Original Article

Clinicopathological profile of breast cancer from Chhattisgarh India: A single-center hospital-based study

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ABSTRACT

Background: Global breast cancer incidence is increasing at an annual rate of 3·1%. Female breast cancer has surpassed lung cancer as the most commonly diagnosed cancer, with an estimated 2.3 million new cases (11.7%). However, the data from different parts of India are still lacking and the study was conducted to assess the burden of disease at tertiary referral centers in central India. **Material and Methods:** Retrospective record analysis (June 2013–June 2017) of data from outdoor clinics and pathology reports. The patients aged <15 yrs, nonresidence of Chhattisgarh, and diagnosed outside the study period were excluded. The triple assessment was used to diagnose all breast lumps (sensitivity 99%). **Results:** Eighty patients were diagnosed having breast carcinoma. The mean age for breast cancer was 39 ± 3.028 years (ranged 31–50 years). Twenty patients had locally advanced breast carcinoma. The predominant religion was Hindu 55.00%. The referral pathway to seek medical care for breast cancer was via a gynecologist in 40% (32/80). Familial breast cancers were in 0.03% (3/80) of patients. None breast cancer patients have previous histology-proven benign breast disease. The mean size of the breast cancer lump was 3.56 cm (ranged 1.0–11.0 cm). Overlying skin ulceration (*n* = 2), skin infiltration/peau-d'-orange (*n* = 2), skin tethering (*n* = 4), and bloody nipple discharge were found in one patient. Breast cancer was diagnosed during lactation (postnatal period) in one patient. The maximum number of patients have tumor size >5 cm (72.6%). Immunohistochemistry and pathological analysis was done on core biopsy (*n* = 20) and surgical procedure (*n* = 60). Modified radical mastectomy was done in 52, breast conservative surgery with Sentinal Lymph node biopsy and axillary lymph node dissection in 6, and toilet mastectomy in two patients. The predominant tumors were solid (*n* = 79/80), with both solid and cystic types (1/80). The solid and cystic lesion on FNAC was of C3b type, and an excision biopsy revealed medullary carcinoma of the breast. Invasive ductal carcinoma-no special type (IDC-NST) was observed to be the most common histopathologic type (*n* = 70/80), followed by medullary carcinoma (*n* = 2), metaplastic carcinoma (*n* = 1), papillary carcinoma (*n* = 4), Paget disease with DCIS (*n* = 1), mucinous carcinoma (*n* = 1), invasive lobular carcinoma (*n* = 1). One male patient with breast cancer and two female patient having bilateral breast cancer also have IDC-NST.Scarff Bloom Richardson Grade was predominantly graded 2 in 46.25% (37/80) of breast cancer patients (Grade 1 = 9, Grade 2 = 37, Grade 3 = 34). Lymphovascular (LVI) and perineural invasion (PNI) were predominantly without LVI and PVI. (Lymphovascular present and perineural invasion present = 4, Lymphovascular present and perineural invasion absent = 32, Lymphovascular absent and perineural invasion absent = 42, Lymphovascular absent and perineural invasion present = 2). Histological examination of axillary lymph nodes showed the presence of malignant cells in all. Triple-negative breast carcinoma was 26.58% (21/79). Most breast cancer presented at stage II A = 37.5% (30/80) and II B = 28.7% (23/80) of the AJCC staging system. **Conclusion:** The clinico-epidemio

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and histological profile of breast cancer in Chhattisgarh is similar to other parts of India. Scarff Bloom Richardson Grade was predominantly grade 2 in 46.25% (37/80) contrary to Grade III (70%) in other series from India.

Keywords: Breast cancer, breast diseases, breast cancer epidemiology, breast cancer screening, Central India, Chhattisgarh, cancer registry, mammography, mastectomy, self-breast examination, triple-negative breast cancer

Background

Global breast cancer incidence is increasing at an annual rate of 3·1%.[1,2] Breast cancer is the most common in Indian women with age adjusted rate as high as 25.8 per 100,000 women and a mortality of 12.7 per 100,000 women.[3] The globally age-adjusted incidence rate of carcinoma of the breast was 42.3 new cases per 100,000 population (using the 2000 World Standard Population).[4] The World Health Organization (WHO) released a Global Brest cancer initiative framework in February 2023. It is a roadmap to attain the target to save 2.5 million lives from breast cancer by 2040. Countries need to ensure that this framework engages and integrates into primary health care for universal health coverage. This framework recommends countries to us on breast cancer early detection programs, so at least 60% of breast cancer patients can be diagnosed and treated as an early stage disease. It has been documented that diagnosing breast cancer within 60 days of the initial presentation can improve survival. The second target of the global breast cancer initiative framework is to start appropriate treatment within three months of the first presentation. The third target is to facilitate treatment facility in such a way that 80 percent of breast cancer-affected females can complete their recommended treatment.[5]

