

Locally Advanced Breast Cancer in Pakistani Women: What Is Different from Rest of the World and Why It Is Difficult to Manage

Muhammad Khalid¹, Noor Ul Wara Rao¹, Farwa Batool Shamsi², Tayaba Kanwal¹, Sana Arshad¹, Muhammad Shahzeb¹, Ameer Alam², Sobia Aleem³, M. Ahsan Iqbal^{3*}

¹Oncology/CCU, Allied Hospital Faisalabad, Faisalabad Medical University, Faisalabad, Pakistan

²Department of Pathology, Faisalabad Medical University (FMU), Faisalabad, Pakistan

³Department of PB & Genetics, University of Agriculture, Faisalabad, Pakistan

Email: *ahsanuaf2003@yahoo.com, *ahsanuaf2003@uaf.edu.pk

How to cite this paper: Khalid, M., Ul Wara Rao, N., Shamsi, F.B., Kanwal, T., Arshad, S., Shahzeb, M., Alam, A., Aleem, S. and Iqbal, M.A. (2022) Locally Advanced Breast Cancer in Pakistani Women: What Is Different from Rest of the World and Why It Is Difficult to Manage. *Journal of Cancer Therapy*, 13, 525-530.

<https://doi.org/10.4236/jct.2022.138046>

Received: May 16, 2022

Accepted: August 21, 2022

Published: August 24, 2022

Copyright © 2022 by author(s) and Scientific Research Publishing Inc. This work is licensed under the Creative Commons Attribution International License (CC BY 4.0).

<http://creativecommons.org/licenses/by/4.0/>



Open Access

Abstract

Locally Advanced Breast Cancer refers to a heterogeneous group of breast cancer with locally extensive disease, which may or may not involve the nodes, without any distant metastases. The study was conducted at Faisalabad Medical University (FMU), Oncology, Allied Hospital Faisalabad (Pakistan). Data of 100 patients with LABC was collected. Demographics were recorded in the form of age, socio-economic status. In clinical data, time of presentation, family history of breast cancer, the presenting symptom in the form of lump, ulceration and other skin changes were noted. Histo-pathological variables including tumor size, histopathology, Bloom & Richardson grading, estrogen receptor (ER), progesterone receptor status (PR) and HER2 status. Results showed that after following a standard trimodality treatment approach in LABC patients, 30 percent died within two years. Disease free survival for more than two years was observed in only 25% of patients. Whereas, 70% patients had eventful (Recurrence/metastases) survival. This poor outcome was observed due to lack of health care facilities, awareness and poor socio-economic status.

Keywords

Oncology Breast, Cancer in Pakistani Women, LABC

1. Introduction

Cancer is a leading cause of death globally and is responsible for an estimated 9.6 million deaths in the world. Breast cancer is most common among women. Lo-

cally advanced breast cancer (LABC) is characterized by the presence of a large primary tumor (>5 cm) or involvement of internal mammary nodes (N1b) associated with or without skin or chest-wall involvement (T4) or with fixed (matted) axillary lymph nodes in the absence of any evidence of distant metastases. LABC may be the result of neglected tumors or if tumor is rapidly growing. These cancers are classified as stage II, IIIA and IIIB according to the AJCC staging system [1]. Asian countries have higher incidence of LABC compared to the western developed countries due to poor socio-economic status. In India and Pakistan, incidence of LABC is 30% - 60%, Malaysia 50% - 60% and Singapore 21%, while in USA only 10% - 20% of all breast cancers present as LABC [2] [3] [4] [5]. Current recommendation for treating LABC are neo-adjuvant chemotherapy followed by surgery and radiation therapy; hormonal treatment is added for receptor positive disease and Trastuzumab Therapy for Her2neu positive patients [6] [7] [8] [9]. Despite of multimodality approach outcome is still very poor. Compared to patients with early breast cancer, patients with LABC are at a significantly higher risk of local recurrence and distant metastases. Even in USA, the five year survival rate for women with LABC is 55% [2]. The present study focused at all such factors and their comparison with rest of world so that treatment strategies can be developed for Pakistani women.

