but microscopically resemble invasive mammary carcinoma cells (American Cancer Society, 2015). Ward et al. (2015) reported a lifetime risk of one in thirty-three for women developing in situ breast cancer. Ductal carcinoma in situ (DCIS) represents stage 0 breast cancer, characterized by malignant epithelial cells confined within breast ducts without stromal invasion (Siziopikou, 2013). Barnes et al. (2012) noted that DCIS lesions can progress to invasive cancer over periods ranging from years to decades. Approximately 20% of all breast cancers are DCIS, accounting for 83% of in situ cases diagnosed between 2010-2014 (American Cancer Society, 2017). Invasive ductal carcinoma originates in milk ducts and penetrates through duct walls into surrounding breast tissue, enabling metastasis through lymphatic and vascular systems (Carcinoma et al., 2016). Zangouri et al. (2018) identified invasive ductal carcinoma as the most prevalent breast cancer subtype, contributing substantially to breast cancer mortality worldwide. Rampaul and Pillarisetti (2006) reported that invasive ductal carcinoma accounts for approximately 70-80% of all breast cancers globally. Invasive lobular carcinoma represents the second most common histologic subtype, accounting for 10-15% of invasive tumors with increasing prevalence in postmenopausal women (Mamtani & King, 2018). Reed et al. (2015) characterized invasive lobular carcinoma cells as small, round, relatively homogenous, and non-cohesive with distinctive single-file stromal infiltration patterns.

Evaluation of estrogen receptor (ER), progesterone receptor (PR), and HER-2/neu expression represents standard practice in breast cancer patient management (Nasrazadani et al., 2018). Combined expression of these three hormone receptors provides the most informative factor for molecular classification, clinical assessment, therapy selection, and prognosis prediction (Kaul et al., 2011). Women with ER and/or PR-negative disease demonstrate higher post-diagnosis mortality risk, while ER-positive and/or PR-positive patients show lower death risk. Triple-negative breast cancer (TNBC), characterized by absence of ER, PR, and HER2 expression, represents an aggressive tumor subtype with early recurrence peaks between first- and third-years post-diagnosis (Cetin & Topcul, 2014; Ismail-Khan & Bui, 2010). Triple-negative breast cancer accounts for approximately 12-20% of all breast cancers worldwide, equivalent to nearly 200,000 annual cases (Maeda et al., 2016). Vanderpuye et al. (2017) demonstrated that African women exhibit higher TNBC incidence, resulting in poorer clinical outcomes compared to other populations. In Tunisia, TNBC represents 23% of all breast cancers, while in Egypt it accounts for 28% (Corbex et al., 2014; Rais et al., 2012). Sayed et al. (2018) reported that among Kenyan breast cancers, 68.8% were ER-positive, 59.4% were PR-positive, and 25.6% were HER2-positive. Groenendijk et al. (2019) identified estrogen receptor variants in ER-positive basal-type breast cancers that respond to therapy similarly to ER-negative tumors.

2.3 Association Between Metastasis and Patient Characteristics

Breast cancer incidence increased by over 20% globally while mortality rose by 14% between reporting periods (Bray et al., 2013). The incidence-to-mortality ratio among African women is 1:2 compared to 1:5 among white Americans, attributed to late presentation and inadequate follow-up (Mutebi, 2014). Lafourcade et al. (2018) found that 15-30% of breast cancer cases manifest with distant metastases at presentation time. Redig and McAllister (2013) identified metastatic

disease as the most significant clinical challenge in solid tumor oncology, responsible for the vast majority of cancer patient deaths. Bone represents the most frequent single metastatic site, accounting for 39.80% of metastatic breast cancer patients, followed by lung metastasis at 10.94% (Wang et al., 2019). Ekpe et al. (2019) reported that among Kenyan metastatic breast cancer patients, 58% had bone metastases, 57% lung, 50% liver, and 14% brain metastases. Seventy-four percent of patients presented with multiple metastatic sites simultaneously (Ekpe et al., 2019). Zhang and Gong (2017) demonstrated that multiple bone metastases conferred 1.72 times higher risk than single bone metastasis, while advanced clinical stage showed 1.49 times higher risk.

