

General Surgery

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**CORRELATION OF CLINICAL EXAMINATION,
MAMMOGRAPHY AND HISTOPATHOLOGY
EXAMINATION IN TUMOUR STAGING FOR
CARCINOMA OF BREAST - TERTIARY
INSTITUTIONAL STUDY, INDIA.**



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ABSTRACT:

Background: The cancer breast is most common malignancy among the rural as well as urban women in India. This study aimed to correlate tumor size by clinical breast examination (CBE), mammogram and post-operative histopathology examination (HPE) early breast cancer.

Materials and methods: The present prospective clinical study was conducted during sept- 2014 to september 2016 among 60 patients of breast cancer in a tertiary care hospital, Andhra Pradesh, India. All these patients were subjected to Clinical examination and mammography pre-operatively and post-operatively, to histopathology examination. All patients with age more than 18 years and less than 70 years, with early breast cancers were included. Results: About 18 (30%) of the patients belonged to 51 – 60 years, 17 (28.3%) to 41 – 50 years, 14 (23.3%) to above 61 years and 11 (18.3%) to 31 – 40 years. Mean age was 51.65±10.79 years. Cancers were more common in the left breast 37 (61.7%) compared to right 23 (38.3%). Tumor was most commonly seen in the upper outer quadrant 35 (58.3%). There was a moderate positive correlation between CBE and HPE ($r = 0.674$, $P 0.000$), thus the best predictor of tumor size was CBE next to HPE. Mammography had comparatively lesser correlation with HPE ($r = 0.473$, $P 0.000$). The correlation between CBE and Mammogram was also good ($r = 0.619$, $P 0.000$).

Conclusion: Clinical Breast Examination is in good agreement with Histopathological examination of breast carcinoma, compared to mammogram. Though CBE might not be confirmatory, it can be used for screening of breast cancers to some extent, especially in low socio-economic situations as in India since mammography is a costly procedure.

INTRODUCTION

Breast cancer is the most prevalent cancer in women worldwide and a leading cause of cancer related deaths in women [1, 2] A total of 14.1 million new cancer cases and 8.2 million cancer deaths were reported in 2012. (3) Worldwide, more than 1 million cases of breast cancer are being diagnosed each year and has now become a major global health problem. It is one of the leading causes of cancer related mortality. (3) In the past two to three decades there has been increasing incidence and mortality from Breast cancer in low and middle resource countries [3]. Of the over million new cases of breast cancer that will be diagnosed worldwide in 2009, low- and middle-resource countries will be burdened with 45% of breast cancer cases

and 55% of breast cancer related deaths [2, 4]

In developing countries like India, inspite of wide information conveyed through multimedia, women seek proper attention at late stages only this may probably explain the high rate of mortality. According to Indian Council of Medical Research (ICMR) registries of cancer in women, the incidence of breast cancer have steadily increased in India. (5) In India, data from the Cancer Atlas reports that amongst the population based cancer registries, Delhi had the highest age adjusted incidence rate of breast cancer at 33.4 per 100,000 females compared to 109.6 per 100,000 white females in San Francisco, California, USA. District wise comparison of minimum age adjusted incidence rates of breast cancer [MAAR] showed that Chandigarh with a rate of 39.5 per 100,000 and North Goa with a rate of 36.8 per 100,000 women exceeded the MAAR of Delhi [6].

Clinical method of palpation of breast cancer for tumor size and axilla remains relevant even today in spite of the advances in technology. Examination of breast and axilla is an integral part of triple assessment of patient with suspected carcinoma breast; the other two being mammography or ultrasonogram (USG) and Fine Needle Aspiration Cytology (FNAC) or core- cut biopsy. USG examination of the axilla has become common practice in the presurgical assessment of breast cancer patients for staging purpose. (7) Clinical Breast Examination [CBE] and Breast self examination [BSE] has been extensively studied as a low cost alternative to mammographic screening aiming to reduce mortality by early detection. Breast cancer mortality reduction has been proven in RCT's for use of CBE's. An estimate based on all randomized clinical trials reported sensitivity of CBE for detection of breast cancer at 54% and specificity at 94% [8].

Berg and others studied the use of ultrasound in addition to mammography to screen 2809 women at high risk for breast cancer [9]. Ultrasound demonstrated a 55% increase in diagnosing breast cancer compared to mammography alone, detection rate increased from 7.6 per 1000 to 11.8 per 1000 due to use of ultrasound in addition to screening mammography. Sensitivity for detection of breast cancer increased to 77.5% from 49% due to addition of screening sonography. However, the drawback with the use of ultrasound is time to perform a whole breast ultrasound which has been reported to be between 10 and 20 mins per bilateral examinations [9 – 12].