For women aged 15–49 years, twice as many breast cancer cases were recorded in developing countries than in developed countries.[1,6] This variation in incidence may be due to multiple factors, including geographic variation, racial/ethnic background, genetic variation, lifestyle, environmental factors, socioeconomic status, presence of known risk factors stage of disease at diagnosis, and the availability of appropriate care.[5,7-9]

The National Cancer Registry Programme (NCRP) was initiated by the Indian Council of Medical Research in 1982 at select hospitals in the country. Up to 2020, NCRP is monitoring 36 Population-Based Cancer Registries and 236 Hospital-Based Cancer Registries. National Centre for Disease Informatics and Research, Bengaluru, Chennai, and Mumbai are monitoring these registries. Simultaneously, hospital-based cancer registries are running at Chandigarh, Thiruanthapuram, Patiala, Naharalagun, Pasighat, Noida, Silchar, and Dhibrugarh. These registries systematically collected data on cancer incidence, mortality, clinical aspects of cancer, estimation of trends, survival, and burden of disease.[7] To date, breast cancer is not a notified disease, therefore is not mandatory to report to healthcare facilities to authorities.[7] These registries follow the active methods of cancer detection. The Central India National Centre for Disease Informatics and Research (NCDIR) and the Indian Council of Medical Research (ICMR) collected data on all cancers from 2012 to 2016.

The Wardha, Nagpur, and Bhopal have published their cancer registries, which showed locally advanced breast cancer as the most common cancer (57.1%) and most common cancer in females.[8,9]

The population of Chhattisgarh is 25.55 million, whereas the rural population constitutes 76.76 percent.[10] The soils of Chhattisgarh is deficient in important mineral, and nutrients like calcium, magnesium, nitrogen, phosphorous, lime, and potash.[11] The main occupations are agriculture, mining, and labor in alloy factories. The extensive forest also provides livelihood, fodder, fuel, and food supplements. The majority of tribes in India are from Chhattisgarh, viz., Gond tribe, Korba, Baiga Tribe, Bison Horn Maria tribe, Abhuj Maria, Muria tribe, Halba tribe, Bhatra, and Dhurvaa tribe.[12] The World Health Organization reported the capital of Chhattisgarh (Raipur) as 3rd most polluted city in 2014 and the 7th most polluted city in 2017.[13] According to Vishwanathan and Gangadharan, 514 industrial units were placed in Chhattisgarh in tribal areas till 1996, which is of great concern as the environmental polycyclic aromatic hydrocarbons (PAHs) and polychlorinated biphenyls (PCBs) in conjunction with certain genetic polymorphisms involved in carcinogen activation and steroid hormone metabolism.[14-17] There is very wide diversity in the literacy rate within the state (maximum 76%).[18] The most common religion in Chhattisgarh is the Hindu religion. Thus, the ecology of Chhattisgarh is slightly different from other parts of India.

The existing data from India show a rising trend in the prevalence and younger age of presentation of breast cancer.[3] However, the data from different parts of the county are still lacking and the study was conducted to fill this data gap. The data might help in further research and planning healthcare policies for better care of breast cancer patients in central India.

Methods

This is a retrospective record analysis (June 2013–June 2017) of data from outdoor clinics, and pathology reports. The study was approved by Institute's Research and Ethical Committee. The patients aged <15 yrs., nonresidence of Chhattisgarh, and diagnosed outside the study period were excluded. A modified B.J prasad scale was used for the socioeconomic status assessment.[19] Clinical breast examination (CBE), radiological imaging (mammography and or ultrasonography), and pathological report (triple assessment) were used to diagnose all breast lumps (sensitivity 99%). The triple assessment was taken as positive if any of the three components were positive, and negative only if all were negative (19). The breast imaging results, mammography, and ultrasonography were interpreted by BI-RADS (Breast Imaging Reporting and Data System (20)). Core

biopsy was a definitive tool in suspicious malignant C3, C4, and C5 FNAC (Cytologic Category Code System).[20] The histological grade of the tumor was based on the Scarff Bloom Richardson grading system.[21] All breast cancer specimens were assessed for steroidal receptor status. ER receptor status was assessed by standard fixation technique and duration, optimal antigen retrieval methods, and the use of a standard set of antibodies for receptor detection to minimize false negative results. The author has not kept a lower limit of cutoff for ER positivity and considered any ER positivity as positive (2001 NIH consensus).[20]

The data were collected for sociodemographic characteristics, referral pathway, risk factors, histopathological characteristics, steroidal receptor status, the delay between the first symptoms and consultation, etc.