Both tumor characteristics and patient characteristics function as prognostic factors for death occurrence after breast cancer diagnosis (Lafourcade et al., 2018). Metastases at diagnosis and treatment response demonstrated statistically significant associations with mortality ($p=0.04$ and $p<0.001$ respectively) using Fisher's exact test. Bidard et al. (2014) established that circulating tumor cell counts confer independent prognostic effects on progression-free survival and overall survival in metastatic breast cancer. However, adding CTC counts to comprehensive clinicopathological predictive models did not improve prognostication beyond existing markers (Bidard et al., 2014). Cancer represents the third leading cause of death in Kenya, accounting for approximately 7% of all deaths annually (Ministry of Health, 2017). Approximately 28,000 new cancer cases occur yearly with 22,000 cancer-related deaths (Ministry of Health, 2017). Over 60% of affected individuals are under 70 years, with 14% lifetime cancer risk before age 75 and 12% death risk. The Kenya National Cancer Registry (2014-2019) determined that seven out of ten cancer cases are diagnosed at late stages, specifically stage III and IV (MOH, 2017).

2.4 Survival Rates and Predictive Factors

Survival rates represent the percentage of individuals enduring a condition like cancer for predetermined periods following diagnosis, enabling medical professionals to provide prognostic assistance (Lynne, 2018). Two-year overall survival for breast cancer patients varies substantially by geographic region and healthcare access, ranging from 63% to 94% across different populations. Lan et al. (2013) reported declining overall survival rates in Vietnam from 94% at one year, 83% at three years, to 74% at five years following breast cancer diagnosis. Tadesse et al. (2018) found that overall estimated two-year survival in Ethiopia was 89.8% using Kaplan-Meier survival estimation methods. Age at diagnosis significantly influences breast cancer prognosis, with younger women under 40 experiencing more aggressive disease than those over 50 years (Sripan et al., 2017). Gender shows significant association with survival, with female breast cancer patients demonstrating different survival patterns than male patients in multivariate analyses. Tumor stage, lymph node involvement, and receptor status represent notable prognostic markers that define early detection steps and improve treatment strategies (Dong et al., 2014). Wang et al. (2021) demonstrated that cervical cancer mortality rates increase with women's age, suggesting age effects on cancer-related deaths across different cancer types.

Cox proportional hazards regression represents the most frequently utilized semi-parametric survival model in health sciences, relying on fewer assumptions than parametric models (Georgousopoulou et al., 2015). Kaplan-Meier survival analysis procedures enable researchers to analyze survival time from predetermined starting points like cancer diagnosis to concluding events like death (Bradburn et al., 2003). Restricted mean survival time (RMST) presents an alternative treatment effect measure with advantages in design, analysis, and interpretation compared to standard measures (Kim et al., 2017). Multivariate Cox regression analysis identifies

parameters predicting overall survival and progression-free survival while eliminating variables with minimal survival rate impact (Smith, 2011). Africa exhibits the highest breast cancer mortality rates globally despite having the lowest incidence rates, reflecting inferior survival outcomes (Joko-Fru et al., 2019). Survival rates in high-income countries like the United States reach 71-89% at five years, attributed to early detection through screening and timely effective treatment (Akpo et al., 2010; Sant et al., 2004). Conversely, survival rates in low-to-middle-income countries remain significantly lower, with Ghana reporting less than 25% and Nigeria only 10% five-year survival (Opuku et al., 2012). Allemani et al. (2015) utilized survival statistics as significant instruments for tracking progress achieved in cancer diagnosis and treatment across 67 countries globally.

3.0 METHODOLOGY

This cross-sectional study was conducted at Alexandria Cancer Center and Palliative Care Hospital in Eldoret, Uasin Gishu County, Kenya. The hospital serves the western region with approximately 24 million people and has a 50-bed capacity providing comprehensive oncology services. The study population comprised 54 breast cancer patients managed between 2016 and 2017 who met inclusion criteria. All patients aged 18 years and above with histologically confirmed breast cancer who completed treatment were included through census sampling. A structured data abstraction tool extracted demographic and clinical variables including age, gender, ethnicity, tumor morphology, metastasis, and treatment response from patient records. Data was entered and cleaned using Microsoft Excel while analysis employed R-3.6.1 software for descriptive statistics, Kaplan-Meier curves, and Cox regression analysis. Ethical approval was obtained from Moi University/MTRH Institutional Research and Ethics Committee with patient data de-identified for confidentiality. Results were presented through tables, graphs, and figures showing frequencies, percentages, means, and survival estimates as appropriate. This hospital-based retrospective study provided local epidemiological data despite limitations in generalizability and inability to capture emerging issues during data collection.