The literature supporting the benefits of screening mammography in reducing mortality from Breast cancer is extensive and the overwhelming body of evidence is strongly in favor of offering this

service to women in countries with a high prevalence of breast cancer. Nevertheless, the controversies and the debate as to when breast cancer screening should commence, how often to screen women, and when to stop screening, rages on. The council of the European Union and the International agency for Research on Cancer expert working group has recommended use of bi-annual mammography for women age 50–69 [13]. In the USA, the Society of Breast Imaging and the Breast Imaging Commission of the American College of Radiology recommends annual screening mammography for Women at average risk to undergo annual screening mammography starting at age 40 [14]. For women with certain risk factors such as having a first degree relative who is BRCA positive, annual screening mammography is recommended starting at age 30 years.

This study was carried out to correlate the stages of carcinoma breast based on clinical, mammography and post-operative histopathology examination (HPE) (which is considered the gold standard)

MATERIAL AND METHODS

The present prospective clinical study was conducted during sept-2014 to september 2016 among 60 patients of breast cancer in a tertiary care hospital, Andhra Pradesh, India. All these patients were subjected to Clinical examination and mammography and post-operatively, to histopathology examination (FNAC/trucut biopsy). The study was carried out in the surgery and radiology departments of the hospital.

Inclusion criteria: Age more than 18 years and less than 70 years, with early breast cancers. Other selection criteria were patients with normal liver function test, renal function test, hematological parameters and echocardiogram.

Exclusion criteria: Patients with already diagnosed breast cancers, those with metastatic breast tumours, pregnant women, other chronic diseases or previous history of other cancers.

Sample size and sampling: A total of 106 women were screened for breast cancers during Sept 2014 to Sept 2016, of which all the 60 patients who fulfilled the inclusion criteria and consented for the study were included in the study.

Procedure: All the study participants were explained about the study in their local language in understandable manner and were free to withdraw from the study anytime at their voluntary will. The confidentiality of the study was assured. A written informed consent was taken from the participant or their guardian, prior to the study. All the participants were subjected to “clinical examination of breasts” and “Mammography” followed by “Histopathological examination (Biopsy)” to assess the size of the tumor (T) by all these methods and correlate the findings. The greatest dimension of the tumor was considered in staging as per the guidelines of AJCC. [15] Based on tumor size (T), staging of breast cancers was done and each method was compared against the HPE (gold standard for diagnosis of breast cancers) findings for any significant difference in staging. Staging of breast cancers was done using the staging guidelines given by AJCC.[15]

Clinical examination of breasts and axillae was done by the treating experienced surgeon. The diameter of breast lump was measured along two perpendicular diameters using Vernier calliper and the mean diameter was calculated.

Mammogram: Bilateral mammogram was performed with dedicated mammographic equipment using standard cranio-caudal (CC) and mediolateral oblique (MLO) with 30° projections with adequate breast compression. Mammogram was performed by technicians under the supervision of experienced radiologist. Depending on breast texture, adjustments were made between 20-35 kV and 30-180 mAs. Mammograms were analysed by an

experienced radiologist and the largest tumor dimension, was recorded.

Biopsy: After these tests, patients underwent FNAC / trucut biopsy for the histological diagnosis of carcinoma breast. After the histological evidence of malignancy the patients were subjected to either wide excision with axillary dissection or modified radical mastectomy. The exact size of the tumor were assessed from the surgical samples by the department of pathology, recorded and compared with pre-operative staging data.

Statistical Analysis: The collected data was entered in Microsoft excel, double checked for errors and analyzed using epi – info software. Results were expressed as percentages, mean and standard deviation. Chi square test was used to compare categorical variables. A P-value of <0.05 is considered statistically significant and 0.000 is very highly statistically significant. Spearman's rank correlation was used to analyze the correlation between procedures.

The study protocol was approved by the ethical committee of the institution.