2. Materials and Methods

The study was conducted at Allied Hospital Faisalabad. One hundred patients of locally advanced breast cancer were treated during the year 2013 to 2015. The data was collected retrospectively from medical record of patients which was present in the record room of hospitals Oncology Centre. Out of 100 patients, most of the patients had T3 or N2 disease. Demographics were recorded in the form of age and socio-economic status of the patients. In clinical data, time of presentation, family history of breast cancer, the presenting symptom in the form of lump, ulceration and other skin changes were noted. Histo-pathological variables studied including tumor size, Bloom and Richardson grading, estrogen receptor (ER) and progesterone receptor status (PR) and HER2neu status. All treatment variables were recorded. Patients were put on three-month follow-up for 2 years. The treatment pattern is described in **Table 1**. This table describes the

Table 1. Treatment patterns.

Treatment modality	Frequency
Neo-Adjuvant Chemotherapy	98%
MRM with ALND	90%
Toilet Mastectomy	7%
Adjuvant Radiotherapy	95%
	5% develop metastatic disease during the course of neo-adjuvant chemo-therapy or after surgery
Hormonal treatment	60%

standard treatment approach for LABC. Neo-Adjuvant Chemo-therapy was done in 98% patients followed by MRM with ALND in 90% patients and Toilet Mastectomy in 7% patients. Ninety five percent (95%) of patients underwent Adjuvant-Radiation Therapy while 5% developed metastatic disease during the treatment.

3. Results

Patient's characteristics and presenting symptoms are summarized in **Table 2(a)** and **Table 2(b)**. Median age was 45 years. Mostly patients were in the age group of 30 to 60 years. Family history of breast cancer was noted in four patient. Information regarding family history was missing in medical record of five patients. Median duration between noticing lump and seeking medical help was eight months.

Tumor characteristics are mentioned in **Table 3**. All tumors were either grade II or grade III, 60% of patients were ER and PR receptors positive. They all receive hormone therapy. Twenty five percent patients (25%) were HER2neu positive. Only about 40 percent were affording for trastuzumab therapy. Five percent patients (5%) did not get their receptor status done.

Clinical outcome is mentioned in **Table 4**.

4. Discussion

We have observed poor outcome of LABC in Pakistani women as compared with developed countries. Although trimodality therapy has improved the outcome but still 30% of LABC patients died at the end of two years after completing their

Table 2. (a) Clinical characteristics of patients with LABC (N = 28); (b) Presenting symptoms of patients.

(a)	
Patients characteristics	Frequency
Female	100%
Family H/O breast cancer	4%
Right sided lesion	64%
Left sided lesion	36%
Median Age	45 Years
Median Duration of presentation	8 months
(b)	
Symptom	Frequency
Lump with skin ulceration	20%
Fungating	10%
Fixed lump	70%

Table 3. Tumor biology.

Tumor characteristics	Frequency
IDC	96% (4% other histology)
Grade II	61%
Grade III	39%
ER+/PR+	60%
ER-/PR-	40%
H2N Positive	25%
Unknown Receptor status	3%
Node positive	74%

Table 4. Clinical outcome of patients.

Survival	Frequency
Mortality within 2-years	30%
Alive more than 2-years	70%
Disease free survival for more than two years	25%
Re-currence/metastases in those survived for more than 2-years	70%

treatment. This number can be even more because some patients lost to follow up. Another study on Pakistani women also reported poor outcome [10]. It's very important to figure out causes of LABC and difficulties being faced by doctors to treat such cases consequently such information will help health authorities to develop plans to deal with LABC in public sector and oncologist to develop management strategies.

In literature, many studies have identified lack of awareness, fear, lower socioeconomic status and illiteracy as main factors leading to late presentation and ending up in Locally advanced disease [11] [12] [13] [14]. These factors are common among all developing countries including Pakistan [15]. Another important factor which could be the cause of locally advanced disease is its aggressive biological behavior as node positive disease was found in 74 percent patients after surgery. Secondly despite the fact that 60 percent were ER/PR receptor positive and they also received hormone therapy even then they develop recurrence or metastatic disease. Racial differences in biology of carcinoma breast have been well described. Japanese women tend to have less aggressive breast cancer among Asians [6]. Within USA Afro-Americans and Hispanic women have more aggressive disease as compare to others USA [7] [8]. Other factors which are compromising outcome are delay in seeking the treatment and unavailability of adequate oncological services [9] [16]. Surgical services are present in every tertiary care center in Pakistan but very few tertiary centers have parallel oncological services which further compromise the management of LABC patients in our pop-

ulation. When we refer them to oncology centers after surgery, most patients get lost because of economic constraints and long waiting time at such centers. These factors are totally manageable so by increasing awareness and oncological facilities to improve the outcome.

