Original Research Article

Growing burden of breast cancer in Bihar a state of eastern India – epidemiology, treatment, and outcome.

Abstract:

Background: Worldwide, the incidence and mortality of breast cancer are rising rapidly, and emerging countries are particularly affected by this change. Globally 25%, or 2.1 million cases, of all female cancers diagnosed in 2018 were breast cancer. The leading cause of death for women is breast cancer. The present study was aimed to report the patient demographics, age, histopathology, stage, and status of presentation, compliance with treatment, follow-up, and survival.

Methods: Our cancer centre has evaluated breast cancer data of (n=422) patients over the period of January 2017 to December 2021. Retrospectively database of patients with breast cancer available in our medical records department and Hospital-Based Cancer Registry software were reviewed. The data were analyzed using IBM SPSS 26.0.

Results: A total of 422 breast cancer cases were registered in our hospital. Of these (n=389; 92.18%) had received treatment. This study has reported a good survival rate of 62.21%, patients (n=242; 62.21%) are alive (n=43; 17.77%) survived with disease free, (n=59; 24.38%) with residual disease and patients (n=84; 19.79%) were expired due to disease progression. The outcomes of triple-negative breast cancer were poor and the treatment options are mainly restricted to systemic chemotherapy. Mortality rates reported in triple negative breast cancer were 80.91%.

Conclusion: The survival rates in this study were reported 62.21%. Breast cancer is spreading aggressively in India. Multicentre clinical trials on breast cancer must be carried out in tier two three cities of India. The requirement is for a strong awareness campaign and the efficient implementation of a national cancer screening programme.

Key words: Bihar, Breast Cancer, Treatment, Outcome, Survival.

Introduction:

In India, breast cancer is very predominant[1]. Breast cancer (BC) is a terrible illness that primarily affects women in India who are of reproductive age and has a significant financial impact[2]. "In 2020, the worldwide cancer incidence and fatalities reached 19.3 million and 10 million, respectively. For the year 2020, the estimated incidence of cancer among females in India was 712758 (104 per 100000)" [3, 4] "the origin of breast cancer is unclear. However, a number of risk factors, including ageing, genetics, radiation exposure, obesity, postponed pregnancy, and alcohol".[5] "According to the 'International Agency for Research on Cancer' (IARC), delayed diagnosis leads to poorer probable outcome or prognosis of breast cancer.[6] It is the most predominant cancer in women, accounting for about a quarter of all cancer cases in Indian cities, and ranking second in rural India" [3 7]. **"**Current trends point out that a higher proportion of the disease is occurring at a younger age in Indian women, compared to the West. In regard to the 5-year overall survival, a study reported it to be 95% for stage I patients, 92% for stage II, 70% for stage III, and only 21% for stage IV patients" [8]. "The survival rate of patients with breast cancer is poor in India compared to Western countries due to earlier age at onset, late stage of disease at presentation, delayed initiation of definitive management, and inadequate/fragmented treatment" [9]. "According to the World Cancer Report 2020, the most efficient intervention for BC control is early detection and rapid treatment" [10]. "A 2018 systematic review of 20 studies reported that BC treatment costs increased with a higher stage of cancer at diagnosis. Consequently, earlier diagnosis of BC can lower treatment costs" [11].

"The Indian Council of Medical Research (ICMR) reported 1.5 lakh new breast cancer cases in 2019, with 70 000 deaths per year. In India, only 66% of women with breast cancer survive for 5 years, compared with 90% of women in the USA" [12]. "The stage of cancer is determined by a series of clinical examinations, radiological modalities (mammography, ultrasonography, PET/CT/MRI, Bone Scans), pathology (aspiration, biopsies) and blood tests. Oncologists use a comprehensive strategy to treat breast cancer such as surgery, hormone/ targeted therapy, chemotherapy, radiation therapy, and biological therapies. Despite advancements in therapy and awareness initiatives, the dangers linked with breast cancer continue to grow in India. Poor diagnosis and costly treatment lead to a high death rate" [13].

