Original Article

Patterns and stages of breast cancer in Northern Kerala, India; Results based on 2016 Hospital-Based Cancer Registry of a Tertiary Cancer Center

ABSTRACT

Background: Breast cancer is leading globally in 2020, with mortality being a concern in developing countries. Cancer registration can help in studying systematically collected data about breast cancer. The aim of this study is (1) to describe demographic aspects, stage at diagnosis, histological types, and treatment availed by evaluating the 2016 Hospital-Based Cancer Registry (HBCR) of a Tertiary Cancer Centre (TCC), (2) to study the relationship between sociodemographic factors, the stage of the disease, the time between diagnosis and registration at TCC and the treatment status.

Methodology: The data of all breast cancer patients who registered at the institution in 2016 was included in the study. The variables in the HBCR core form were used as a baseline for collecting data from hospital records.

Results: The number of patients registered in 2016 was 534. The mean age was 53.8 (SD 53.8 ± 12.11). Majority (59.2%) presented in the early stages. Seventy-two percent were from rural areas, and 59.5% had a middle school education and above. Our study found a significant association between education status, the stage of disease, and treatment status.

Conclusion: Education level plays an important role in early presentation and treatment completion. Registry data analysis can be used as a guideline for understanding patterns and for formulating cancer control activities in the state.

KEY WORDS: Breast cancer, cancer registry, Kerala

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INTRODUCTION

Breast cancer is the most commonly diagnosed cancer (11.7% of total cases) and the leading cause of cancer death among women globally.[1] It has the highest incidence among women in most countries, accounting for one in four cancer cases and one in six cancer deaths.[1] Rising incidence in developing countries is due to sociocultural and lifestyle changes, delayed marriage, late first pregnancy, and an increase in workforce participation by women, which decreases opportunities for breastfeeding.[1] Though, developing Asian countries have lower incidence compared to developed countries, mortality due to breast cancer is higher, which demands immediate attention.[2,3]

Breast and cervical cancers are the most common among Indian women, accounting for 39.4% of total cancers.[2] As per the National Cancer Registry Program (NCRP) report, there has been a significant annual increase in incidence rate across all Population-Based Cancer Registries (PBCR).[4] The projected rate of breast cancer in the country is 230,000 in 2025.[5] Pooled data from 58 HBCRs in India reports 57% being diagnosed in locally advanced or loco-regional states, requiring a multimodality treatment approach.[4]

Breast is the leading site of cancer among women in Kerala, accounting for 29.1% in Northern Kerala.[6] The Age-Adjusted Incidence Rate reported in 2007 is 29.4 per 100,000 women in Southern Kerala.[7] Studies have predicted an overall increase from 43.4 in 2013 to 57 per hundred thousand women in 2020.[8]

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Cancer registration is a process of providing reliable statistical information about cancer, which in turn gives the status of disease and the efficacy of control measures in society. In 1965, the first PBCR in India was started in Mumbai, and the country got away with conventional methods such as surveys to a more reliable approach to cancer data collection.[9] While the PBCR collects data from selected geographical locations, HBCR collects data from patients who visit a specific hospital that treats cancer. It provides an estimate of cancer incidence, cancer survival, and public health initiatives associated with cancer control.[9] However, there is a scarcity of research outputs associated with breast cancer from Northern Kerala. This necessitates a study on the patterns of breast cancer among patients registered in the HBCR of the TCC and associated factors.

AIMS AND OBJECTIVES

This paper aims to study the patterns of breast cancer and the factors associated with stages, time to registration, and treatment sought.

The objectives are:

1. To analyze the profile of breast cancer patients from HBCR (2016) of a TCC in Northern Kerala
2. To study the stage of presentation of breast cancer in the TCC and the associated factors
3. To study the time to registration after diagnosis of breast cancer and the associated factors
4. To study the status of treatment sought from TCC, and the factors associated with it.

METHODOLOGY

Study setting

The TCC caters to the cancer treatment needs of all northern districts of Kerala and the adjoining states of Tamil Nadu, Karnataka, and the Union Territory of Puducherry. A detailed description of the same is given in the study protocol elsewhere.[10] The annual HBCR report published by the TCC gives data on cancer patients in Northern Kerala. It also has a PBCR which gives information on trends and the burden of cancer in the area.