4.0 Findings and Discussion

This chapter presents findings from 54 breast cancer cases that met inclusion criteria out of 89 patients initially considered at Alexandria Cancer Center and Palliative Care Hospital. The results address study objectives examining histopathological subtypes, metastasis patterns, and two-year survival outcomes. Data analysis employed descriptive statistics, Kaplan-Meier survival estimates, and Cox proportional hazards regression to identify significant predictors of mortality.

4.1 Histopathological Subtypes of Breast Cancer

Invasive ductal carcinoma represented the predominant histological subtype, accounting for 88.9% (48 of 54) of all breast cancer cases examined in this study. Other subtypes included breast lymphoma at 3.7% (2 cases), while ductal carcinoma in-situ, invasive lobular carcinoma, and breast sarcoma each constituted 1.9% (1 case each) of the total cases. The overwhelming predominance of invasive ductal carcinoma aligns with global epidemiological patterns where this subtype consistently represents the majority of breast cancer diagnoses across diverse populations.

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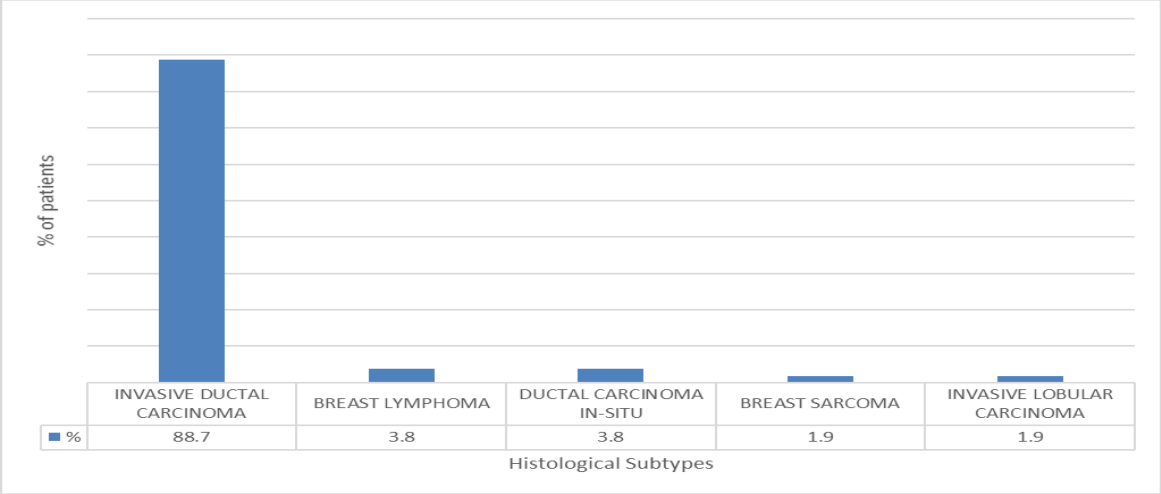

Figure 1: Histopathological Description of Breast Cancer

Hormone receptor status analysis revealed significant data gaps, with 46.3% of patients lacking documented hormone receptor results in their medical records. Among the 29 patients with known HR/HER2 status, double positive tumors (ER+/PR+) and triple-negative breast cancer each accounted for 37.9% (11 cases) of documented cases, representing the leading molecular subtypes. The high proportion of triple-negative breast cancer is concerning given its association with aggressive disease behavior and limited targeted treatment options. This finding suggests that a substantial proportion of patients in this cohort had biologically aggressive disease at presentation.