Statistics

Data analysis was performed using Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, USA) version 20. General and clinical characteristics were analyzed by descriptive statistics. Mean and standard deviation were described for the continuous variable with normal distribution and range for the continuous variable with skewed distribution. Statistical significance was set at a *P* value < 0.05.

Results

In four year period, 399 patients with breast lumps presented to unit III of the Department of Surgery. The most common symptom was mastalgia and the most common pathology was benign breast disease [Table 1]. The age range for breast pathologies was 12 yrs–75 yrs. The mean age for breast cancer

patients was 39 ± 3.028 years (31–50 years). The histological diagnosis of breast carcinoma was made in 80 patients. The data analysis of demography and clinicopathological findings in 80 breast cancer patients was done. Twenty patients presented with locally advance breast carcinoma were referred to regional cancer center for chemo-radiotherapy.

The demography of breast cancer patients is shown in Table 2, Figure 1. 19 % of Patients were illiterate or obtained only primary education. The predominant religion was Hindu 55.00. The regional distribution of breast cancer patients in Chhattisgarh is shown in Table 3.

The referral pathway to seek medical care for breast cancer in a tertiary healthcare center was via a gynecologist in 40% (32/80) of patients [Figure 2]. However, a breast cancer awareness camp conducted by the institute at schools/colleges/dental/ ayurvedic and Homeopathic colleges among educated girls over one year reported. eight cases shows awareness camp would be very effective in the detection of early breast cancer. The ultrashort duration breast cancer awareness camp conducted at different education institutes by healthcare workers also motivated a significant number of patients for Clinical Breast Examination.[22,23]

The percentage of breast cancer patients having cumulative risk factors for breast cancer in Figures 3-5. Family history of familial breast cancer was present in only 0.03% (3/80) of

Table 1: Spectrum of common breast pathology

Nature of breast lump (based on a triple assessment)	*n*	%
Mastalgia (cyclical and noncyclical)	126	31.5
Fibroadenoma	82	20.5
Breast cancer	80	20
Breast abscess (Bacterial)	50	12.5
Fibroadenosis without mastalgia	35	9
Ductal ectasia	14	3.5
Breast abscess (Mycobacterial)	8	2
Breast cyst	4	1
Total patients	399	
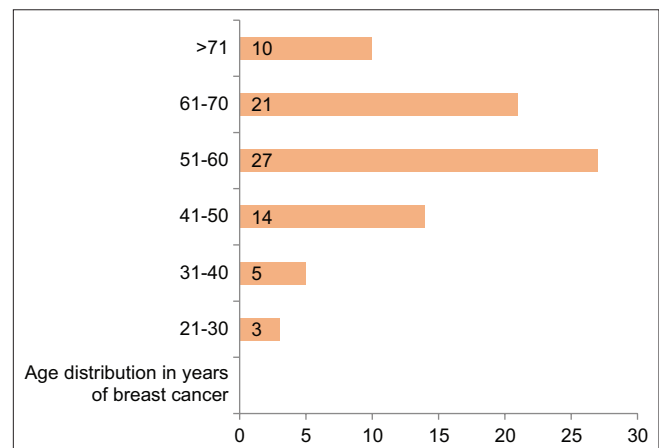
Figure 1: The age distribution of breast cancer patients

Table 2: The demography of breast cancer patients

Education status of patients	*n* (%)	The religion of breast cancer patients	*n* (%)	Occupation	*n* (%)
Illiterate	4 (5.0%)	Hindu (including Sindhi)	44 (55.0%)	Housewife	42 (52.5%)
Primary	16 (20.0%)	Muslim	19 (23.75%)	Agriculture	33 (41.2%)
Middle	16 (20.0%)	Sikh	8 (10.0%)	Private Job	2 (2.5%)
Highschool	10 (12.5%)	Christian	5 (6.2%)	Self Employed	2 (2.5%)
Intermediate	23 (28.75%)	Parsi	2 (2.5%)	Teacher	1.25 (%)
Graduate & above	11 (13.75%)	Jain	2 (2.5%)	Others	-
Total	80	Total	80	Total	80

