Presentation, diagnosis and management of locally advanced breast cancer: Is it different in low/middle income countries?

Shahneela Manzoor1, Mariyah Anwer2, Salim Soomro3, Dileep Kumar4

ABSTRACT
Background and Objective: Breast cancer incidence is increasing and it is highest in low income countries. The main challenge is regarding awareness, screening, late presentation and its management in a third-world country. Our objective was to share the experience faced in various presentations, diagnosis and management of locally advanced breast cancer (LABC) in a third world country and discuss if they are different with respect to developed countries.

Methods: It is a retrospective case series study performed at Jinnah Postgraduate Medical Centre Karachi, from January 2015 to December 2017, over period of three years. Data was collected from the record maintained by authors about patients presenting in breast clinic. Patients of breast cancer were managed in breast clinic over 3 years. Our study included patients who presented with LABC based on their clinical presentation confirmed by histopathological diagnosis and followed by surgical management. Statistical analysis for students t-test was performed using SPSS (version 20.0). A p-value less than 0.05 was considered statistically significant.

Results: One hundred twelve patients presented with LABC over period of 3 years. All but two were female. Mean age was 52 years (range 26-78 years), SD 18.96. On presentation size of tumor was 5cm & more in 103 (91.9%) patients. Involvement of axilla was in 86 (76.7%). Chest wall was involved in 22 (19.6%). Total T3 and T4 were 71 (63.3%) and 41 (36.6%) respectively Diagnosis of all patients was confirmed by histopathology. Neoadjuvant was given to all patients to downstage the tumor. ER/PR was positive in 46(41.1%), HER-2/neu positive in 31 (27.6%). On staging breast carcinoma was metastatic in 13(11.6%) with liver, lung and bone in 4 (3.5%), 3 (2.7%) and 6 (5.3%) respectively. Breast conservation was done in 6 (6.1%) patients, Modified Radical Mastectomy was done in 86 (86.9%), Radical Mastectomy in 3 (3.03%), Toilet Mastectomy in 4 (4.045) and 13 (11.6%) patients were not operated.

Conclusion: In our series 65% of all breast cancers are LABC at presentation. In low/middle income countries high percentage of LABC at presentation result in high metastatic disease, poor prognosis and limits conservation of breast. Awareness and education can improve outcomes.

KEYWORDS: Breast Cancer, Third-World Countries.

How to cite this: Manzoor S, Anwer M, Soomro S, Kumar D. Presentation, diagnosis and management of locally advanced breast cancer: Is it different in low/middle income countries (LMICs)?. Pak J Med Sci. 2019;35(6):1554-1557.
doi: https://doi.org/10.12669/pjms.35.6.165

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/3.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

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. Since 2008, breast cancer incidence has increased by over 20% and breast cancer deaths have risen by 14%. 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.

The majority of women present with advanced disease stage III and IV and the 5-year survival rate in less than 50%. Advance breast cancer and its high mortality are seen with delay in diagnosis and treatment. 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. Our aim of study was to share the experience faced in various presentations, diagnosis and management of locally advanced breast cancer (LABC) in a third world country and discuss if they are different with respect to developed countries.

METHODS

It is a retrospective case series study done in surgical ward of a teaching hospital Jinnah Postgraduate Medical Center in Karachi Pakistan, in three years from January 2015 to December 2017. Data was collected from the record maintained by authors about patients presenting in breast clinic. Total 172 patients of breast cancer were managed in breast clinic over three years. Patients admitted in surgical ward from surgical OPD were enrolled in the study after taking informed consent. Our study included 112 patients i.e. 65% of total patients, who presented with LABC based on their clinical presentation confirmed by histopathological diagnosis and followed by surgical management. Patients of early breast cancer were excluded.

Statistical analysis for students t-test was performed using SPSS (version 20.0). A p-value less than 0.05 was considered statistically significant. The study was approved by the JPMC Ethics Committee (F2-81-GENL/JPMC).

