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Original Article

Locally Advanced Breast Cancer in Pakistani Women: Clinical Features and Prognostic Factors

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ABSTRACT

Locally advanced breast cancer poses a significant health challenge due to delayed diagnosis and limited access to healthcare resources among Pakistani women. Understanding the clinical features and prognostic factors specific to Pakistani women can help healthcare professionals identify high-risk patients, initiate timely interventions, and improve survival rates. **Objective:** To investigate the clinical features and prognostic factors associated with locally advanced breast cancer (LABC) in Pakistani women. **Methods:** The study was carried out at the Department of Surgery, Liaquat University of Medical & Health Sciences, Jamshoro. 300 patients with LABC had their data gathered. Age and socioeconomic status were recorded under the category of demographics. Clinical information included the date of presentation, family history of breast cancer, the lump that was the presenting symptom, the ulceration, and other skin changes. Tumour size, histopathology, Bloom & Richardson grading, estrogen receptor (ER), progesterone receptor (PR), and HER2 status are histopathological factors. **Results:** The study showed that 30% of LABC patients who received standard Tri modality treatment died within two years. Only 25% of patients were found to have more than two years of disease-free survival. On the other hand, 70% of patients survived with eventful (recurrence/metastases) survival. **Conclusions:** Though there is a substantial mortality rate within one year, a significant proportion of patients survive beyond one year. Disease recurrence or metastases are prevalent as per the current study, emphasizing the need for comprehensive follow-up and targeted therapies to improve long-term outcomes.

INTRODUCTION

Breast cancer in LMICs often presents with locally advanced breast cancer (LABC) [1]. LABC accounts for 40-60% of all breast cancers on presentation in developing countries [2]. One of the most important prognostic factors of survival in breast cancer is the clinical stage at diagnosis [3]. Since 2008, breast cancer incidence has increased by over 20% and breast cancer deaths have risen by 14% [4]. Breast cancer is the commonest female malignancy all over the world including Pakistan and a 2nd leading cause of death from cancer in female population due to late presentation and advance stage of disease [5]. A large primary tumour (>5 cm) or involvement of internal mammary nodes (N1b) in conjunction with or without skin or chest wall involvement (T4) or with fixed (matted) axillary lymph nodes in the absence of any indication of distant metastases define locally advanced breast cancer (LABC). LABC may develop as a result of untreated tumours or if the tumour is expanding quickly. The AJCC staging system classifies these cancers as stage II, IIA, and IIB [6]. Due to their low socioeconomic status, Asian countries have a higher incidence of LABC than western developed nations. While the incidence of LABC varies between 30% and 60% in India and Pakistan, 50% to 60% in Malaysia, and 21% in Singapore, only 10% to 20% of all breast cancers in the USA present as LABC [7-10]. Neo-adjuvant chemotherapy, followed by surgery and radiation therapy are the current recommended treatments for LABC; hormonal treatment is added for receptor positive disease and Transtuzuumab

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Therapy for Her2neu positive patients [11-14]. The majority of women present with advanced disease stage III and IV and the 5-year survival rate in less than 50% [3]. Advance breast cancer and its high mortality are seen with delay in diagnosis and treatment [15]. Third world breast cancer is characterized by late presentation, advance stage of disease with a worse biologic behavior and occurrence relatively at a younger age than that reported in western literature [16]. Our aim of study was to investigate the clinical features and prognostic factors associated with locally advanced breast cancer (LABC) in Pakistani women and discuss if they are different with respect to developed countries.

METHODS

The cross-sectional descriptive study was conducted at the Department of Surgery, Liaquat University of Medical & Health Sciences, Jamshoro, over the period of 2021 to 2022, involving 300 patients diagnosed with locally advanced breast cancer (LABC) who received treatment. (Sample size was calculated via WHO open epi sample size calculator by taking the proportion of locally advance breast cancer among all breast cancers as 26.4% [8]. Patients were chosen via convenient sampling. Data for the study were obtained retrospectively from the patients' medical records, which were archived in the record room of cancer ward in the hospital. Women aged more than 18 years with locally advanced breast cancer, defined as stage III or stage IV disease were included in the study while those with metastasis and with early stage breast cancer were excluded from the study. Among the 300 patients included in the study, a majority of them exhibited T3 or N2 disease, indicating an advanced stage of LABC. Demographic information such as age and socioeconomic status of the patients was recorded as part of the data collection process. Clinical details encompassed the date of presentation, presence of a family history of breast cancer, the primary symptom of presentation (a palpable lump), as well as the presence of ulceration and other skin changes. Details about prognostic factors included TN staging, HER2/neu status, histological grading, involvement of localized lymph nodes and response to the treatment. For 1 years, patients were monitored every three months. Data were analyzed via SPSS version 22.0 and qualitative data were measured in frequency and percentages while the quantitative data were expressed in means ± SD.

RESULTS

The study revealed that the median age of the patients with locally advanced breast cancer (LABC) was 45, with a majority falling within the age range of 30 to 60. On presentation size of tumor was 5cm & more in 91.9% patients. Involvement of axilla was in 76.7%. Chest wall was involved in 19.6%. Total T3 and T4 were 63.3% and 36.6% (Table 1).