Study population

This is described in phase 1 of the study protocol elsewhere.[10] The cohort has not only breast cancer patients who were newly diagnosed in 2016 (either in the TCC or elsewhere) but also those diagnosed in any other year and reporting for posttreatment follow-up or mammogram or for treatment of metastasis. Those patients coming for a second opinion reported only once, as they do not intend to take treatment here. Facilities for surgery in breast cancer care are also available in various private setups in Kerala, and some women prefer them. They may register in the TCC for adjuvant treatment such as radiotherapy or chemotherapy and may undergo follow-up either here or at the initial center. Analyzing a heterogenous group may not be meaningful; hence, we intend to do further analysis in groups of women of interest.

Data collection: Data of all breast cancer patients registered in the TCC from January 1, 2016, to December 31, 2016, and included in the HBCR of the year was collected from medical records. The records were accessed by utilizing the Unique Hospital Identity (UHID) obtained from the Department of Cancer Registry. This is described in detail elsewhere.[10]

Data variables: The variables were adapted from the HBCR core form of ICMR, described in detail elsewhere.[10]

Ethical considerations: Ethics committee clearance was obtained both from the TCC and the research scholar's center of study.[10]

Analysis: Univariate analysis was given as means and standard deviation and for bivariate analysis, the Chi-square test was used.

RESULTS

A total of 534 patients (age range from 25 years to 85 years) were registered in the TCC in 2016. The mean age was 53.8 years, 95% CI [52.79, 54.8]. Patients mainly belonged to the district where TCC was located (52.3%), other northern districts (46%), and a few (0.16%) from neighboring states of Karnataka and the Union Territory of Puducherry. Except for two women, all were Malayalam-speaking. Eighty-two percent were diagnosed in 2016, 6.7% in 2015, and 12% between 1991 and 2014. One-fourth of women visited the TCC only once. The reasons were that those diagnosed before 2016 have visited either for follow-up or treatment for a second malignancy or recurrence or may have completed part of their treatment elsewhere and visited only for a second opinion regarding further treatment.

The sociodemographic characteristics of the cohort are given in Table 1.

Pathomorphological features of the cohort are given in Table 2.

Majority (47%) have registered in TCC within one week of diagnosis and 31% between 8 and 30 days of diagnosis. The date of diagnosis is taken as the date of reporting of cytology or histopathology, extracted from the lab reports in the patient records. Microscopic confirmation of diagnosis was available with 83.9% at the time of registration, with cytology of primary being 53% followed by histology (41%). Among imaging diagnostic modality (9.9%), half was mammography ($n = 28$). Early stage (stage 1 or 2) was seen among 59.3%, and 39% were in late stages when diagnosed [AJCC 7th edition[11]]. Among metastasis, the most common was bone (18.2%), and multiple secondaries were found in 41%.

Table 1: Sociodemographic profile of the breast cancer patients (*n*=534)

	n (%)
Age	
<50 years	211 (39.5)
>50 years	323 (60.5
Sex	
Female	532 (99.6)
Male	2 (0.4)
Location	
Urban	149 (27.9)
Rural	385 (72.1)
Marital status	
Unmarried	35 (6.6)
Married	400 (74.9)
Widowed	85 (15.9)
Divorced	12 (2.2)
Unknown	2 (0.4)
Mother tongue	
Malayalam	529 (99.0)
Kannada	3 (0.6)
Others	1 (0.2)
Unknown	1 (0.2)
Religion	
Hindu	339 (63.5)
Muslim	131 (24.5)
Christian	64 (12)
Job	
Home maker	458 (85.8)
Manual laborer	15 (2.8)
Professional	19 (3.6)
Others	42 (7.9)
Education	
Illiterate	61 11.4)
No formal schooling	45 (8.4)
Primary	105 (19.7)
Middle	123 (23)
Secondary	131 (24.5)
College and above	64 (12)
Unknown	5 (0.9)