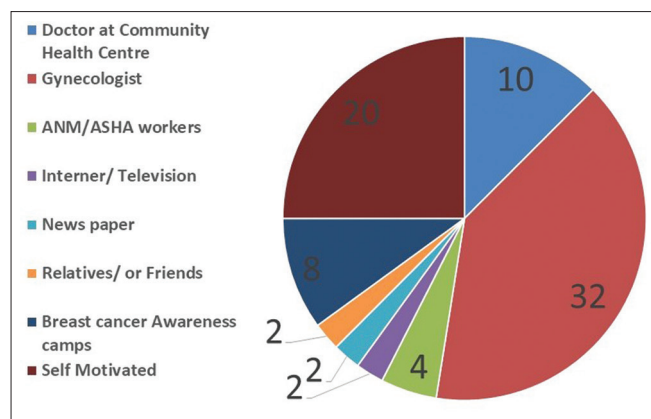patients [Figure 6]. No breast cancer patient was found to have previous histology-proven benign breast disease.

The mean size of the breast cancer lump was 3.56 cm (ranged 1.0–11.0 cm). Overlying skin ulceration ($n = 2$), skin infiltration/ peau-d'-orange ($n = 2$), skin tethering ($n = 4$), and bloody nipple discharge were found in one patient. Breast cancer was diagnosed during lactation (postnatal period) in one patient. The maximum number of patients having tumor size >5 cm (72.6%). Breast cancer most commonly involved the upper outer quadrant at 48.75% (39/80) [Figure 7]. The axillary lymph node was palpable in all patients [Figure 8].

Immunohistochemistry and pathological analysis was done on tissue obtained either via core biopsy ($n = 20$) or surgical procedure ($n = 60$). Modified radical mastectomy was done in 52, breast conservative surgery with Sentinal Lymph node biopsy and axillary lymph node dissection in 6, and toilet mastectomy in two patients. The predominant tumor type was solid ($n = 79/80$), both solid and cystic (1 patient). The solid and cystic lesion on fine needle aspiration cytology was of C3b type, and excision biopsy revealed medullary carcinoma of the Breast. Invasive ductal carcinoma-no special type (IDC-NST) was observed to
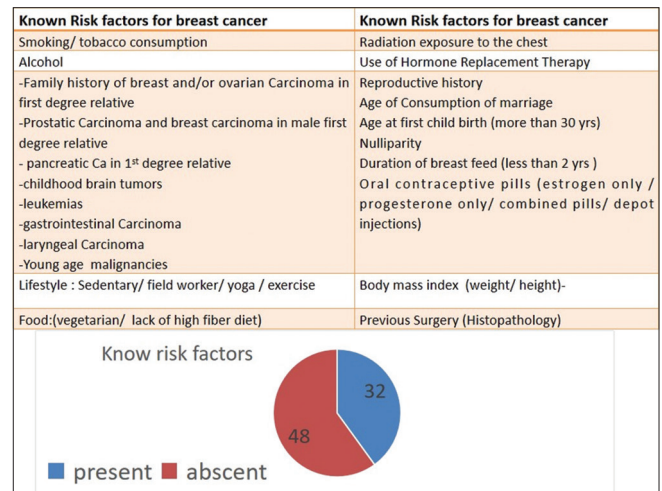
be the most common histopathologic type ($n = 70/80$). Others were medullary carcinoma ($n = 2$), metaplastic carcinoma ($n = 1$), papillary carcinoma ($n = 4$), Paget disease with DCIS ($n = 1$), mucinous carcinoma ($n = 1$), invasive lobular carcinoma ($n = 1$).

