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Original Research Article

The study of role of mammography and fine needle aspiration cytology in the diagnosis of early breast carcinoma

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ABSTRACT

Background: Epidemiologically breast cancer is the most common form of cancer among women. Prevalence rate of breast cancer is higher in urban women of middle age group. Early diagnosis of breast carcinoma is required for effective treatment else it may lead to mortality if advanced to stage 3 or 4. At present, there are different diagnosis modalities for early stage breast carcinoma. Currently triple diagnostic assessment including clinical, radiological and pathological examinations with 99% sensitivity is used in diagnosing all palpable breast lumps. The aim of the study was to determine the sensitivity and specificity of mammogram and Fine needle aspiration cytology (FNAC) in diagnosing breast cancer.
Methods: A cross sectional study was conducted on total 80 female patients above 30 years of age with a palpable breast lump. Patients were sent for mammography, fine needle aspiration cytology and histopathological examinations. Results of mammography, FNAC and HPR were compared and statistically correlated.
Results: Sensitivity of mammogram diagnosis was observed to be 92.857%, specificity as 86.842%, positive and negative predictive values to be 88.636% and 91.667% respectively. Therefore, current study findings revealed accuracy of mammogram to be 90.000%. Sensitivity of FNAC diagnosis was observed to be 92.857% and specificity to be 100%, positive and negative predictive values were observed to be 100% and 92.683% respectively. The study results revealed that FNAC diagnosis exhibited accuracy of 96.250%.
Conclusions: Current investigation findings revealed that FNAC has more accuracy in predicting breast cancer than mammogram. Also, it was concluded that there is a significant association between FNAC and mammogram diagnosis.

Keywords: Breast cancer, FNAC, Mammography, Histopathology, Breast lump, Sensitivity, Specificity, Accuracy

INTRODUCTION

According to published data; epidemiologically cancer is considered to be one of the leading causes of mortality worldwide.[1,2] Breast cancer originates from breast tissues mainly milk ducts or lobules and is considered to be the second most common type of cancer worldwide.[3] Among women, breast cancer is the most common type of cancer accounting for 25% of all cancers which closely approximates to more than one in ten new cancer cases diagnosed every year.[4] In Indian females breast cancer has emerged as the most common type of cancer with a high mortality rate equivalent to almost 13 per 100,000 women.[5] It was also published in several global and Indian studies that there is a significant rise in the incidence and cancer-associated morbidity and mortality in Indian population.[6] Breast cancer has evolved as a multifactorial disease with varied factors like genetic, environmental, demographic, lifestyle, hormonal, reproductive, race, ethnicity among few that contribute towards its occurrence.[7]

Evolution of breast cancer is slow and silent and the breast tumor can progressively spread hematologically and lymphatically to distant metastasis leading to poor prognosis.[8] Mostly the breast cancer is detected

accidentally during routine checkups or due to some physical changes like change in breast shape or size or change in the rate of nipple discharge.[9] Delayed diagnosis of breast cancer leading to late implementation of treatment strategies (surgery, chemotherapy, radiation) increases the risk of patient mortality and lowers the survival rate. Currently imaging techniques; like mammography, ultrasound or MRI, physical examination, biopsy techniques like fine needle aspiration cytology**,** core needle biopsy**, s**urgical biopsy**,** image-guided biopsy or sentinel lymph node biopsy are commonly used techniques for diagnosing breast cancer.[10]

In mammography high amperage and low voltage X-ray is utilized to examine the soft tissues of the breast, after placing the breast in contact with ultrasensitive film and exposing to the above mentioned X-rays.[11] Calcifications, stellate, nipple changes and axillary lymphadenopathy are revealed by mammography in case of breast malignancy.[12] Mammogram helps to detect the size and shape of lesion in relation to the breast size, it helps to assess the breast quadrants with tumour involvement, multifocality and multicentricity and to determine skin changes and axillary lymph node involvement.[13] The American college of radiology developed breast imaging reporting and data assessment (BIRADS score) to categorize the diagnosis made through mammography. BIRADS score I indicates negative (no findings), BIRADS score II indicates benign appearance, BIRADS score III indicates probable benign appearance (less than two percent chance of malignancy), BIRADS score IV indicates findings suspicious of malignancy, BIRADS score V indicates highly suspicious of malignancy (more than 90% chance of malignancy).[14] Limitations of mammography as an individual diagnostic technique is 5 percent chances of carcinomas not being apparent, relatively expensive investigation and least accurate in younger patients with dense breast.[15]