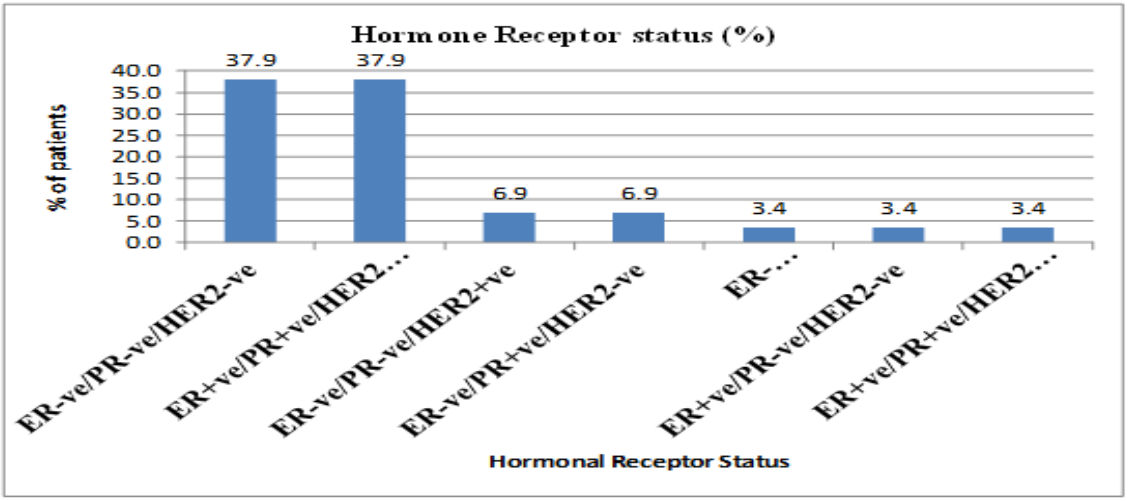

Figure 2: Hormone Receptor Status

4.2 Clinical Presentation and Metastasis Patterns

The majority of breast cancer patients (52.8%) were diagnosed through histology of the primary tumor site, establishing definitive tissue diagnosis as the primary diagnostic approach. Laterality analysis revealed that the right breast was affected in 53.7% of patients, while the left breast was involved in 46.3% of cases. No bilateral breast cancer presentations were documented during the study period, indicating that all cases represented unilateral disease at diagnosis.

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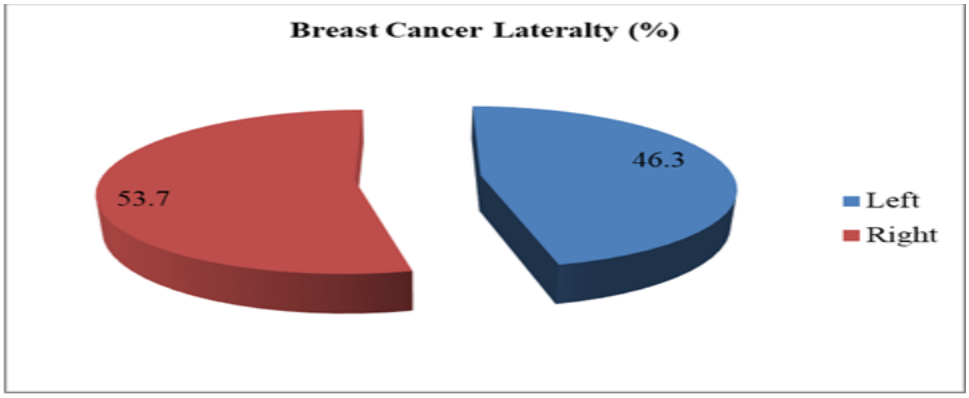

Figure 3: Method of Tissue Examination

Metastatic disease at diagnosis was absent in 57.4% of patients, while 42.6% presented with metastasis, indicating substantial late-stage disease at presentation. Among patients with metastatic disease, bones and lungs emerged as the most commonly affected organs, each accounting for 13.0% of all patients. Multiple organ metastases were encountered in several cases, including complex patterns involving combinations of bones, brain, spine, liver, lungs, and thyroid. This high proportion of metastatic presentation at diagnosis reflects significant barriers to early detection and suggests delays in seeking healthcare or accessing diagnostic services.

4.3 Treatment Modalities and Patient Status

Chemotherapy administered as a single modality represented the most commonly employed treatment approach, accounting for 39.6% of all patients without combination with other anticancer treatments. This predominance of chemotherapy-only regimens may reflect limitations in access to multimodal therapy or patient presentation at advanced stages where systemic treatment was prioritized. Combined treatment approaches were also utilized, though less frequently than chemotherapy alone.