Meterials and Methods:

This was a descriptive study carried out at a tertiary cancer center in Patna, India. Retrospectively, data analysis was done for (n=422) histopathologicaly confirmed cases of breast cancer patients over the period of 5 years (January 2017 – December 2021). Medical Record Department and Hospital-Based Cancer Registry databases were analyzed. The data were collected in a standard pro forma. The variables used for analysis were the mode of patient demographics, histology, age, stage and clinical presentation, compliance with treatment, follow-up, and survival. The details of inclusion and exclusion criteria, sample size, data collection, and analysis are given below:

Inclusion criteria:

- Women between 18 – 75 years of age were included in the study.
- Willing to give their consent for data analysis and paper publications.

Exclusion criteria:

- Child bearing/ lactating women.
- Not willing to give consent.

Sample size: 422 confirmed cases of breast cancer patients.

Data collection tools: Electronic Case Report Form (eCRF).

Source of data: Medical Record Department & Hospital-Based Cancer Registry Software.

Statistical analysis: The data were analyzed using IBM SPSS 26.0 package. Descriptive analysis was provided for the qualitative variables by frequency and percentages.

Ethics clearance will not be obligatory because this review has involved data available in our medical records and Hospital-Based Cancer Registry software.

Mode of contact: Status at last follow-up was confirmed either through medical records or telephonically.

Result:

A total of (n=422) breast cancer patient data were studied. All cases were identified to have registered with Savera Cancer and Multispeciality Hospital from January 2017 – December 2021. The variables were classified as per age, gender, clinical presentation, ECOG score and stage, imaging modalities, treatment procedures, follow-up and their geographical location in the

state of Bihar. Patients were found to be suffering from breast cancer in Stage I – Stage IV. Patients from different regions of Bihar were included in the study.

Age distribution

In this study, we demonstrated patient age groups of 21-40, 41-60, and 61-85. It is seen that patients below 20, that is, relatively young in age and diagnosed with BC were rare to find, the ones in the age group of 21-40 were maximum (n= 101; 23.93%) in number. Patients in age brackets of 41-60 were the highest (n= 219; 51.90%) in number and age groups of 61-85 were (n=102; 24.17%).

Geographical distribution

Area wise distribution of breast cancer patients was done and interesting observation is seen. Maximum number of cases registered are residents of rural districts of Bihar, in fact, 62.32% (n=263) of all cases were registered from Patna. State capital Patna registered approximately 37.44% (n=158) patients. Cases from rural areas were the highest may be due to lack of awareness, missed diagnosis, untrained practitioners, infrastructures, etc.

Breast cancer patients clinically presented with painful lumps (n= 89; 21.09%), painless lumps (n=167; 39.57%), nipple discharge with ulcerative lesions and axillary lymph nodes (n=131; 31.04%) and (n=35; 8.29%) patients were presented with distant metastasis. ECOG performance status scale was used to clinically measure an individual's ability to engage in physical activity and care for self. This study demonstrated ECOG Scale 0 (n=24; 5.69%), 1 (n=89; 21.09%), 2 (n=122; 28.91%), 3 (n=112; 26.54%), 4 (n=76; 18.01%) patients respectively.

Depending on the frequency, data of 5 major types of breast cancer patients were reviewed for the study: Ductal carcinoma in situ (DCIS; 44.08%), Infiltrating ductal carcinoma (IDC; 40.52%), Infiltrating lobular carcinoma (ILC; 5.21%), inflammatory breast carcinoma (3.03%), and Mixed Carcinoma (1.10%). Alone, DCIS and IDC types were highest in number (88.60%). Another important variable we observed in this study was the anatomical site of the breast. Right and left breast cancer patients were 53.55% and 45.97%, where as bilateral involvement was only (n=3; 0.71%). Breast cancer staging was done as per the TNM AJCC 7th Edition guidelines. In Stage I (0.24%), Stage II (16.59%), Stage III (55.21%), and Stage IV (12.80%) BC patients were reported to our cancer centre. Mammography and USG was performed in 78.44% patients as a preliminary investigation to rule out breast malignancy as per BIRADS criteria. Then CT/PET was advised in 31.28% BC patients to rule out the extent of the disease (metastasis).

MRI of the breast was also advised in a few patients (9.72%). Histopathology was done in 90.05% patients. IHC markers ER, PR positive (9.74%), Her 2 Neu positive (6.05%), ER, PR, Her 2 Neu positive (2.37%) and Triple Negative was found in 8.68% patients. Only 1.32% patients were advised to do FISH test.