Table 3: Regional distribution of breast cancer patients at Chhattisgarh

Region from Chhattisgarh	n (80)	Region from Chhattisgarh	n (80)
Raipur	39	Korea	0
Bilaspur	3	Dhamtari	5
Durg	14	Kanker	0
Raigarh	1	Kawardha	1
Bastar	0	Dantewada	0
Sarguja	0	Narayanpur	0
Rajnandgauv	0	Bizapur	0
Korba	1	Balod	0
Janjgir-Champa	1	Bemetara	0
Mungeli	1	Baloda Bazar	2
Gariyaband	0	Kondagav	0
Sukma	0	Balrampur	0
Surajpur	0	Bhilai	13
Total			80

Figure 2: The referral pathway to seek medical care for breast cancer

| Known Risk factors for breast cancer	Known Risk factors for breast cancer
Smoking/ tobacco consumption	Radiation exposure to the chest
Alcohol	Use of Hormone Replacement Therapy
-Family history of breast and/or ovarian Carcinoma in first degree relative	Reproductive history
-Prostatic Carcinoma and breast carcinoma in male first degree relative	Age of Consumption of marriage
- pancreatic Ca in 1st degree relative	Age at first child birth (more than 30 yrs)
-childhood brain tumors	Nulliparity
-leukemias	Duration of breast feed (less than 2 yrs)
-gastrointestinal Carcinoma	Oral contraceptive pills (estrogen only / progesterone only/ combined pills/ depot injections)
-laryngeal Carcinoma	
-Young age malignancies	
Lifestyle : Sedentary/ field worker/ yoga / exercise	Body mass index (weight/ height)-
Food:(vegetarian/ lack of high fiber diet)	Previous Surgery (Histopathology)

Figure 3: The percentage of breast cancer patients having cumulative risk factors for breast cancer
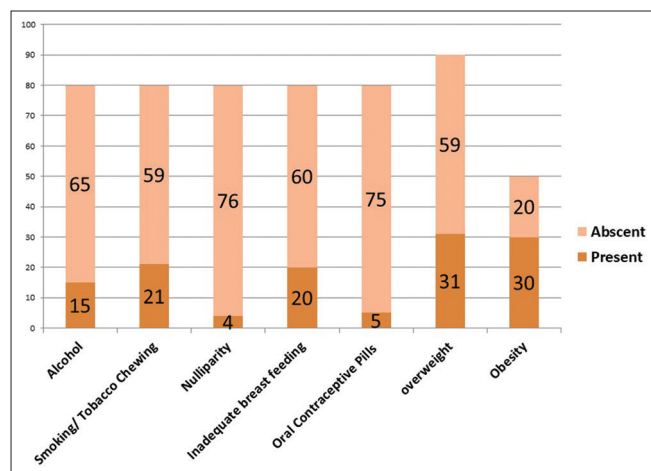
Figure 4: The percentage of breast cancer patients having the proportion of individual risk factors for breast cancer
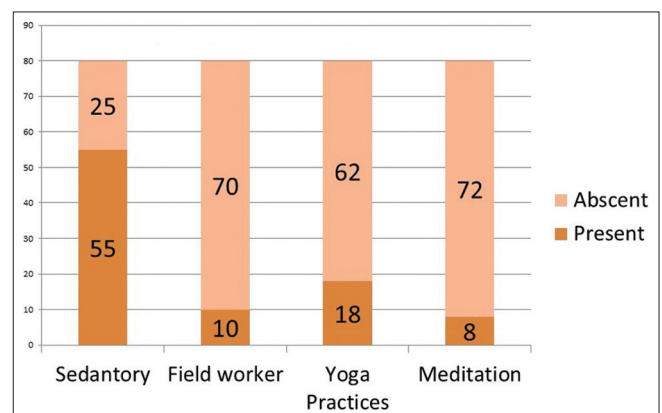
Figure 5: The percentage of breast cancer patients having lifestyles
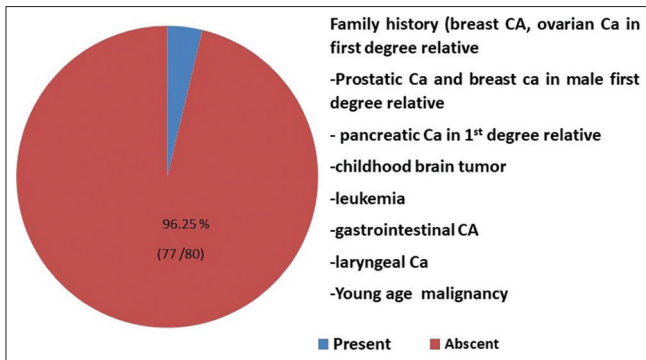
Figure 6: Patients profile of the family history of familial breast cancers

One male patient with breast cancer and two female patients having bilateral breast cancer also have IDC NST. having bilateral breast cancer also have IDC-NST.

Scarff Bloom Richardson Grade was predominantly grade 2 in 46.25% (37/80) of breast cancer patients (Grade 1 = 9, Grade 2 = 37, Grade 3 = 34).