Fine needle aspiration cytology (FNAC) is least invasive technique in which with the aid of a 22 gauze needle solid and cystic lesions can be differentiated and carcinoma cells can be detected.[16] FNAC is a simple and safe technique of collecting and reading the appearance of diagnostic smears for determining the pathological nature of the breast lumps with least requirement of specialized expertise or expensive material.[17] In FNAC after locating the mass clinically it is fixed in position over the puncture site which is prepared with alcohol or betadine. The needle point is touched to the skin and introduced into the located fixed mass swiftly piercing the tissue.[18] Once the needle enters the tumor which is indicated by resistance to the needle, full vacuum is applied while the needle is moved back and forth in 3-4 directions within the mass with short strokes. The needle is then withdrawn from the mass and temporarily removed from the syringe which is filled with air by pulling back the plunger, the needle is then reattached and the specimen is transferred to a glass slide and smeared with a second slide and then immersed in 95% fixative solvent ethyl alcohol. If aspirate is thick the slides are pressed against each other, if blood is aspirated, the same procedure is repeated using thinner needle till a clear aspirate is obtained. It was observed that prior wetting of needle lumen with heparin substantially increases the cell yield.[16-18] Limitations of FNAC includes lack in reproducibility of results which varies on an average of 5-10% depending on individual performing FNAC, chances of false negative results or false positive results, sampling errors or errors in cytological interpretation, ductal carcinoma having a high degree of differentiation present difficulty in diagnosis since these cells have a monomorphic appearance and may be confused with normal ductal epithelium, in small lesion needle may not strike the tumor and hence the representative cells may not be obtained in aspiration, sclerotic or inflammatory type of malignancy may produce acellular aspirates, in cystic and large necrotic lesions the aspirate may not contain diagnostic cells.[19,20] Therefore neither mammogram nor FNAC individually can be considered as a standard diagnosis in detecting breast cancer. However published study reports have shown that in combination FNAC and mammogram diagnosis have proved to detect breast carcinomas in their early stages, thus current study was conducted to compare the diagnostic ability of these two modalities in diagnosing breast cancer which was later confirmed by the histopathology reports.

Aim and objectives

The aim and objectives of the study was to compare the efficacy of mammography and FNAC in predicting positive histopathological report in breast cancer and to determine the agreement between mammogram and FNAC in diagnosing breast carcinoma diagnosed through histopathological reports. Current study did not intend to draw any conclusion related to replacement of one diagnostic modality by other.

METHODS

Study design, location and duration

Present study is a cross sectional study conducted in the department of general surgery at tertiary care centre of Government medical college Thrissur which is a 1700 bedded multispeciality hospital, providing tertiary care to Thrissur, Malappuram and Palakkad. Districts. The study was conducted from December 2010 to December 2011.

Inclusion criteria

Inclusion criterion in current study was all female patients above 30 years of age with a palpable breast lump registered in surgery outpatient department.

Exclusion criteria

Exclusion criteria for current study were patients with ulcerative lesion or skin involvement; patients with

palpable axillary lymph node; and patients who were unwilling to participate.

Sample size and sampling technique

Sample size for current study was calculated considering the lowest difference in sensitivity and specificity. According to calculations, sample size needed for the study was 70 thus 80 consecutive patients with palpable breast lump satisfying the sample size registered or admitted in the department of general surgery, medical college, Thrissur were selected as study participants. The sample size was calculated at 5% significance level using the following equation:

$$N = \frac{[Z_{1-\frac{\alpha}{2}}\sqrt{2\pi_0(1-\pi_0)} + Z_{1-\beta}\sqrt{\pi_1(1-\pi_1)+\pi_2(1-\pi_2)}]^2}{(\pi_1-\pi_2)^2}$$

Where Z=1.96, power was taken as 80%, π_1=sensitivity/specificity of the reference HPR test=100%, π_2= sensitivity of mammogram=78% and specificity of FNAC=83%.

$$\pi_0 = \pi_1 + \frac{\pi_2}{2}$$

Tools and data collection techniques

Semi structured questionnaire and laboratory results were used as data collection tools in current study. Data was collected using interview method, clinical examination or laboratory investigations.

Procedure

Total 80 female patients above 30 years of age with a palpable breast lump visiting the outpatient department were examined and detailed patient history including the onset and duration of the breast lump occurrence were documented. Patients were selected regardless of their religion, occupation and financial status. The patients were then send for mammography and fine needle aspiration cytology (FNAC) from the breast lump and surgery was offered in the form of lumpectomy, wide excision and mastectomy. The procedure of mammography and FNAC was performed by trained personnel in the pathology and radio diagnosis department following a uniform protocol. All pathology specimens underwent a histopathological (HPR) study and results of mammography, FNAC and HPR were documented, compared and correlation was sought. The results obtained were tabulated and analysed statistically in terms of sensitivity, specificity, positive predictive values and negative predictive values.