Table 2: Pathomorphological profile of the breast cancer patients (*n*=534)

	n (%)
Stage at presentation (AJCC 7th edition)	
Stage 1	30 (5.6)
Stage 2	286 (53.6)
Stage 3	129 (24.2)
Stage 4	83 (15.5)
Unknown	6 (1.1)
Morphology	
Invasive duct ca-ET	461 (86.3)
Lobular ca-ET	8 (1.5)
Papillary ca-ET	6 (1.1)
Carcinoma NOS	14 (2.6)
Phyllodes tumor	3 (0.6)
mucinous ca	9 (1.7)
medullary ca	2 (0.4)
DCIS	5 (0.9)
Others	8 (1.5)
Unknown	18 (3.4)
ER PR status	
ER PR positive	234 (43.8)
ER PR negative	162 (30.3)
ER positive PR negative	42 (7.9)
ER negative PR positive	5 (0.9)
Unknown	91 (17.0)
HER2 status	
HER 2 (0/1+)	148 (27.7)
HER 2 2+	47 (8.8)
HER 2 2+ (amplified by FISH)	15 (2.8)
HER 2 2+ (not amplified by FISH)	25 (4.68)
HER 2 2+ (FISH not performed)	7 (1.3)
HER 2 3+	233 (43.6)
Unknown	106 (19.9)
Ki67 status	
0-2% grade 1	11 (2.1)
2-20% grade 2	104 (19.5)
>20% grade 3	156 (29.2)
Inconclusive	34 (6.4)
Unknown	229 (42.9)

In 97.8% of patients, the breast was the primary site of malignancy. Among 12 patients who had two primary, breast was in the sequence of first of the two primary in 2.8% and second in sequence in 1.5%. The most common sites of the second primary were endometrium and ovary.

Triple negative reports were found in 32.4% and 43.8% were ER PR positive. Ki67% was unknown in 47%, as only the newly diagnosed cases had it detected from the TCC. Those with HER2 neu (Human Epidermal growth factor Receptor2) IHC 2+ (equivocal) underwent FISH for confirmation.

Thirty percent (n = 163) have received either partial or complete treatment from elsewhere before registration. Surgery either mastectomy (MRM) or breast conservation surgery (BCS) was the most common (65, 39.4%).

Three-fourths of patients underwent some form of treatment for TCC. Intention to treat was radical in 74.4% and palliative in one-fifth of patients. Of them, ten percent were advised either symptomatic treatment or best supportive care (4.4%). In 54.5% of patients, treatment was started within 30 days of registration in the TCC. Cancer-directed treatment included surgery (MRM or BCS), chemotherapy, radiotherapy, targeted therapy with trastuzumab, hormones, or a combination of these treatment modalities according to the clinical and pathological stage of the disease. MRM was conducted in 55% including bilateral MRM in 11 patients. In addition, some underwent treatment with bone-strengthening agents, Xeloda, radiation, or surgical oophorectomy as per the stage of the disease. In our study, the treatment interval (time between diagnosis and initiation of definitive treatment) was within 30 days in 36% and between 30 and 60 days in 30%.

The stage and type of treatment taken by the cohort are given in Figure 1.

Among the two male breast cancers, one presented in an advanced stage, and the other reported with a second malignancy and died shortly after due to old age.

For the present exercise, 437 patients who were diagnosed in 2016 were included for analysis [Figure 2]. Ninety-two percent took treatment from TCC, of which 73.1% completed treatment

within one year. Those who underwent anti-HER2 treatment with trastuzumab took a longer time as the treatment schedule was one year.[12] We tried to find out whether there was an association between sociodemographic variables and factors like stage of disease [Table 3], diagnosis to registration time [Table 4], and treatment status [Table 5]. It was found that educational status was associated with the stage of disease and treatment status with a significant *P* value. Sixty percent had middle-level education and above in our study. Other factors such as age, religion, place of stay, and occupation did not find any association.

