

## Original Research Article

# Lessons from a clinicopathological study of breast cancer

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### ABSTRACT

**Background:** It is estimated for every two new breast cancer cases diagnosed, one breast cancer death is reported in India. It is important regional variations in disease behaviour and health care delivery are studied to understand the elevated mortality of breast cancer in India.

**Methods:** In this retrospective study, 198 patient records were scrutinized for breast cancer related demographic data, disease related information, treatment and pathological data.

**Results:** The median age at presentation was 52 years. The results replicated national trends with regards to menopausal status, menarche, parity and breast feeding. Low parity and age at presentation had a strong inverse correlation ( $P < 0.001$ ). EBC (61%) was the commonest with LABC (28%) and Metastatic disease (13.6%) also prevalent. HR positive (47%) molecular type was the commonest with HER 2 neu (30%) and TNBC (22%) types also noted. Core biopsy was the preferred diagnostic test. Metastatic work up had a yield of 13.6%. Mastectomy was the only surgery procedure; none had BCS or sentinel node biopsy. Surgery done by surgical oncologist had better oncological outcomes.

**Conclusions:** Epidemiological profile of breast cancer in south India confirms to national trends. BCS and sentinel node biopsy are considered standard of care in breast cancer care however seems unavailable in government funded hospitals in south India.

**Keywords:** Breast cancer, Clinicopathological study, South India

### INTRODUCTION

Breast cancer is the commonest cancer among women. GLOBOCAN 2012 report indicates breast cancer has relegated cervix cancer to become the leading cancer among Indian women.<sup>1</sup> National cancer registry data (2007-2011) clearly highlight the breast cancer related public health issues in India. Increasing incidence, younger age at diagnosis and presentation at advanced stage are thought to translate into higher mortality observed compared to other developed nations.<sup>2</sup>

It is estimated for every two new cases diagnosed, one breast cancer death is reported in India.<sup>3</sup> The reasons for

this elevated mortality is unknown, apart from health service related issues like lack of screening, accessibility and availability of quality cancer care, several disease related factors unique to the Indian women may be causative.

The Indian subcontinent is geographically vast with a diverse demographic profile, it is important regional variations in disease behavior and health care deliveries are studied to understand the issues highlighted above. A review of breast cancer care at a tertiary care cancer center was planned to assess the factors intrinsic to breast cancer behavior and cancer care delivery in southern India.

## METHODS

A retrospective analysis of 198 patient records treated at the breast cancer clinic of our tertiary cancer care center was done. Demographic data were collected; disease related information including clinical presentation and pathological data were accrued. Treatment data were analyzed for type of surgery, requirement of radiotherapy and chemotherapy. Issues identified at initial analysis were further evaluated by collection of additional information. Statistical analysis was done using SPSS software version 22. A P value of <0.05 was considered a

statistically significant result. The students-t test was used for continuous variables and Fisher's exact test for categorical variables. The spearman rho was used for testing association between two continuous variables.

## RESULTS

The median age of the study patients was 52 years (range 24-82 years). All were females with no male breast cancer treated during the study period. A marginal predominance of left sided cancers was noted 53 % (n=105).