Statistical analysis

Descriptive statistics parameters like sensitivity, specificity, positive predictive value and negative predictive value of mammography and FNAC were calculated using formulae:

$$\text{Sensitivity} = \text{True positives} \div \text{True positives} + \text{False negatives} \times 100$$

$$\text{Specificity} = \text{True negatives} \div \text{True negatives} + \text{False Positives} \times 100$$

$$\text{Positive predictive value} = \text{True positives} \div \text{True positives} + \text{False positives} \times 100$$

$$\text{Negative predictive value} = \text{True negatives} \div \text{True negatives} + \text{False negatives} \times 100$$

Overall sensitivity and specificity was calculated using the formula mentioned below:

$$\text{Overall sensitivity} = \text{Sensitivity}_1 + \text{Sensitivity}_2 (\text{Sensitivity}_1 \times \text{Sensitivity}_2)$$

$$\text{Overall specificity} = \text{Specifity}_1 \times \text{Specifity}_2$$

Where subscript 1 represents sensitivity/specificity of reference tests and sub script 2 represents sensitivity/specificity of new tests.

RESULTS

Majority of the patients (43.75%) amongst total 80 cases that were included in current study belonged to the age group of 30 to 39 years; whereas 21.25% patients belonged to the age group of 40 to 49 years and 35% belonged to the age group above 50 years (Table 1). Seventy patients (87.5%) attained menarche after 12 years of age whereas fifty (62.5%) patients were premenopausal and 30 (37.5%) patients were postmenopausal of which, 11 of post-menopausal patients had age of menopause <50 years and rest of postmenopausal women had menopause age of >50 years (Table 1).

Of the studied patients 66 (82.5%) were married and the rest were unmarried. Of the study population, 62 (77.5%) were multiparous and 18 (22.5%) were nulliparous. Family history was found to be positive in 10 out of 80 patients constituting 12.5% (Table 1).

Upper and outer quadrant was the most common quadrant involved in both benign (26.25%) and malignant (27.5%) lesion; whereas central zone of breast was least involved in benign (3.75%) and malignant (0%) lesions (Table 2). Among the 38 cases diagnosed to have benign lesions of the breast by histopathology 68.42% were in the age group 30 to 39 years and 15.78% cases were equally found in the age group of 40 to 49 and above 50 years

(Table 3). Whereas of the 42 malignant lesions, 21.4% were in the age group of 30 to 39 years, 26.19% were in the age group of 40 to 49 years and 52.38% were in age above 50 years. This study substantiates the fact that as the age group increases the breast lesions occurring tends to be more malignant. Out of total 80 patients sent for mammogram, 36.25% patients were diagnosed to have BIRADS IV and 18.75% were diagnosed to have BIRADS V, among the rest of the study population, 30% were diagnosed to have BIRADS II and 15% were included in BIRADS III (Table 4) (Figure 1).

In FNAC study; carcinoma was observed to be the most common indication seen in 39 (48.75%) patients, 12.5% cases were diagnosed to have fibroadenoma, 28.75% exhibited fibrocystic disease, 3.75% were having galactocele and 6.25% with breast abscess. All the lumps were subsequently subjected to surgery, in which 38 out of total 80 (47.5%) cases were proved to be benign and the remaining 42 (52.5%) were proved to be malignant on the histopathological examination (Table 4) (Figure 2). Amongst the 36 patients who were diagnosed to have benign disease through mammogram analysis, 3 patients turned out to have malignancy in histopathological examination. Among the 44 patients diagnosed to have malignancy in mammogram, 5 were proven to have benign disease in histopathology (Figure 3).

So, the sensitivity of mammogram was observed as 92.857% and specificity as 86.842%. Positive predictive value of mammogram was observed to be 88.636% and negative predictive to be 91.667%. Therefore, from current study findings accuracy of mammogram was predicted to be 90.000%. Statistical analysis showed a Chi square value of 51.201 and statistically significant $p<0.001$ for observed results of mammogram (Table 5). A variety of radiological patterns were seen in mammography. Definitive diagnoses were made from hard lumps, which produced stellate, or spiculated appearances. False negative or indeterminate diagnoses were concluded from soft, cystic or ill-defined lumps, and lumps close to chest wall. With improved technology and experience a high specificity is expected from mammography.