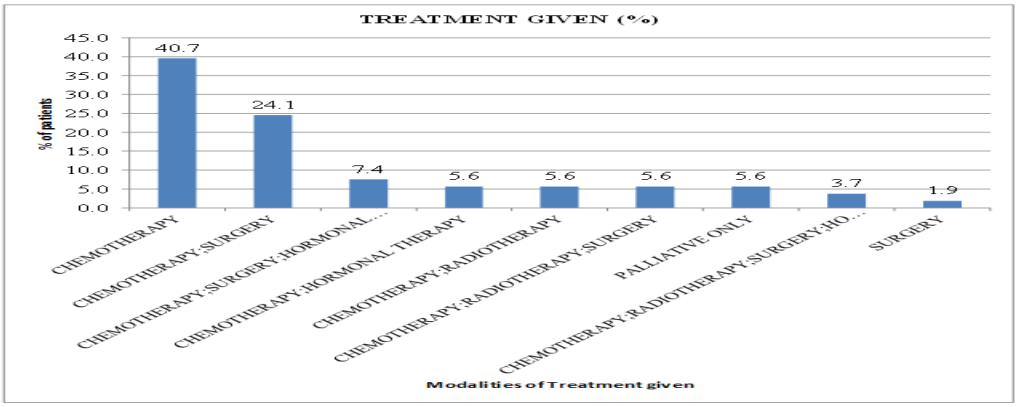

Figure 4: Treatment Given to Patients with Breast Cancer

At the time of last contact with healthcare providers, 66% of patients with breast cancer were alive, while 34% had died from the disease or related complications. This survival status reflects outcomes following various treatment modalities administered during the study period. The mortality rate underscores the serious nature of breast cancer in this population and highlights the need for improved early detection and comprehensive treatment approaches.

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4.4 Factors Associated with Mortality

Bivariate analysis using Fisher's exact test identified significant associations between death and specific clinical variables among the study population. Metastasis sites demonstrated significant association with mortality (p=0.041), with deceased patients showing higher frequencies of metastatic involvement across various organs. Treatment response showed the strongest association with death (p<0.001), where 78.9% of deceased patients experienced disease progression during treatment compared to only 22.9% among survivors. Conversely, stable disease was observed in 71.4% of living patients but only 21.1% of deceased patients, while partial response occurred in 5.7% of survivors with no deceased patients achieving this outcome.

Other clinical characteristics showed no significant associations with mortality outcomes. Histological subtype demonstrated no significant relationship with death (p=0.832), with invasive ductal carcinoma representing similar proportions among both survivors (88.6%) and deceased patients (89.5%). Laterality of breast involvement showed no significant association (p=0.110), though right breast cancer occurred more frequently in deceased patients (68.4%) compared to survivors (45.7%). Age group distribution revealed no significant relationship with mortality (p=0.660), with relatively similar proportions across age categories. Gender showed no significant association (p=0.288), as all deceased patients were female compared to 94.3% among survivors. Treatment modality similarly showed no significant association with death (p=0.359), though chemotherapy alone was more common among deceased patients (57.9%) than survivors (31.4%).