Table 3: Sociodemographic factors and stage of presentation (*n*=437)

Factor	Early stage *n* (%)	Late stage *n* (%)	Total	*P*
Education				
Below 5th std	105 [59.7]	71 {40.3}	176	0.03*
Above 5th std	181 {69.3}	80 {30.7}	261	
Total	286 {65.4}	151 {34.6}	437	
Urban/rural				
Urban	82 {65.6}	43 {35.4}	125	0.98
Rural	204 {65.4}	108 {34.6}	312	
Marital status				
Married	217 {65.8}	118 {35.2}	335	0.59
Others	69 {67.6}	33 {32.4}	102	
Total	286 {65.4}	151 (34.6)	437	
Age				
<50 years	128 {69.9}	55 {30.1}	183	0.09
50 years and above	158 {62.2}	96 {37.8}	254	
Total	286 {65.4}	151 {34.6}	437	
Religion				
Hindu	193 {67.0}	95 {33.0}	288	0.32
Muslim	58 {59.2}	40 {40.8}	98	
Christian	35 {68.6}	16 {31.4}	51	
Total	286 {65.4}	151 {34.6}	437	
Occupation				
Homemakers	241 {65.5}	127 {34.5}	368	0.96
Employed	45 {65.2}	24 {34.8}	69	
Total	286 {65.4}	151 {34.6}	437	

**P* significant at *P*<0.05

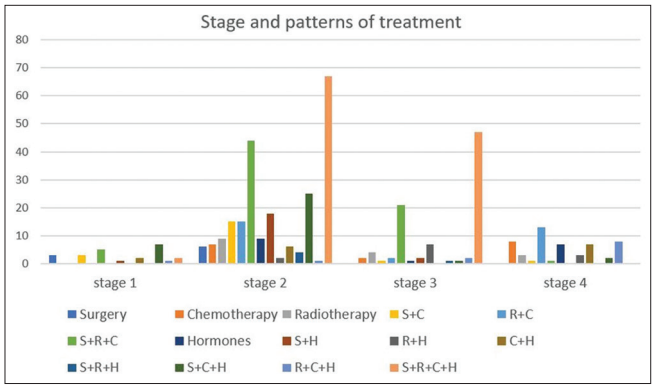

Figure 1: Stages and patterns of treatment of breast cancer patients in the HBCR of 2016. S+C -Surgery + Chemotherapy, R+C -Radiotherapy + Chemotherapy, S+R+C-Surgery + Radiotherapy + Chemotherapy, S+H -Surgery + Hormones, R+H -Radiotherapy + Hormones, C+H -Chemotherapy + Hormones, S+R+H -Surgery + Radiotherapy + Hormones, S+C+H -Surgery + Chemotherapy + Hormones, R+C+H -Radiotherapy + Chemotherapy + Hormones, S+R+C+H -Surgery + Radiotherapy + Chemotherapy + Hormones

DISCUSSION

The mean age in our cohort was 53.8 years (SD 53.8 ± 12.11). More than half of women were aged between 40 and 59 years, maximum between 45 and 54 years of age. Studies from Kerala[7,13,14] and other parts of India[15,16] also reflect similar age group patterns, stressing the fact that in India, younger age is a major risk factor, and results are comparable with the report of NCRP 2021.[17-19] Women in developing countries get the disease one decade earlier compared to developed countries.[2] In a study based on HBCR in Sri Lanka, the mean age was 56 years and the majority were between 50 and 59 years.[20]

In our study, 6.2% belonged to 35 years or lesser age category, which is also known as young breast cancer. Though this is between 2% and 3% in developed countries, Indian studies show results ranging from 8% to 10%,[21-23] while developing Asian countries have 25% leading to poor prognosis.[2]

In our study, the majority of patients were from rural areas in Northern Kerala. Urban areas have a higher incidence compared to rural areas in Kerala.[24] Globally, access to care is a major reason for late-stage presentation.[25] Poor access to medical facilities causes a higher incidence mortality ratio in rural areas.[17] Majority of the our reported patients were from the district of TCC and nearby northern districts, suggesting better rural access. As in a study from western India,[26] the rural operational area of the TCC contributed to better accessibility and a higher presentation in the early stages (59.3%). Only 39% were diagnosed in the late stages, which is contrary to the rest of India (57%).[4] The TCC's engagement in regular public campaigns on cancer may have resulted in increased awareness and early-stage presentation, an indication of health promotion activities reflecting as changes in the community.[25]

Studies show that the stage of presentation was associated with demographic factors like income, educational status,