Lymphovascular (LVI) and perineural invasion (PNI) were predominantly without LVI and PVI. (Lymphovascular present and perineural invasion present = 4, Lymphovascular present and perineural invasion absent = 32, Lymphovascular absent and perineural invasion absent = 42, Lymphovascular absent and perineural invasion present = 2).

Histological examination of the axillary lymph node showed the presence of malignant cells in all patients 100% (80/80).

Estrogen/progesterone receptor and human epidermal growth factor (Her 2 Neu) receptor status are shown in Figure 9. Triple-negative breast cancer (estrogen negative, progesterone negative, Her2/Neu overexpression absent) breast carcinoma was 26.58% (21/79) [Figure 9].

Most of the patients having breast cancer were presented at stage II A 37.5% (30/80) and II B 28.7% (23/80) of the AJCC staging system [Figure 10].

Discussion

Breast cancer is the most common cancer in females, with the trend to involve younger population.[24] It is very difficult to imagine a house without a female. She is the backbone of every family. According to International Agency for research on cancer in 2020, approximately 4.4 million women died of cancer 2020, and nearly 1 million children were orphaned by cancer, 25% of which were due to breast cancer. The Orphaned children experience health, education, and social life disparity that triggers long-term social and financial disharmony in society.[25] Worldwide there are more than 2.3 million cases of breast cancer occur each year. However, data from a few counties are still missing because of the lack of cancer registries in many
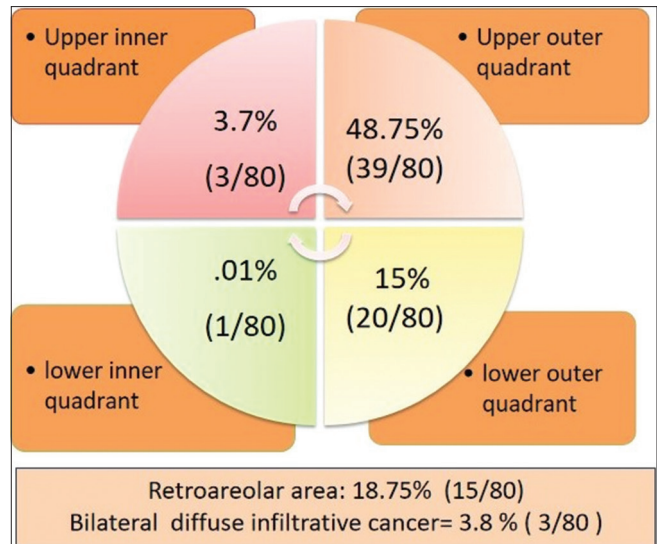
Figure 7: Frequency of breast cancer involving different breast quadrants

developing countries. Survival is quite variable among different countries. Within India, five-year survival is 76.3% in localized breast cancer and 47.4 percent in regional breast cancer, which is very less compared to the west 89.6% and 75.4%, respectively. A probable reason for variation in survival rate is the access to the best healthcare services in different countries. Painless lump adds to delay in treatment-seeking behavior in 50% to 70% of the cases in rural areas of India.[26] Worldwide 80% of deaths from breast and cervical cancer occur in low- and middle-income countries.[27]

In resource-limited countries, targeted breast cancer screening can also be performed as per the WISDOM (Women Informed to Screen Depending on Measures of Risk) trial. This clinical trial is going on black African women to do annual mammography in women having high-risk factors, viz., genetic makeup, family history, and other factors.[28,29]

The NCDIR recommended making all cancer a notifiable disease to enable increased coverage by Indian registries and the establishment of registries in areas in uncovered regions.[7] India is a country having variable geography, local ecology, cultural background, etc. Chhattisgarh state in India has unique ecology as the incidence of sickle cell trait and sickle cell disease is very much higher. So, our study aims to generate baseline data for the demography and histology of the most prevalent variety of breast cancer in this area.