RESULTS

About 18 (30%) of the patients belonged to 51 – 60 years, followed by 17 (28.3%) to 41 – 50 years, 14 (23.3%) to above 61 years and 11 (18.3%) to 31 – 40 years. Mean age was 51.65±10.79 years. Cancers were more common in the left breast 37 (61.7%) compared to right 23 (38.3%). Tumor was most commonly seen in the upper outer quadrant 35 (58.3%). Only 1 (1.7%) tumor was present since 4 years while all the remaining tumors 59 (98.3%) were present from < 1 year, of which majority, 48 (80%) existed since < 6 months. About 22 (36.7%) women were post-menopausal, 20 (33.3%) pre-menopausal and 18 (30.0%) peri-menopausal. (Table 1)

TABLE 1 Characteristics of the Breast cancers

Characteristic	Number	Percentage
A. Laterality	23	38.3
1. Right	37	61.7
2. Left		
B. Quadrant	35	58.3
1. Upper outer quadrant	16	26.7
2. Upper inner quadrant	7	11.7
3. Lower outer quadrant	2	3.3
4. Lower inner quadrant		
C. Duration in months	48	80.0
1. 1 – 6	11	18.3
2. 7 – 12	0	0
3. 13 – 24	0	0
4. 25 – 36	1	1.7
5. > 36		
D. Menopausal status	20	33.3
1. Pre-menopausal	18	30.0
2. Peri-menopausal	22	36.7
3. Post-menopausal		

STAGING OF TUMORS BY THREE PROCEDURES

By clinical examination, 41 (68.3%) were stage II tumors, 17 (28.3%) stage III and 2 (3.3%) stage I tumors. By mammography, 43 (71.7%) were stage II tumors, 11 (18.3%) stage I and 6 (10%) were stage III tumors. Histopathologic examination of the tumors following trucut biopsy is considered gold standard for the diagnosis of breast cancers. By HPE, 42 (70%) were stage II, 13 (21.7%) stage III and 5 (8.3%) were stage I tumors.(Table 2)

TABLE 2 STAGING OF tumors by CBE, Mammogram and HPE

Tumor Stage (t)	Clinical Examination Number (%)	Mammogram Number (%)	HPE (Biopsy) Number (%)
1	2 3.3	11 18.3	5 8.3
2	41 68.3	43 71.7	42 70.0
3	17 28.4	6 10.0	13 21.7
TOTAL	60 100.0	60 100.0	60 100.0

COMPARISON BETWEEN PROCEDURES

CBE Vs HPE: Clinical breast examination and HPE both could detect 2 (40%) of the stage I tumors while CBE overestimated 3 (60%) of the histopathologically stage I tumors as clinically stage II tumors. HPE detected 42 stage II tumors, of which CBE could pick up 35 (83.3%) as stage II correctly, while overestimating 7 (16.7%) as clinically stage III tumors. Similarly HPE detected 13 stage III tumors, of which CBE could pick up 10 (76.9%) as stage III correctly, while underestimating 3 (23.1%) as clinically stage II tumors. These differences in the diagnosis of stage I,II and III tumors by CBE and HPE were statistically significant (Corrected Chi square 41.597 P 0.000).

Mammogram Vs HPE:

Mammography and HPE both could detect 4 (80%) of the stage I tumors while mammogram overestimated 1 (20%) of the histopathologically stage I tumors as stage II tumors. Of the 42 stage II tumors detected by HPE, mammogram could pick up 34 (61.0%) of stage II tumors correctly, while overestimating 2 (4.8%) as stage III tumors and underestimating 6 (14.3%) as stage I tumors. Similarly HPE detected 13 stage III tumors, of which mammogram could pick up only 4 (30.8%) as stage III correctly, while underestimating 8 (61.5%) as stage II tumors and 1 (7.7%) as stage I tumors. These differences in the diagnosis of stage I,II and III tumors by mammogram and HPE were statistically significant (Corrected Chi square 21.363 P 0.000).

CBEVs Mammogram

CBE could detect 2 (3.3%) of stage I tumors, 41 (68.3%) of stage II tumors and 17 (28.3%) of stage III tumors. Mammography could detect 11 (18.3%) of stage I tumors, 43 (71.7%) of stage II tumors and 6 (10%) of stage III tumors. The concordance between CBE and mammogram was seen in 2 (3.3%) of stage I tumors, 33 (55%) of stage II tumors and 5 (8.33%) of stage III tumors. These differences in the diagnosis of stage I, II and III tumors by CBE and mammogram were statistically significant (Corrected Chi square 18.931 P 0.001).

In comparison of CBE and mammography with HPE, there was a moderate positive correlation between CBE and HPE ($r = 0.674, P 0.000$), thus the best predictor of tumor size was CBE next to HPE. Mammography had comparatively lesser correlation with HPE ($r = 0.473, P 0.000$). The correlation between CBE and Mammogram was also good ($r = 0.619, P 0.000$). Physical examination overestimates and mammogram underestimates breast tumor classification.(Table 3)

Procedures		Spearman's rho	P value
HPE with	CBE	0.674	0.000
	Mammogram	0.473	0.000

DISCUSSION

Breast cancer is the most prevalent cancer in women worldwide and a leading cause of cancer related deaths in women. This tertiary institutional study was conducted to correlate the stages of carcinoma breast based on clinical, mammographic USG and post-operative histopathology (HPE) (which is considered the gold standard) examination.