Table 1: Bivariate Test of Association Between Death and Patient Characteristics

	Alive (N=35)	Dead (N=19)	p value
Female	33 (94.3%)	19 (100.0%)	0.288
Male	2 (5.7%)	0 (0.0%)	
Below_39	11 (31.4%)	6 (31.6%)	0.660
40-49	13 (37.1%)	5 (26.3%)	
Above_50	11 (31.4%)	8 (42.1%)	
BREAST LYMPHOMA	1 (2.9%)	1 (5.3%)	0.832
BREAST SARCOMA	1 (2.9%)	0 (0.0%)	
DUCTAL CARCINOMA IN-SITU	1 (2.9%)	1 (5.3%)	
INVASIVE DUCTAL CARCINOMA	31 (88.6%)	17 (89.5%)	
INVASIVE LOBULAR CARCINOMA	1 (2.9%)	0 (0.0%)	
HEMATOGENOUS	7 (20.0%)	3 (15.8%)	0.497
LOCAL INFILTRATION	6 (17.1%)	2 (10.5%)	
LYMPHOID	11 (31.4%)	10 (52.6%)	
UNKNOWN	11 (31.4%)	4 (21.1%)	
LEFT	19 (54.3%)	6 (31.6%)	0.110
RIGHT	16 (45.7%)	13 (68.4%)	
No	23 (65.7%)	7 (36.8%)	0.164
Yes	12 (34.3%)	12 (63.2%)	
BONES	5 (14.3%)	2 (10.5%)	0.041
BONES;BRAIN;SPINE	0 (0.0%)	1 (5.3%)	
BONES;LIVER	1 (2.9%)	0 (0.0%)	
BONES;LUNGS;LIVER	0 (0.0%)	1 (5.3%)	
BRAIN	0 (0.0%)	1 (5.3%)	
BRAIN;SPINE	1 (2.9%)	0 (0.0%)	
BRAIN;THYROID	0 (0.0%)	1 (5.3%)	
LUNGS	3 (8.6%)	4 (21.1%)	
LUNGS;BRAIN	0 (0.0%)	1 (5.3%)	
LUNGS;LIVER	2 (5.7%)	0 (0.0%)	
NONE	23 (65.7%)	8 (42.1%)	
CHEMOTHERAPY	11 (31.4%)	11 (57.9%)	0.359
CHEMOTHERAPY; HORMONAL THERAPY	3 (8.6%)	0 (0.0%)	
CHEMOTHERAPY; RADIOTHERAPY	2 (5.7%)	1 (5.3%)	
CHEMOTHERAPY;RADIOTHERAPY;SURGERY	2 (5.7%)	1 (5.3%)	
CHEMOTHERAPY;RADIOTHERAPY;SURGERY;HORMONAL THERAPY	1 (2.9%)	1 (5.3%)	
CHEMOTHERAPY;SURGERY	10 (28.6%)	3 (15.8%)	
CHEMOTHERAPY;SURGERY;HORMONAL THERAPY	4 (11.4%)	0 (0.0%)	
PALLIATIVE ONLY	1 (2.9%)	2 (10.5%)	
SURGERY	1 (2.9%)	0 (0.0%)	
PARTIAL RESPONSE	2 (5.7%)	0 (0.0%)	**< 0.001**
PROGRESSION	8 (22.9%)	15 (78.9%)	
STABLE DISEASE	25 (71.4%)	4 (21.1%)	

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4.5 Survival Analysis Outcomes

Kaplan-Meier survival analysis estimated the two-year overall survival rate at 64.8%, with 19 participants (35.2%) experiencing death within the 24-month observation period following diagnosis. The majority of deaths occurred within the first 20 weeks post-diagnosis, indicating that early post-diagnosis period represents the highest risk time for mortality. The survival curve demonstrates this pattern with an initial steep decline during the first 20 weeks, followed by a more gradual decrease in survival probability. The dotted lines above and below the survival curve represent the 95% lower and upper confidence bands, indicating the precision of the survival estimate. This two-year survival rate reflects the challenges of managing breast cancer in this population and highlights opportunities for improving early detection and treatment outcomes.

Multivariate Cox proportional hazards regression analysis identified three statistically significant predictors of survival time among breast cancer patients. Gender emerged as a significant predictor (p=0.0014), with females demonstrating 12.7% increased hazard of death compared to males, with hazard ratio of 1.127 and 95% confidence interval of 3.99-24.4. Age showed significant association with survival (p=0.046), where each additional year of age corresponded to 10.4% increase in hazard of death, with confidence interval of 1.961-2.02. Presence of metastasis at diagnosis significantly predicted mortality (p=0.029), with metastatic patients showing 20.9% higher hazard of death compared to patients without metastatic disease, with confidence interval of 1.876-12.67. Their median survival time was also lower than non-metastatic patients. Laterality of breast involvement showed no significant association with survival outcomes (p=0.923). These findings underscore the importance of age, gender, and metastasis in predicting survival outcomes and guide clinical decision-making for risk stratification.