Treatment and outcome

Management of BC is multidisciplinary and has come a long way. Breast cancer is commonly treated by various combinations of surgery, chemotherapy, radiation therapy, hormone therapy, and targeted therapy via a multimodality approach. Text Figure 03 illustrates the management of breast cancer patients at our centre. A total of (n=389; 92.18%) patients administered different treatments including Surgery alone (25.69%), surgery and chemotherapy (14.93%), surgery + chemotherapy + radiation therapy (12.32%), chemotherapy + radio therapy (9.24%), chemotherapy + hormonal/ targeted therapy (9.48%) and others were 8.53%).

"The field of breast surgery has also evolved from total mastectomy to breast conservation therapy to oncoplastic breast surgery. The rapidly advancing field of oncoplastic breast surgery offers a pragmatic alternative to total mastectomy and breast conservation therapy. It is currently nascent but expected to attain mainstream status in the near future as oncoplastic breast surgery has economic feasibility and cost-effectiveness and is well suited for a low-resource setting such as India" [33].

At the end of the result we concluded with response evaluation, post-treatment and during the routine follow-up of the patients. In figure 04, patients (n=389; 92.18%) had received treatment at our centre, patients (n=242; 60.21%) are alive (n=43; 17.77%) survived with disease free, where as in (n=59; 24.38%) cases residual disease reported, patients (n=84; 19.79%) were expired due to disease progression and approximately (n=33; 7.82%) patients refused treatment due to financial reasons or referred to higher centers.

Outcome

This study has reported a good survival rate of 62.21%. The outcomes with triple-negative breast cancer were poor and the mortality rate alone reported was 80.91%. The treatment options are mainly restricted to systemic chemotherapy. Patients approaching from rural areas were highest in number (62.33%).

Discussion:

The median age of presentation was 43 years, so most of the patients were below 50 years. Studies suggested that the disease peaks at 40–50 years in Indian women [14]. "Literatures from West revealed the median age of women at the time of diagnosis of breast cancer is approximately 61 years in the Western world, with the peak age being 60 to 70 years; however, in India, a higher proportion of patients with breast cancer tend to be premenopausal, and the peak age is between 40 and 50 years" [15, 16]. Our study demonstrated 55.21% BC patients presented to our hospital in Stage III. According to various studies, the majority of BC cases in the west reported in stage I and II, whereas in India 45.7% reported in advanced stages [17, 18]. Gogia et al have shown in their study nearly 60% of BC patients were diagnosed at stage III [19].

The initial presentation of BC is a lump which is generally not associated with pain. This adds to the delay in seeking treatment in 50%-70% of the cases in rural areas. Our study illustrated 39.57% BC patients presented with painless lump, ulcerative lesions with nipple discharge, and axillary lymph nodes in (31.04%) and (27.29%) patients were presented with distant metastasis. A study by Shinde S et al found similar clinical presentations, changes in the shape/ size of the breast, discharge from nipple, and inverted nipple as danger signs of breast cancer [20].

20. Shinde S, Kadam S. Breast cancer awareness among women in Vikhroli: a suburban area of Mumbai, Maharashtra, India. Int J Community Med Public Heal. 2016; 3(8):2281–6.

Mammography is one of the most effective and popular modalities presently used for breast cancer screening and detection. Mammography and USG breast data suggested a 78% BC patients went through this modality. Barton MB et al. found that "clinical breast examination along with mammography, as screening tools; have a role in reducing mortality" [21].

Mammography is the gold standard in breast cancer imaging. However, it is restricted to detection in dense breast tissues [22]. Greenwood et al. have shown in their study, mammography reduces the mortality rate about 20–40% [23]. The United States Preventive Services Task Force (USPSTF) has recommended mammography every 2 years and after the age of 50 [24]. Majority of the patients (80%) in this study were evaluated by sonomammography followed by core biopsy of the breast. Khan et al also observed in their study the sensitivity of sonomammography in detecting benign breast lesions is 95.23% while that of malignant is 100% [25]. Similarly, Badu-