In our study, 30% of the patients belonged to 51 – 60 years, 28.3% to 41 – 50 years, 23.3% to above 61 years and 18.3% to 31 – 40 years. Mean age was 51.65±10.79 years.

There were no patients above 70 years and below 30 years, which shows that the prevalence of carcinoma breast is low in young age group and very old age group. In our study group, 36.7% patients were post-menopausal, indicating that the incidence is higher in post-menopausal women. Similar findings in relation to age distribution and menopausal state have been reported by Rony J et. al (7). In our study, in comparison of CBE and mammography with HPE, the best predictor of tumor size was CBE ($r = 0.674, P 0.000$). Mammography had comparatively lesser correlation with HPE ($r = 0.473, P 0.000$). The correlation between CBE and Mammogram was also good ($r = 0.619, P 0.000$). These correlation among procedures

are well in consistence with the findings by J Herrada et. al (16). However, one of the studies revealed that the correlation coefficient between ultrasound and pathological size ($r=0.68$) was significantly better than the correlations between physical examination and pathological size ($r=0.42$) and mammographic and pathological size ($r=0.44$). Physical examination overestimated and ultrasound underestimated breast tumour classification (17). In our study, CBE overestimated pathologic size in 10 cases and underestimated pathologic size in 3 cases, which is quite different from the findings reported by Anees B. Chagpar (18), in which Physical Examination (CBE) underestimated pathologic size in 19 cases and overestimated in 5 cases. Similarly, in our study, mammogram overestimated and underestimated pathologic size in 3 cases and 15 cases respectively, which is different from a study which revealed that mammography underestimated in 13 cases and overestimated in 19 (18). Overall, the agreement between clinical and pathologic measurement was only good, with correlation coefficients 0.674, and the agreement between mammography and pathologic measurement was only fair, with correlation coefficients slightly over 0.4 in this study.

Various studies have reported the correlation between pathologic (HPE) tumor size and tumor size by Clinical Breast Examination (Physical Examination), Ultrasonography and Mammography. Some reported moderate correlation and some fair. A review of 9 published papers suggests that clinical approaches for measuring tumor size, especially ultrasonography, may be reasonably accurate in selected patients who do not receive neoadjuvant chemotherapy (Table 4).(17, 19 – 26)

TABLE 4 Correlation Between Pathologic Tumor Size and Preoperative Tumor Size Estimated by Physical Examination or Imaging in Patients Not Treated With Neoadjuvant Chemotherapy

Reference year	n	Spearman's rank correlation co-efficient		
		Physical examination	Ultrasonography	Mammography
Fornage et al 19 (1987)	31	0.79	0.84	0.72
Madjar et al 20 (1993)	100	0.77	0.91	0.79
Davis et al 21 (1996)	1	NS	0.45	0.46
Yang et al 22 (1997)	38	NS	0.93	0.84
Tressera et al 23 (1999)	174	NS	0.72	NS
Hieken et al 24 (2001)	146	NS	0.63	0.40
Bosch et al 17 (2003)	73	0.42	0.68	0.44
Golshan et al 25 (2004)	202	NS	0.48	0.66
Pritt et al (2004) 26	129	NS	0.82	NS
1. IDC	41		0.81	
2. ILC	40		0.67	
3.IDC/ILC				
NS: Not specified, IDC: Invasive ductal carcinoma, ILC: Invasive lobular carcinoma				

While these r values are statistically significant, this significance indicates only that there is an association between the two measurements. Indeed, it would be surprising if there were not such an association, since the same physical object is being measured. This does not indicate, however, that the clinical size estimates or mammographic size estimates are accurate predictors of pathologic size. To yield a prediction that is even 50% better than a random guess, the correlation must be at least 0.86.(27)

CONCLUSIONS

This study concludes that Clinical Breast Examination is in good agreement with Histopathological examination of breast

carcinoma, compared to mammogram. Though CBE might not be confirmatory, it can be used for screening of breast cancers to some extent, especially in low socio-economic situations as in India since mammography is a costly procedure. However, the ultimate diagnosis can only be confirmed by Histopathologic examination of the biopsy specimen, which is the gold standard modality. Although, many studies have revealed combination of procedures yield accurate and reliable results in screening and diagnosis of breast cancers.

LIMITATIONS

The staging of cancers for the study was based only on the size of primary tumor and lymph nodes status and metastasis were not considered. This is because the idea was to compare the correlation between procedures in assessment of tumor size.

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