RESULTS

One hundred twelve patients presented with LABC over period of three years. All but two were female. Mean age was 52 years (range 26-78 years), SD 18.96. On presentation size of tumor was 5cm & more in 103 (91.9%) patients. Involvement of axilla was in 86 (76.7%). Chest wall was involved in 22 (19.6%). Total T3 and T4 were 71 (63.3%) and 41 (36.6%) respectively (Fig.1). Diagnosis of all patients was confirmed by histopathology. Neoadjuvant was given to all patients to downstage the tumor. ER/PR was positive in 46(41.1%), HER-2/neu positive in 31 (27.6%). On staging breast carcinoma was metastatic in 13(11.6%) with liver, lung and bone in 4 (3.5%), 3 (2.7%) and 6 (5.3%) respectively (Table-I). Breast conservation was done in 6 (6.1%) patients, Modified Radical Mastectomy was done in 86 (86.9%), Radical Mastectomy in 3 (3.03%), Toilet Mastectomy in 4 (4.04%) and 13 (11.6%) patients were not operated.

Table-I: Result showing Clinical presentation, diagnosis and management of LABC in LMIC.

| Characteristics                                  | n=112(%) |
|-------------------------------------------------|----------|
| Age in years                                    |          |
| Mean                                            | 52       |
| Range                                           | 26-78    |
| Presentation                                    |          |
| Size of tumor 5cm & more                       | 103 (91.9%) |
| Skin involvement                               | 77 (68.7%)  |
| Fungating mass                                  | 17 (15.2%) |
| Discharging sinus                               | 14 (12.5%) |
| Nipple excoriation                              | 19 (16.9%) |
| Axilla involvement                              | 86 (76.7%) |
| Chest wall involvement                         | 22 (19.6%) |
| T3                                              | 71 (63.3%) |
| T4                                              | 41 (36.6%) |
| Diagnosis                                       |          |
| Histopathology                                  | 112 (100%) |
| Neoadjuvant Chemotherapy                        | 112 (100%) |
| ER/PR status                                    |          |
| ER and/or PR positive                           | 46 (41.1%) |
| ER and/or PR negative                           | 66 (58.9%) |
| HER-2/neu status                                |          |
| Positive                                        | 31 (27.7%) |
| Negative                                        | 81 (72.3%) |
| Staging                                         |          |
| Non-metastatic                                  | 99 (88.4%) |
| Metastatic                                      | 13 (11.6%) |
| Liver                                           | 4 (3.5%)  |
| Lung                                            | 3 (2.7%)  |
| Bone                                            | 6 (5.3%)  |
| Surgery                                         |          |
| Breast conservation                             | 6 (6.1%)  |
| Modified radical mastectomy                     | 86 (86.9%) |
| Radical Mastectomy                              | 3 (3.03%) |
| Toilet Mastectomy                               | 4 (4.04%) |
| Not operated                                    | 13 (11.6%) |
DISCUSSION

Our study supports the literature that patient’s delay (delay between individuals’ first awareness of breast abnormality and initial medical consultation) is a common factor that contributes to late detection of breast cancer and presentation at any healthcare facility. It is believed that around 20–30% of women with symptoms of breast cancer wait three months before consulting their physicians.8 This is explained by many facts; as it has also been shown that even cells from in situ carcinoma can metastasize.9 In the USA, breast cancer death rates decreased by 36% between 1989 and 2012.10 These improvements were driven by combined improvements in early detection and adjuvant systemic therapy.11 The implementation of screening and treatment policies for breast cancer control that have shown success in high-income settings might be beyond the reach of many countries.12 The common occurrence of late presentation and advanced stage in LMICs compared with UMICs13 contributes to morbidity, a substantial loss of productive life for patients and productive capacity within the community, and, ultimately, to increased breast cancer mortality.13,14 Data that support the benefits of early detection stems from UMICs,15,16 where resources are limitless. Thus, only one in seven women (15%) in UMICs present with locally advanced or metastatic breast cancer.16 This is in contrast to LMICs, where nearly two of three women have locally advanced or metastatic disease at the time of presentation.13

Our series describes that 65% of our breast cancers are locally advanced at presentation. In developing world late presentation due to mainly social factors leads to compromised outcome for the patients. As opposed to the Western societies where majority of patients are presenting with early cancers, our numbers are telling the story of high morbidity and mortality.

In absence of National screening programs and widely available Mammography due to lack of resources leads to delayed pick up of disease relying on patient’s self-pick up of the disease. Ironically recent studies show breast physical examination and breast self-examination to be unhelpful in reducing stage at diagnosis17 which we used to advocate to our patients initially.