Peprah et al assessed "the overall sensitivity and specificity of mammography and sonomammography that was found to be 73%, 80% and 100%, 80.4% respectively" [26]. "MRI imaging is more sensitive than mammography and ultrasound in the diagnosis of breast cancer, and it is relatively cost-effective. Studies have shown that MRI has detected 14.7 new cases of cancer per 1000 people when used as a complementary method in people who have already had mammography and ultrasound" [26]. We also found that only 9.72% patients underwent MRI in the present study. A study by Phillips et al revealed a major challenge of MRI for breast imaging along with the high cost and time of the scan as patients' difficulty in maintaining proper posture [28]. In the present study, the majority of the BC patients underwent upfront surgery, 35% were treated with NACT regime, and 15% administered palliative treatment. The primary means of local and regional breast cancer treatment remains surgical intervention. Fischer et al and Veronesi et al reported that "survival with lumpectomy and radiation was equivalent to that with mastectomy in the treatment of early breast cancer".

Krop et al found in randomized trials that patients with HER2-positive metastatic breast cancer received taxane along with trastuzumab and pertuzumab as first-line therapy and had a better prognosis [31]. This study found that the survival rate of breast cancer patients in India is only 62% where as in the west it is 90-%. A recent Lancet publication on global data showed age-standardized net survival with breast cancer of 80% or more in 34 countries [32]. TNBC is still a continuing challenge to treat. Our study data reported an 80% mortality rate alone in this setting. Triple-negative breast cancer tends to be more aggressive, harder to treat, and more likely to recur than other forms of the disease, such as hormone receptor–positive or HER2-positive breast cancer. Conventional chemotherapy drugs have not been effective against triple-negative breast cancer, and new treatment options are needed.

Conclusion:

To conclude, the BC burden is rising at a rate much faster than it was a decade ago. Breast cancer is one of the foremost cancers in India now would be the first step towards making people cognizant of the disease. This study reported 62% survival rate only where as in the west it is 90%. A robust awareness campaign and effective implementation of a national cancer screening program are the need of the hour. A large multicentre clinical trial on TNBC needs to be conducted in tier 2/3 cities of India. Additionally, PBCR programs must be implemented in

cancer institutions based in Bihar. To combat the consequences as a country, better preparedness is essential. We also need to stand up and deliver on the healthcare front. The shortage of skilled manpower and infrastructural requirements needs to be met, and for this, the total healthcare budget of the country needs to be increased.

Consent

As per international standard or university standard, patient(s) written consent has been collected and preserved by the author(s).

Abbreviations:

AJCC	: American Joint Committee on Cancer
BC	: Breast cancer
BIRADS	: Breast imaging reporting and data system
CHEMO	: Chemotherapy
eCRF	: Electronic case report form
ECOG	: Eastern Cooperative Oncology Group
ER	: Estrogen receptor
HBCR	: Hospital Based Cancer Registry program
Her-2/Neu	: Human epidermal growth factor receptor 2
IHC	: Immunohisto cytology
ICMR	: Indian Council of Medical Research
MMG	: Mammography
MRD	: Medical Record Department
MRM	: Modified radical mastectomy
NACT	: Neo-adjuvant chemotherapy
PBCR	: Population-Based Cancer Registry Program
PR	: Progesterone receptor
RT	: Radiation therapy
SCMH	: Savera cancer and multispeciality hospital
TNBC	: Triple negative breast cancer