Table 2: Multivariate Cox Regression Analysis of Predictors of Survival

Variable	Estimate	Std. Error	Statistic	p-value	Hazard Ratio	95% CI Lower	95% CI Upper
Gender (Female vs Male)	0.120	1.050	3.280	0.001*	12.70	3.99	24.40
Age (per year increase)	0.093	0.016	-0.459	0.046*	1.093	1.96	2.02
Laterality (Right vs Left)	9.650	0.037	-0.096	0.923	0.965	0.47	1.99
Metastasis (Yes vs No)	0.192	0.938	-0.002	0.029*	1.209	1.88	12.67

Hazard ratios are calculated as exp(estimate). Values greater than 1 indicate increased hazard of death, while values less than 1 indicate decreased hazard. The 95% confidence intervals that exclude 1 indicate statistically significant effects. In hazard regression analysis, significant coefficients are interpreted by checking whether the 95% confidence interval for the hazard ratio excludes one. When the confidence interval excludes one, a statistically significant effect is concluded. All presented coefficients in the analysis are statistically significant based on this criterion. The coefficients in the table are rounded to two decimal points for presentation clarity, while in the descriptive text they are presented to three decimal places for greater precision in interpretation.

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Schoenfeld's procedure was employed to evaluate the proportional hazards assumptions for the Cox regression model. The residual plots against time for gender, age, laterality, and metastasis all demonstrated straight lines passing through residual value of zero with zero gradient, indicating that all variables satisfy the proportional hazards assumptions and are thus time-independent. This validation confirms the appropriateness of the Cox proportional hazards model for this dataset and ensures the reliability of the hazard ratio estimates and their associated confidence intervals.

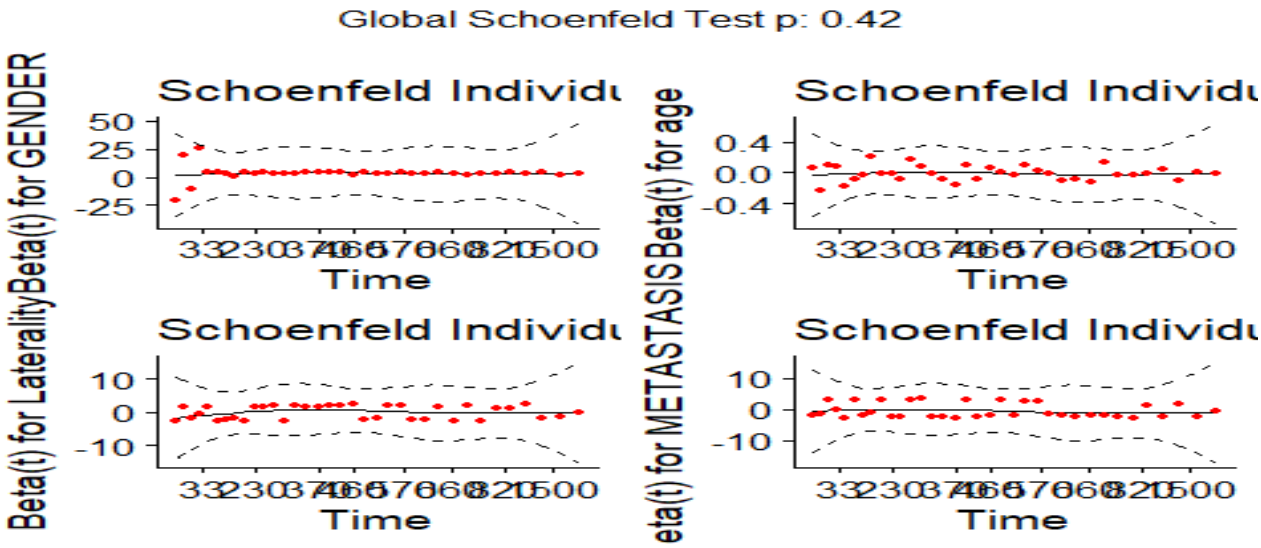

Figure 5: Proportional Hazard Assumptions - Schoenfeld Residuals Plot

5.0 Conclusion

The most affected age group was 40 to 49 years with invasive ductal carcinoma being the most common histological sub-type of breast cancer. Two-year survival rate among the study population was 64.8%. Metastases at diagnosis and disease progression increased the risk of death from breast cancer.

6.0 Recommendation

This study recommends that there should be efficient role out of breast cancer prevention and screening programs targeting the middle-aged group (40 to 49 years).

There should be targeted technology enhanced screening for early detection and treatment aimed at improving 2-year survival rate to above 65%.

Timely efficacious evidence-based treatment should be provided to prevent disease progression.

There should be additional research into using a bigger sample size to increase validity and reliability of the findings and should be conducted in multiple centers to reduce any bias.

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