**Table 1: Baseline and demographic characteristics.**

Variable		Sample size (N=198)	P value (If applicable)
Age at presentation median 52 years (24 -82 years), Menarche Mean 13 years		198	
Laterality	Right	93 (47%)	
	Left	105 (53%)	
Menopausal status	Pre	74 (37%)	
	Post	124 (63%)	
Parity Median age years	Nullipara 37 years	12 (06%)	P=0.2 (Parity & Incidence) P<0.001 (Parity & age of presentation)
	1 49 years	28 (14%)	
	2 50 years	87 (44%)	
	>3 53 years	71 (36%)	
Breast fed	Yes	190 (96%)	
	No	08 (04%)	
Detection	Symptomatic	193(97%)	
	Incidental	04 (02%)	
	Screen detected	01(0.005%)	
Tumor stage	T1	31 (16%)	
	T2	90 (45%)	
	T3	46 (23%)	
	T4	31 (16%)	
Clinical stage	I	31 (16%)	
	II	84 (42%)	
	III	56 (28%)	
	IV	27 (14%)	
Diagnostic Modality	FNA	15 (7.5%)	
	Core biopsy	160 (81%)	
	Excision biopsy	15 (7.5%)	
	Frozen section	08 (04%)	
Surgery	Mastectomy	163(100%)	
	Breast conservation	0	
	Sentinel node biopsy	0	
	Reconstruction	0	
Molecular type	HR positive	76 (47%)	
	Her 2 neu	50 (30%)	
	TNBC	36 (22%)	
	Missing data	36 (18%)	
Histology	IDC	187 (94%)	
	Lobular	06 (03%)	
	Metaplastic	02 (0.01%)	
	Medullary	03 (0.01%)	

Pre and post-menopausal women constituted about 37 % (n=74) and 63 % (n=124) of the study cohort. The average age of menarche was 13 years and only 6 % (n=12) were nulliparous, 96% of the women had history of having breast fed. Most women had at least two children 79 % (n=158) however increasing parity (P=0.2) was not statistically correlated with increasing incidence. The median age of presentation had a strong inverse correlation with lower parity P<0.001 (Table 1).

Only 0.005 % of the cancers (n=1) were screen detected, an overwhelming majority of 96.4 % (n=191) being symptomatic for tumor or were incidentally diagnosed 0.02 % (n=4). Core biopsy was the preferred diagnostic modality used in 81 % (n=160) of the cases, excision biopsy, frozen section and fine needle cytology (FNAC) were utilized in the others. Interestingly in 7.5 % (n=15) the surgeons had proceeded to surgery relying only on aspiration cytology report without performing a core biopsy. Infiltrating ductal carcinoma (n=187) and lobular carcinoma (n=6) were the two major histological types, though other histological types like metaplastic (n=2) and medullary (n=3) were also observed. Metastatic disease at presentation was diagnosed in 13.6% (n=27) while the remaining 61 % (n=121) were early breast cancers (EBC) and another 28 % (n=56) locally advanced breast cancers (LABC). Molecular typing results were available in only 162 case records with hormone receptor positive subtype noted in 47 % (n=76), HER 2 neu in 30 % (n=50) and triple negative type observed in 22 % (n=36).

An detection rate of 13.6 % (n=27) was noted for metastatic workup with CT scan (51%) and bone scan (58%) yielding the most. Mastectomy was the only surgery performed irrespective of tumor size with no breast conservation procedures done on the study cohort. None of the mastectomy patients had breast reconstructive surgery. The above results are shown in Table 1.

**Table 2: Factors affecting sensitivity of FNA.**

Variable	P value
Age Less than or above 40 years	P=0.38
Laterality- Right vs Left	P=.67
T size less than or above 35 mm	P=0.008
Tumor quadrant	P=0.56

It was observed some surgeons practiced curative surgery based only on a positive aspiration cytology results without performing a core biopsy. Consequent to this, data related to accuracy and diagnostic yield of aspiration cytology was done by recollecting additional information from the patient records. It was observed that FNA had a sensitivity of only 88 % compared to core biopsy (98 %) and excision biopsy (100%). Factors leading to a false negative result were analyzed, except tumor size less than 3.5 cms (P=0.008) none of the other variables assessed like age less than 40 years (P=0.38), laterality (P=0.67), tumor quadrant (P=0.56) were significant Table 2.

The data also revealed all the mastectomies in the study group were done either by general surgeons or by surgical oncologists, hence pathological data were reviewed to check for differences in surgical quality. The variables assessed showed significant differences in nodal harvest (9 vs 15 nodes p=0.0001) and margin positivity (12 vs 02, P=0.01) in favor of surgical oncologists but requirement for revision surgery was not significant P=0.13(0 vs 5) Table 3.