As per the ICMR-PBCR (Population-based cancer Registry) data, breast cancer is the most commonest cancer among women in urban registries of Delhi, Mumbai, Ahmedabad, Calcutta, and Trivandrum where it constitutes >30% of all cancers in females.[8] The age-standardized incidence rates (AARs) range from 6.2 to 39.5 per 100,000 Indian women.[8] The AARs vary by region, ethnicity, and religion, with the highest incidence reported at 48.3 per 100,000 women in the Parsi community of Mumbai. The

breast cancer projection for India in 2020 is supposed to go up to 1797900.[8] Westernization of lifestyle has led to an increase in the incidence of breast cancer in India.[30] The main risk factors related to breast cancer are hormonal factors related to premenopausal estrogenic impregnation, genetic predisposition, and environmental factors.[26] The protective effects of a diet high in vegetables, fruits, legumes, whole grains, turmeric, green tea, and lean protein on breast cancer are proven in different studies. In developing countries, primary healthcare workers need to make aware of modifiable risk factors via delayed conception, reduced (<2 yrs.) total duration of breastfeeding practices, early menarche, sedentary lifestyle, postmenopausal obesity, and lack of high-fiber diet, excessive intake of processed food, consumption of alcohol and smoking.[26]

A large difference has been observed in the behavior of the tumor, clinical manifestation, treatment, response, and prognosis. The mortality rate of breast cancer varies proportionally with the age of the patient, stage of disease, prompt management, type and extent of the tumor, complacency, and response to initial treatment. The Indian government should make more canters involved in cancer registries to approach the periphery and private hospitals to get the exact burden of disease. Cancer screening facilities (a qualified radiologist and mammography machine) must be available at all peripheral healthcare centers for early detection of breast cancer.[7]

Disease patterns and presentation of breast cancer in India differ from the west. While the majority of breast cancer patients in western countries are postmenopausal (the 60s and 70s years), in India premenopausal patients constitute about 50% of all patients.[1]

The average age of presentation in our study was (31 yrs to 50 yrs). The mean age for breast cancer patients was 39 ± 3.028 years, which is slightly earlier than mentioned in various population-based studies (51–53 yrs) in India.[31] In our study, four patients were younger than 35 yrs. Overall, about 5% of all breast cancer patients had a family history of breast cancer.[15]

The average stage of breast cancer presentation in India is Stage I: 1–8%; Stage II: 23–58%; Stage III: 29–52%; Stage IV: 6–24%. Sixty percent of breast cancer present in stage III of AJCC.[26,32] Contrarily, in our study, the maximum number of patients were from Stage II of AJCC. This might be selection bias, as advanced breast cancers are usually referred to the regional cancer center, Higher rates of breast cancer among Indians were observed amongst Christians and Parsis, than in Hindus and Muslims.[3] We predominantly found the Hindu religion having breast cancer which could be due to differences in the regional distribution in our state.

The study found invasive ductal carcinoma not otherwise specified (IDC NOS) as the most common type (88%), similar to those reported from other parts of India[26,32] IDC NOS was followed by infiltrating lobular carcinoma (3.7%), colloid carcinoma (1.1%), ductal carcinoma *in situ* (DCIS) (1.1%), and metaplastic types (0.9%).

Scarff Bloom Richardson Grade was predominantly grade 2 in 46.25% (37/80) contrary to Grade III (70%) in other series from India.[33]

India has a higher proportion of ER-negative breast cancer compared to the west (34). Triple-negative breast cancer (TNBC) is an aggressive subtype that lacks the expression of ER, PR, and the absence of overexpressed or amplified HER2. In the western world breast cancer, TNBC constitutes approximately 12%–17% of all invasive breast cancers. In India, overall
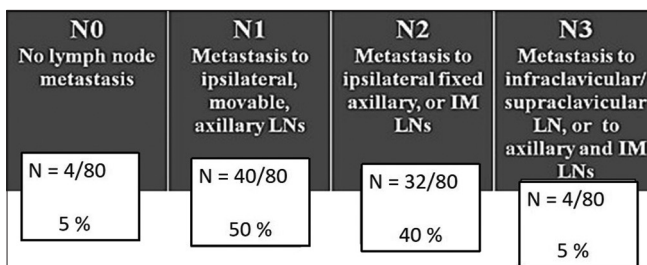