It is also seen that effective therapy may help lower breast cancer death rates after detection18,19 but still mortality remains high. Neoadjuvant chemotherapy is recommended for women with LABC. Chemotherapy recommendations according to national resources have also been published by the Breast Health Global Initiative.20

National diagnostic and treatment guidelines are needed to establish a “standard of care” and promote the rational use of existing resources and greater equity in access to treatment, as stated by WHO.21 It cannot be stressed enough that educating women is suggested in all countries to help achieve early detection and treatment.22 Evidence-based guidelines outlining optimal approaches to breast cancer detection, diagnosis and treatment have been well developed and disseminated in several high-resource countries.23 Breast imaging, initially with ultrasound and, at higher resource levels, with diagnostic mammography, improves pre-operative diagnostic assessment, and also permits image-guided needle sampling of suspicious lesions. Diagnostic mammography and magnetic resonance imaging (MRI), while helpful for breast-conserving surgery, are not mandatory in LMCs when these resources are lacking.24 The ability to perform modified radical mastectomy (MRM) is the mainstay of locoregional treatment at the basic level of breast healthcare.25

CONCLUSION

In our series 65% of all breast cancers are LABC at presentation. In low/middle income countries high percentage of LABC at presentation result in high metastatic disease, poor prognosis and limits conservation of breast. Awareness and education about breast cancer can have long term impact to reduce the suffering and improve outcomes.
REFERENCES

1. Ogundiran TO, Ayandipo OO, Ademola AF, Adebamowo CA. Mastectomy for management of breast cancer in Ibadan, Nigeria. BMC Surg. 2013;13:59. doi: 10.1186/1471-2482-13-59

2. El Saghir NS, Khalili MK, Eid T, El Kinge AR, Charafeddine M, Geara F, et al. Trends in epidemiology and management of breast cancer in developing Arab countries: a literature and registry analysis. Int J Surg. 2007;5:225-233. doi: 10.1016/j.ijsu.2006.06.015

3. Burstein, HJ, Harris, JR, Morrow, M. Malignant tumors of the breast. In: DeVita, VT, Lawrence, TS, Rosenberg, SA, eds. Cancer: Principles and Practice of Oncology. Philadelphia, PA: Lippincott Williams & Wilkins; 2011:1606–1645.

4. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer. 2015;136(5):E359-E368. doi: 10.1002/ijc.29210

5. Mahmood S, Rana TF, Ahmad M. Common determinants of Ca breast - a case control study in Lahore. Ann King Edward Med Coll. 2006;12(2):227-228. doi: 10.21649/akemu.v12i2.880

6. Montazeri A, Ebrahimi M, Mehrdad N, Ansari M, Sajadian M, Delayed presentation in breast cancer; a study in Iranian women. BMC Women Health. 2003;3:4. doi: 10.1186/1472-6874-3-4

7. Stanley NC Anyanwu. Temporal trends in breast cancer presentation in the third world. J Exp Clin Cancer Res. 2008;27:17. doi: 10.1186/1756-9966-27-17.

8. Ramirez AJ, Westcombe AM, Burgess CC, Sutton S, Littlejohns P, Richards MA. Factors predicting delayed presentation of symptomatic breast cancer: a systematic review. Lancet. 1999;353:1127-1131. doi: 10.1016/S0140-6736(99)02142-X

9. Husemann Y, Geigl JB, Schubert F, Musiani P, Meyer MA, Burghart E, et al. Systemic spread is an early step in breast cancer. Cancer Cell. 2008;13:58-68. doi: 10.1016/j.ccr.2007.12.003

10. DeSantis CE, Lin CC, Mariotto AB, Siegel RL, Stein KD, Kramer JL, et al. Cancer treatment and survivorship statistics, 2014. CA Cancer J Clin. 2014;64(4):252-271. doi: 10.3322/caac.21235

11. Berry DA Cronin KA, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer. 2015;136(5):E359-E368. doi: 10.1002/ijc.29210

12. Stanley NC Anyanwu. Temporal trends in breast cancer presentation in the third world. J Exp Clin Cancer Res. 2008;27:17. doi: 10.1186/1756-9966-27-17.