Conflicts of Interest

There is no conflict of interest. This is a research/analysis based work.

References

- [1] Singletary, S.E., Allred, C., Ashley, P., Bassett, L.W., Berry, D., Bland, K.L., *et al.* (2002) Revision of American Joint Committee on Cancer Staging System for Breast Cancer. *Journal of Clinical Oncology*, **20**, 3628-3636. <https://doi.org/10.1200/JCO.2002.02.026>
- [2] Giordano, S.H. (2003) Update on Locally Advanced Breast Cancer. *Oncologist*, **8**, 521-530. <https://doi.org/10.1634/theoncologist.8-6-521>
- [3] Hisham, A.N. and Yip, C.H. (2003) Spectrum of Breast Cancer in Malaysian Women. *World Journal of Surgery*, **27**, 921-923. <https://doi.org/10.1007/s00268-003-6976-x>
- [4] Ten, E.Y., Wong, H.B., Ang, B.K. and Chan, M.Y. (2005) Locally Advanced and Metastatic Breast Cancer in a Tertiary Hospital. *Annals of the Academy of Medicine of Singapore*, **34**, 595-601.
- [5] Agrawal, G., Paradeep, P.V., Aggarwal, V., Yip, C.H. and Cheung, P.S. (2007) Spectrum of Breast Cancer in Asian Women. *World Journal of Surgery*, **31**, 1031-1040. <https://doi.org/10.1007/s00268-005-0585-9>
- [6] Edwards, M.N., Grornel, J.W. and Vaughn, W.P. (1998) Infiltrating Ductal Carcinoma of the Breast: The Survivors Impact of Race. *Journal of Clinical Oncology*, **16**, 2693-2699. <https://doi.org/10.1200/JCO.1998.16.8.2693>
- [7] Gililand, F.D., Hunt, W.C. and Key, C.R. (1998) Trends in the Survival of American, Indian, Hispanic and Non-Hispanic White Cancer Patients in New Mexico and Arizona, 1969-1994. *Cancer*, **82**, 1769-1783.
- [8] Joslyn, S.A. and West, M.M. (2000) Racial Differences in Breast Carcinoma Survival. *Cancer*, **88**, 14-23. [https://doi.org/10.1002/\(SICI\)1097-0142\(20000101\)88:1%3C114::AID-CNCR16%3E3.0.CO;2-I](https://doi.org/10.1002/(SICI)1097-0142(20000101)88:1%3C114::AID-CNCR16%3E3.0.CO;2-I)
- [9] Thongsuksai, P., Chongsuvativitwong, V. and Sriplung, H. (2000) Delay in Breast Cancer Care: A Study in Thai Women. *Medical Care*, **38**, 108-114. <https://doi.org/10.1097/00005650-200001000-00012>
- [10] Iqbal, J., Bano, K., Saeed, A., Akram, M. and Aziz, Z. (2010) Survival of Women with Locally Advanced Breast Cancer at a Teaching Hospital in Lahore. *Journal of Pakistan Medical Association*, **60**, 721-725.
- [11] Hackett, T.P., Casscm, N.H. and Raker, J.W. (1973) Patient Delay in Cancer. *New England Journal of Medicine*, **289**, 14-20. <https://doi.org/10.1056/NEJM197307052890104>
- [12] Adams, S.A., Homer, J.K. and Vessey, M.P. (1980) Delay in Treatment for Breast Cancer. *Community Medicine*, **2**, 195-201.
- [13] Nichols, S., Waters, W.E., Fraser, J.D., Wheeler, M.J. and Ingham, S.K. (1981) Delay in the Presentation of Breast Symptoms for Consultant Investigation. *Commu-*

nity Medicine, **3**, 217-225.

- [14] Elzawawy, A. (1999) Delay in Seeking Medical Advice by Breast Cancer Patients Presenting with Breast Lump. *Cancer Strategy*, **1**, 16-19.
- [15] Malik, L.A. (2002) Clinico-Pathological Features of Breast Cancer in Pakistan. *Journal of Pakistan Medical Association*, **52**, 100-104.
- [16] Arndt, V., Sturmer, T., Stegmaier, C., Ziegler, H., Dhom, G. and Brenner, H. (2000) Patient Delay and Stage of Diagnosis among Breast Cancer Patients in Germany—A Population Based Study. *British Journal of Cancer*, **86**, 1034-1040.
<https://doi.org/10.1038/sj.bjc.6600209>