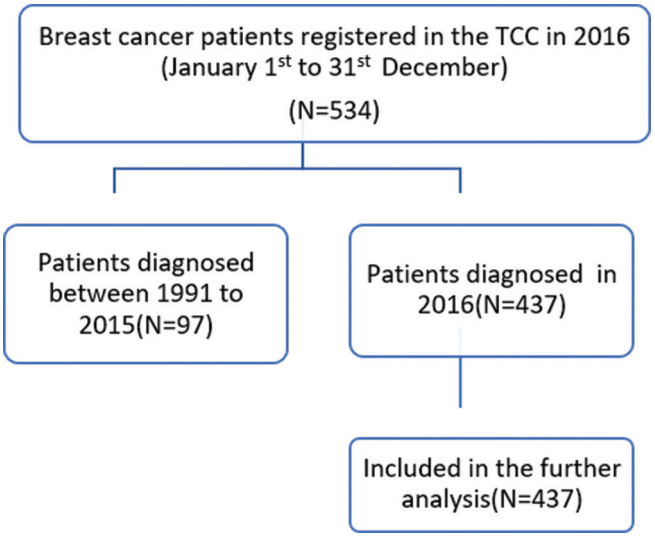

Figure 2: A description of the cohort of breast cancer patients in the HBCR of 2016

marital status, occupation, ethnicity, and age.[7,13,25,27] Women who were unmarried, widowed, or divorced and those with lower education were at risk of presenting at late stages.[17] There were also studies where demographic factors were not associated with the stage of presentation.[27] In our study, education level and stage at presentation were significantly associated. This is in confirmation with other studies from Kerala and other parts of India.[7,28-30] Contrary to other studies, age,[31] marital status,[7,32] and place of residence[33] were not associated with the stage of disease in our study.

Majority had a microscopic diagnostic report at the time of registration, cytology being the commonest test. This shows the operational area of HBCR has better accessibility for the diagnosis of breast cancer. In our study, the time between diagnosis and registration did not find an association with any of the demographic factors.

Triple-negative cases (TNBC) in our study were 32%. This is in confirmation with studies from North India (28% to 39%), though a majority was estrogen progesterone receptor positive.[16,21]

Sixty-five women preferred initial surgery from elsewhere before coming to TCC, which may be due to either societal stigma or apprehension to approach the government system.[27]

Definitive cancer treatment was started in about half of women within 30 days of registration at TCC and in 16.3% between 30 and 60 days. This interval, described as in-hospital interval,[34] is consistent and even lesser than in other studies.[19] This could be achieved due to initiatives at the center like monthly audits of the patient waiting time and formulating plans for improvement. There may be unavoidable delays like time for diagnostic workups, cross consultation for treatment fitness, and long waiting lists due to patient load, as experienced in other places.[35] Studies show that delays of more than 45 days have decreased survival.[19]

Table 4: Factors affecting time between diagnosis and registration at TCC (*n*=437)

Factor	Within 1 month	Above 1 month	Total	*P*
Education				
Below 5th std	162 {92.0}	14 {8}	176	0.15
Above 5th std	229 {87.7}	32 {12.3}	261	
Total	391 {89.5}	46 {10.5}	437	
Urban/rural				
Urban	115 {92}	10 {8}	125	0.27
Rural	276 {88.5}	108 {34.6}	312	
Total	391 {89.5}	46 {10.5}	437	
Marital status				
Married	295 {88.1}	40 {11.9}	335	0.08
Others	96 {94.1}	6 {5.9}	102	
Total	391 {89.5}	46 {10.5}	437	
Age				
<50 years	161 {88}	22 {12}	183	0.38
>50 years	230 {90.6}	24 {9.4}	254	
Total	391 {89.5}	46 {10.5}	437	
Religion				
Hindu	264 {91.7}	24 {8.3}	288	0.08
Muslim	85 {86.7}	13 {13.3}	98	
Christian	42 {82.4}	9 {17.6}	51	
Total	391 {89.5}	46 {10.5}	437	
Occupation				
Homemaker	330 {89.7}	38 {10.3}	368	0.75
Employed	61 {88.4}	8 {11.6}	69	
Total	391 {89.5}	46 {10.5}	437	

Table 5: Factors affecting treatment status of the patients (*n*=437)