13. El Saghir NS, Khalili MK, Eid T, El Kinge AR, Charafeddine M, Geara F, et al. Trends in epidemiology and management of breast cancer in developing Arab countries: a literature and registry analysis. Int J Surg. 2007;5:225-233. doi: 10.1016/j.ijsu.2006.06.015

14. Burstein, HJ, Harris, JR, Morrow, M. Malignant tumors of the breast. In: DeVita, VT, Lawrence, TS, Rosenberg, SA, eds. Cancer: Principles and Practice of Oncology. Philadelphia, PA: Lippincott Williams & Wilkins; 2011:1606–1645.

15. Ogundiran TO, Ayandipo OO, Ademola AF, Adebamowo CA. Mastectomy for management of breast cancer in Ibadan, Nigeria. BMC Surg. 2013;13:59. doi: 10.1186/1471-2482-13-59

16. American Cancer Society: Breast Cancer Facts and Figures 2015-2016. Atlanta, GA, American Cancer Society, 2016.

17. Thomas DB, Gao DL, Ray RM, Wang WW, Allison CJ, Chen FL, et al. Randomized trial of breast self-examination in Shanghai: final results. J Natl Cancer Inst. 2002;94(19):1445-1457. doi: 10.1093/jnci/94.19.1445

18. Harmer V. Breast cancer, part 2: present and future treatment modalities. Br J Nurs. 2008;17(16):1028-1030. doi: 10.12968/bjon.2008.17.16.31068

19. Wadler BM, Judge CM, Prout M, Allen JD, Geller AC. Improving breast cancer control via the use of community health workers in South Africa: a critical review. J Oncol. 2011;2011:1-8. doi: 10.1155/2011/150423

20. Anderson BO, Yip CH, Smith RA, Shyryan R, Seener SF, Eniu A, et al. Guideline implementation for breast healthcare in low-income and middle-income countries: overview of the breast health global initiative global summit 2007. Cancer. 2008;113(Suppl.2):2221-2243. doi: 10.1002/cncr.23844

21. Executive summary of the national cancer control programs: policies and managerial guidelines. World health Organization: Geneva 2002; pp 1-24

22. Ghoncheh M, Pournamdar Z, Salehiniya H. Incidence and mortality and epidemiology of breast cancer in the world. Asian Pac J Cancer Prev. 2016;17(33):43-46. doi: 10.7314/APJCP.2016.17.S3.43

23. Goldhirsch A, Wood WC, Gelber RD, Coates AS, Thürlimann B, Senn HJ, et al., Progress and promise: highlights of the international expert consensus on the primary therapy of early breast cancer 2007. Ann Oncol. 2007;18(7):1333-1344. doi: 10.1093/annonc/mdm271

24. Nadkarni MS, Gupta PB, Parmar VV, Badwe RA. Breast conservation surgery without pre-operative mammography-A definite feasibility. Breast. 2006;15(5):595-600. doi: 10.1016/j.breast.2006.01.010

25. Eniu A, Carlson RW, El Saghir NS, Jose Bines J, Bese SM, Geara F, et al. Trends in epidemiology and management of breast cancer in Ibadan, Nigeria. BMC Surg. 2013;13:59. doi: 10.1186/1472-6874-3-4

Author’s Contribution:

SM did data collection and manuscript writing.
MA conceived, designed and did statistical analysis & editing of manuscript.
SS did review and final approval of manuscript.
DK did data collection.

Authors:

1. Dr. Shahneela Manzoor, MBBS, FCPS Trainee (General Surgery).
2. Dr. Mariyal Anwer, MBBS, FCPS. Assistant Professor of Surgery.
3. Dr. Salim Ahmed Soomro, MBBS, FCPS. Professor of Surgery.
4. Dr. Dileep Kumar, MBBS, FCPS. Associate Professor of Surgery.
5. Dr. Nadeem Jaffar, MBBS, FCPS. Assistant Professor of Surgery.

Correspondence:

Dr. Mariyal Anwer, MBBS, FCPS.
Assistant Professor of Surgery.
Ward 2, Jinnah Postgraduate Medical Center, Rafiqlu Shaheed Road,
Karachi, 75510 Pakistan.
Email: medbooksall@yahoo.com