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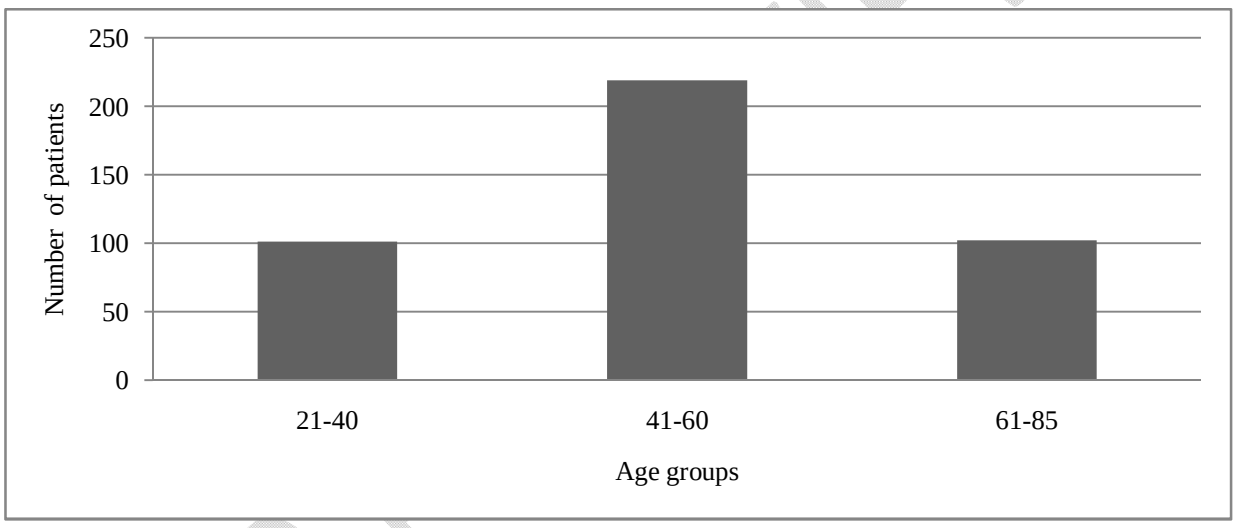
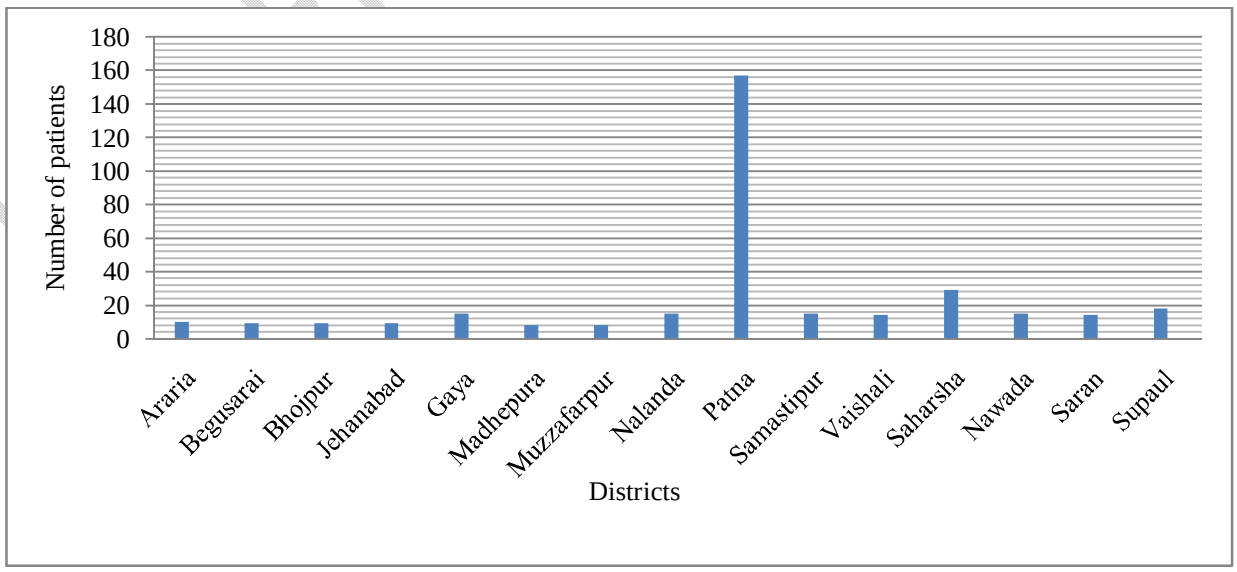
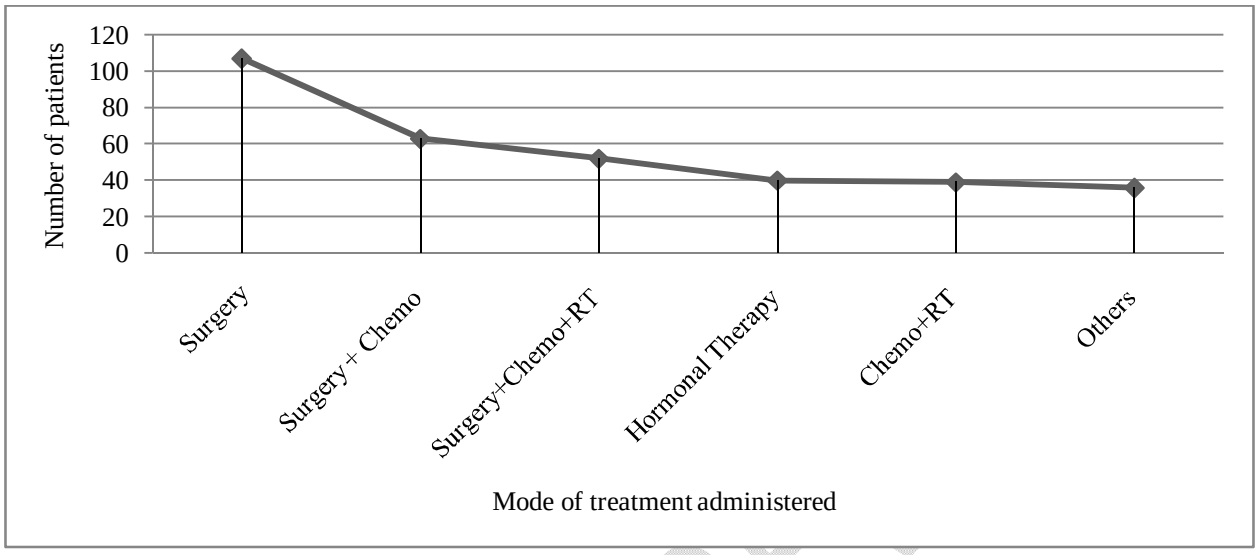
Figures:



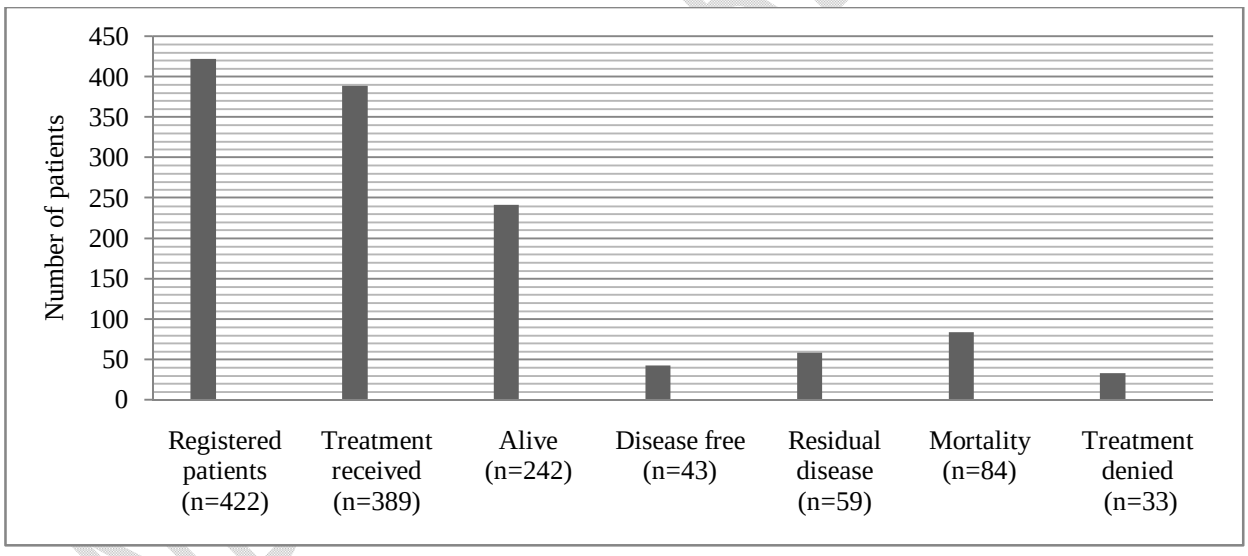
Text Fig.01- Graph depicting cancer frequency Vs number of patients in different age groups.



Text Fig.02 - Graph representing the number of patients from different districts of Bihar



Text Fig 03: Graph demonstrating patients received types of treatment.



Text fig 04: Illustrating the status of patients