**Table 3: Comparison of surgical quality between surgical oncologist and non-oncology trained surgeons.**

Variable	Surgical oncologist versus Non oncology trained surgeons
Mean axillary nodal yield	15 vs 9 nodes (P=0.0001)
Margin positivity	02 vs 12 (P=0.01)
Revision surgery	0 vs 05 (P=0.13)

## DISCUSSION

### Patient factors

The median age of disease presentation was 52 years with majority of patients between 51-60 years. This contrast slightly from data published from north India where a median of 46 years has been reported, however a similar regional study (south India) reports a mean of 51.4 years.<sup>4,5</sup> Most breast cancers were noted in the fifth decade and these results are concordant with published data from other parts of India confirming earlier presentation of breast cancer in Indian women compared to western women.<sup>6,7</sup> The reason for these observed trends remains undefined. With regards to menopausal status, age of menarche, parity and breast feeding our data conforms to the national trends.<sup>4,6,7</sup> Present data also indicate parity and age at presentation were inversely related and this has been observed in western women.<sup>8</sup>

### Tumor factors

A majority reported with symptomatic disease and a few were physician detected; only one screen detected cancer was diagnosed. This trend is universally observed in India.<sup>4,6</sup> In contrast to assumption that Indian women present in advanced stages our data indicate most are early breast cancers (61%) and recent publications (EBC vs LABC 55 vs 33%) have reported this changing paradigm in India.<sup>4,5,7</sup> IDC continues to be the predominant histology, interestingly hormone receptor positive cancers constituted 47 %, her 2 positive 30% and triple negative 22% in present data. Another regional study reported similar proportion of hormone positive cancers but lower (18%) her 2 positive and higher (34%) triple negative molecular types.<sup>5</sup> A similar observation was noted in a study from Karnataka, the reasons for the higher her 2 positive and lower TNBC in present study is not known.<sup>7,9</sup>

Fine needle aspiration cytology had a lower diagnostic sensitivity in our patients (88% vs 91%) however sensitivity is known to vary with number of attempts, 61% with single and 91% with three or more attempts and it has been recommended that a negative result should be considered as indeterminate and core biopsy performed particularly if clinical suspicion of cancer is high.<sup>10</sup> A tumor size of less than 3.5 cms was associated with false negative result in our study however an inadequate aspirate and smear appears to be the major reason for a false negative result but could not be evaluated due to retrospective nature of this study.

### **Treatment factors**

All breast cancer surgeries were mastectomies with none treated with breast conservation or reconstruction. This trend was noticed despite maximum proportion of cases in T2 category. Mastectomy as the predominant surgery is an universal observation from studies across India however breast conservation surgery rates have in recent times increased from 12% to 59%.<sup>11,12</sup> A study from southern India reported a mastectomy rate of 93 % and the reasons for this remain unclear.<sup>11</sup> In present public funded institute non availability of linear accelerator to deliver satisfactory whole breast radiation is the primary reason to offer mastectomy to patients otherwise suitable for breast conservation surgery. Present study demonstrated mean nodal yield and margin positivity after mastectomy were influenced by the training background of the operating surgeon. The above are important prognostic determinants and are a prerequisite in adjuvant therapy treatment decisions. A suboptimal oncological outcome has been observed in mastectomy by non-oncology trained surgeons.<sup>13</sup> The reasons for such quality disparity may be related to surgical training and expertise, this issue requires further evaluation by a clinical trial.

### **CONCLUSION**

Epidemiological profile of breast cancer in south India confirms to national trends except for a higher median age at presentation. A higher proportion of Her 2 and a lower TNBC were observed in this study compared to regional trends. Breast conservation surgery including reconstructive procedures and sentinel node biopsy techniques are considered standard of care in breast cancer care however seems unavailable in government funded hospitals. These standard treatment modalities have to be immediately incorporated in to public sector health services in this region. Disparity in surgical quality between surgeons offering mastectomy needs further evaluation by a well-designed study.

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