Figure 8: Frequency of breast cancer involving axillary lymph node status
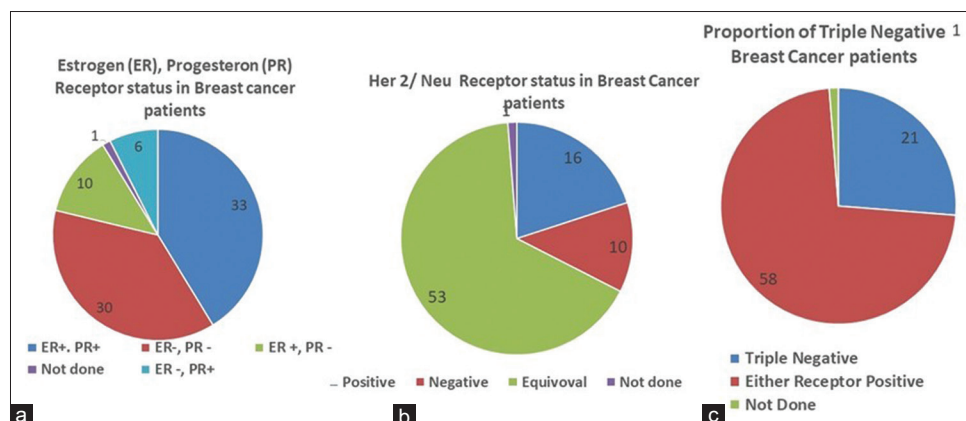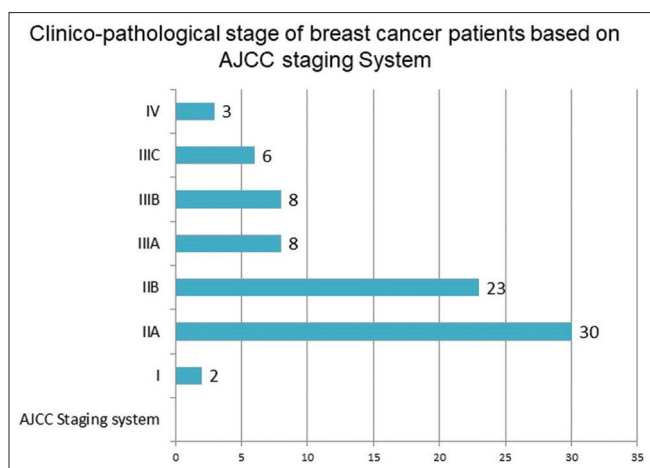

Figure 9: Proportion of (a) estrogen, progesterone, (b) Her 2 Neu, and (c) triple-negative receptor status in breast cancer patients

Figure 10: Clinicopathological staging of breast cancer patients according to American Joint cancer on Cancer (AJCC)

prevalence of TNBC in the north, south, east, and west of the country was 28%, 34%, 30%, and 31%, respectively.[34,35] This study found more than 75% of TNBC in our sample population. TNBC occurs more frequently in younger women, we also had a higher proportion of young age females having breast cancer.[35]

The advanced stage (stage III and Stage IV) constituted 31.2% (25/80) of our patients. A high proportion of patients were reported to have a high S-phase fraction, aneuploidy, and other poor prognostic features on histology.[36] These breast cancer patients have higher locoregional recurrences and poorer overall survival.[37]

The lacuna of study: The data regarding the distribution of breast cancer patients in different districts of Chhattisgarh might have Berkson's bias or selection bias as the study was based on an analysis of hospital records. A long-term follow-up study of these patients is needed for a better understanding of the disease in the local region.

Conclusion

Scarff Bloom Richardson Grade was predominantly grade 2 in 46.25% (37/80) contrary to Grade III (70%) in other series from India.[33] Breast cancer awareness programs conducted by the author in the institute had some influence on the health-seeking behavior of patients. The study found the referral pathway of breast cancer patients to surgeons, is predominantly via gynecologists, so healthcare policy can be advocated accordingly to promote active involvement of gynecologists in breast cancer screening programs.

Key points

- This study found no ecological or histological variation in the presentation of breast cancer, except the early age of presentation and predominant grade 2, Scarff Bloom Richardson Grade for breast cancer from Chhattisgarh.
- The Indian government should involve cancer registries to

approach the periphery and private hospitals to explore more about breast cancer disease more.
- A qualified radiologist and mammography machine must be available at all peripheral healthcare centers and gynecologist clinics for early detection of breast cancer.

Take home message

Countries with weaker health systems are least able to manage the increasing burden of breast cancer. Breast cancer places tremendous strain on individuals, families, communities, health systems, and economies, so it must be a priority for ministries of health and governments everywhere. Making breast cancer a notifiable disease might increase the chance to identify the health facility access gap and take the necessary steps to fill this gap. Strengthening and awarding gynecologist clinics for early cancer detection and early referral might increase the treatment-seeking behavior of patients.

Ethical approval

The Bioethics Committee of All India Institute of Medical Sciences, Raipur, Chhattisgarh. India approved the study.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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