Factor	Treatment completed	Not taken	Incomplete treatment	Total	*P*
Education					
Below 5th std	117 {66.5}	23 {13.1}	36 {20.5}	176	0.0006*
Above 5th std	182 {69.7}	56 {21.5}	23 {8.8}	261	
Total	299 {68.4}	79 {18.1}	59 {13.5}	437	
Urban/rural					
Urban	79 {63.2}	31 {24.8}	15 {12.0}	125	0.06
Rural	220 {70.5}	48 {15.4}	44 {14.1}	312	
Total	299 {68.4}	79 {18.1}	59 {13.5}	437	
Marital status					
Married	231 {69.0}	64 {19.1}	40 {11.9}	335	0.17
Others	68 {66.7}	15 {14.7}	19 {18.6}	102	
Total	299 {68.4}	79 {18.1}	59 {13.5}	437	
Age					
<50 years	127 {69.4}	35 {19.1}	21 {11.5}	183	0.55
>50 years	172 {67.7}	44 {17.3}	38 {15.0}	254	
Total	299 {68.4}	79 {18.1}	59 {13.5}	437	
Religion					
Hindu	205 {71.2}	46 {16}	37 {12.8}	288	0.32
Muslim	61 {62.2}	24 {24.5}	13 {13.3}	98	
Christian	33 {64.7}	9 {17.6}	9 {17.6}	51	
Total	299 {68.4}	79 {18.1}	59 {13.5}	437	
Occupation					
Homemaker	247 {67.1}	66 {17.9}	55 {14.9}	368	0.752
Employed	52 {75.4}	13 {18.8}	4 {5.8}	69	
Total	299 {68.4}	79 {18.1}	59 {13.5}	437	

*P significant at P<0.05

More than half of women underwent MRM, while one-sixth underwent BCS. That most women preferred mastectomy even after they were counseled for BCS based on assessment, was confirmed in an Indian study.[36]

In our study, out of the 49% who were positive for HER2, 42.4% took trastuzumab, a targeted monoclonal antibody therapy for breast cancer positive for HER2.[37] Other studies reported only 30% of the eligible patients receiving anti-HER2 treatment.[21] In Kerala, there are treatment schemes supported by the government, which can be availed by enrolled patients. The scheme provides five lakh per family per year for hospitalization in the empanelled health care facility for secondary and tertiary care.[38] Some treatment modalities may not be covered by these schemes. Hence, patients may stop such treatments due to financial constraints, as reported earlier.

It was also noted that few discontinued treatment (13.7%). Reasons documented include voluntary decline (10.8%), poor tolerance to treatment (12.9%), death (9.4%), comorbidities, aging, alternative and herbal treatment (3.2%), and financial especially in taking targeted therapies. A study from Africa found that religion, ignorance regarding health insurance, and belief in traditional medicine have led to incomplete treatment.[39] In our study, treatment status was found to have a significant association with education.

About 70% started their treatment within 60 days of diagnosis. Our treatment intervals were comparable with other studies (ranging from 29 to 54.7 days).[34,40] Since the majority were diagnosed before registering at TCC, this time interval also includes the delay before reporting at TCC, which does not come under the scope of this study.

Registry can give exclusive data on treatment patterns, incidence, and trends, but PBCR-based cancer data are available only in 20% of Asian countries, covering only part of the population.[3,24,41] Though HBCRs give data on breast cancer in a particular hospital, since most of them are in regional cancer centers, the data may also represent cancer patterns in the area.[42]

CONCLUSION

Breast cancer is on the rise in Northern Kerala, and younger age of presentation is a concern. Our study shows that education and access to health facilities plays an important role in early-stage diagnosis of the disease and treatment completion. Majority of our patients were from rural areas; the rural location of the TCC might have helped in early-stage diagnosis, though it could not be proved statistically in the study. Registries have to be strengthened with completeness of information and wider population coverage for understanding trends and patterns of breast cancer in the area.

Strength and limitation

The study involves patients from a single center only. The strength is that our study addresses the knowledge gap and provides data about breast cancer in Northern Kerala, which is scarce. As the TCC caters to the cancer treatment needs of majority of districts in North Kerala, this study gives a picture of breast cancer in the area.

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Conflicts of interest

There are no conflicts of interest.

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