Table 1: Clinical characteristics of locally advanced breast cancer (LABC) patients

Clinical Characteristics	N (%) N= 300
Median Age	45 years
Age Range	30-60 years
Tumor Size ≥ 5cm	275 (91.7)
Axillary Involvement	230 (76.7)
Chest Wall Involvement	59 (19.7)
Tumor Staging	
T3 Stage	190 (63.3)
T4 Stage	110 (36.7)
Histopathological Factors	
ER/PR Positive	123 (41)
HER-2/neu Positive	83 (27.7)
Staging and Metastasis	
Metastatic Breast Carcinoma	35 (11.7)
Liver Metastasis	10 (3.3)
Lung Metastasis	8 (2.7)
Bone Metastasis	16 (5.3)

Diagnosis of all patients was confirmed by histopathology. Neoadjuvant was given to all patients to downstage the tumor. ER/PR was positive in 41.1%, HER-2/neu positive in 27.6%. On staging breast carcinoma was metastatic in 11.6% with liver, lung and bone in 3.5%, 3 2.7% and 5.3% respectively. Breast conservation was done in 17 patients, Modified Radical Mastectomy was done in 248 patients, Toilet Mastectomy in 21 patients and 14 patients were not operated (Figure 1).

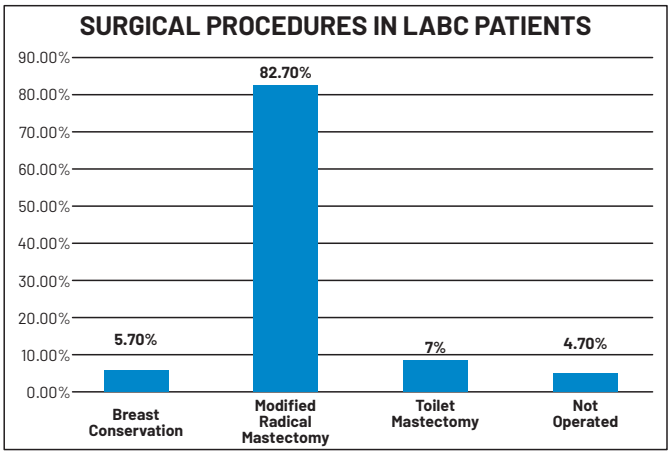

Figure 1: Surgical Procedures in LABC Patients

Among the 300 patients, 30% (90 patients) experienced mortality within one year. 70% (210 patients) were alive beyond one year, indicating survival beyond the initial diagnosis. Out of the total sample, 25% (75 patients) achieved disease-free survival for more than one year, while a substantial proportion of 62% (186 patients) experienced disease recurrence or metastases (Table 2).

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Table 2: Clinical Outcomes of LABC Patients

Survival	Percentage
Mortality within 1-year	30%
Alive more than 1-year	70%
Disease free survival for more than 1 year	25%
Recurrence/metastases	62%

DISCUSSION

In Pakistani women, LABC results were poor compared to those in developed nations. Despite the fact that Tri modality therapy has improved the results, 30% of LABC patients still passed away two years after finishing their treatment. This figure may be higher given that some patients were lost to follow-up. Iqbal *et al.*, in 2010 reported similar poor among [17]. Understanding the causes of LABC and the challenges that doctors face in treating such cases will enable health authorities to develop plans for dealing with LABC in the public sector and help oncologists develop management strategies. Many studies reported lack of knowledge, fear, low socioeconomic status, and illiteracy as major contributors to late presentation and locally advanced breast cancer among women [18-21]. Malik *et al.*, in 2002 reported lack of awareness, fear of illness and unavailability of accessible health services as contributing factor to late presentation of advanced breast cancers [22]. As node positive disease was discovered in 74 percent of patients after surgery, its aggressive biological behaviour is another crucial factor that could be the cause of locally advanced disease. Second, even though 60% of patients had ER/PR positive status and were also receiving hormone therapy, they still developed recurrence or metastatic disease. Breast cancer biology racial differences have been well described. Among Asian women, Japanese women typically have less aggressive breast cancer [11]. Afro-Americans and Hispanic women in the USA have more severe diseases than other Americans [12, 13]. Delay in seeking treatment and the lack of adequate oncological services are additional factors that are counterproductive [14, 23]. The clinical features of LABC in Pakistani women are similar to those in other populations. The most common symptom is a palpable breast lump, which is often painless. Other symptoms include breast pain, nipple discharge, and skin changes, such as dimpling or redness. However, due to the lack of awareness and cultural barriers, many women in Pakistan delay seeking medical attention until the disease has progressed to an advanced stage [24]. Several prognostic factors have been identified in LABC, including tumor size, lymph node involvement, hormone receptor status, and HER2/neu status. In Pakistani women, the majority of LABC cases are hormone receptor-positive, which means that the cancer cells grow in response to estrogen or progesterone. This subtype of breast cancer is associated with a better prognosis and response to hormonal therapy. However, HER2/neu overexpression is also common in Pakistani women with LABC, which is associated with a poorer prognosis and resistance to chemotherapy, as reported by Talib *et al.*, in 2014 [25]. Every tertiary care facility in Pakistan offers surgical services, but very few of these facilities also offer parallel oncological services, which further complicates the management of LABC patients in our population. Most patients lose their way after surgery when we refer them to oncology centers because of financial limitations and lengthy wait times at such facilities. These factors are entirely controllable, so by raising awareness and providing more oncological resources, the outcome can be improved.

CONCLUSIONS

Though there is a substantial mortality rate within one year, a significant proportion of patients survive beyond one year. Disease recurrence or metastases are prevalent as per the current study, emphasizing the need for comprehensive follow-up and targeted therapies to improve long-term outcomes.

Authors Contribution

Conceptualization: RK
Methodology: RK, FH, AMB
Formal Analysis: FH, AIM, IK, N
Writing-review and editing: RK, AMB, AIM, IK, N

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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