Amongst the 41 patients who were diagnosed to have benign disease through FNAC analysis, 3 were proven to have malignancy in histopathological report whereas all 39 patients who were diagnosed to have malignancy in FNAC were also proven to have malignancy in histopathology examination. Therefore, the sensitivity of FNAC diagnosis was observed to be 92.857% and specificity to be 100%. Positive predictive value of FNAC was observed to be 100% and negative predictive value to be 92.683%. The study results exhibited that FNAC has an accuracy of 96.250% (Table 5). Chi square test analysis showed a value of 68.850, with statistically significant $p<0.001$ for observed results of FNAC. False positive diagnoses were very minimal and false negative and inconclusive reports were seen from acellular aspirates from very hard lumps, hemorrhagic aspirates from highly vascular tumors and aspirates from cystic lumps.

Through the current study findings, the overall sensitivity and specificity calculated as per the formula mentioned in method section were observed to be 92.8% and 84.2% respectively. Also, the overall positive and negative predictive values calculated from current study results were 86.67% and 91.43% respectively (Table 6). Thus, the current study findings revealed that FNAC was more accurate in predicting breast cancer than mammogram.

Also, a significant association was observed between FNAC results and mammography results ($p=0.875$) (Table 7).

Table 1: Distribution of patients based on age, menstrual profile and obstetric status of patients (n=80).

Parameters		N	%
Age group (years)	30-39	35	43.75
	40-49	17	21.25
	>50	28	35.00
	Total	80	100
Age of menarche (years)	≤12	10	12.5
	>12	70	87.5
Menstrual status	Pre-menopausal	50	62.5
	Post-menopausal	30	37.5
Age of menopause (years)	≤50	11	36.67
	≥50	19	63.33
Marital status	Unmarried	14	17.5
	Married	66	82.5
Parity	Nulliparous	18	22.5
	Multiparous	62	77.5
Family history	Yes	10	12.5
	No	70	87.5

Table 2: Distribution of breast lumps in relation to the quadrants of breast.

Quadrant of breast	Benign		Malignant		Total	
	N	%	N	%	N	%
Upper outer quadrant	21	26.25	22	27.5	43	53.75
Upper inner quadrant	9	11.25	14	17.5	23	28.75
Lower outer quadrant	3	3.75	4	5	7	8.75
Lower inner quadrant	2	2.5	2	2.5	4	5
Areolar	3	3.75	0	0	3	3.75
Total	38	47.5	42	52.5	80	100

Table 3: Distribution of patients in relation to the histopathology of breast masses.

Age group (years)	Benign		Malignant	
	N	%	N	%
30-39	26	68.42	9	21.4
40-49	6	15.78	11	26.19
>50	6	15.78	22	52.38
Total	38	100	42	100

Table 4: Mammography and FNAC findings in the study group.

Findings	N	%
Mammogram		
BIRADS I	0	0
BIRADS II	24	30
BIRADS III	12	15
BIRADS IV	29	36.25
BIRADS V	15	18.75
Total	80	100
FNAC		
Fibroadenoma	10	12.5
Fibrocystic disease	23	28.75
Galactocele	3	3.75
Breast abscess	5	6.25
Carcinoma	39	48.75
Total	80	100

Table 5: Mammogram vs histopathology and FNAC vs histopathology results.

Findings		Histopathology		Total	χ^2	P value
		Benign	Malignant			
Mammogram						
Benign	N	33	3	36	51.201	<0.001
	%	41. 25	3.75	45		
Malignant	N	5	39	44		
	%	6.25	48.75	55		
Total	N	38	42	80		
	%	47.5	52.5	100		
Sensitivity	92.857					
Specificity	86.842					
Positive predictive value	88.636					
Negative predictive value	91.667					
FNAC						
Benign	N	38	3	41	68.85	<0.001
	%	47.5	3.75	51.25		

Continued.

Findings		Histopathology		Total	χ^2	P value
		Benign	Malignant			
Malignant	N	0	39	39		
	%	0	48.75	48.75		
Total	N	38	42	80		
	%	47.5	52.5	100		
Sensitivity	92.857					
Specificity	100.000					
Positive predictive value	100.000					
Negative predictive value	92.683					

Table 6: Combined efficacy of mammogram and FNAC.

Findings	Malignant	Benign	Total
Mammogram (test A)			
Malignant	39	5	44
Benign	3	33	36
Total	42	38	80
Sensitivity$_1$	92.85%		
Specificity$_1$	86.84%		
FNAC (test B)			
Malignant	0	1	1
Benign	3	32	35
Total	3	33	36
Sensitivity$_1$	0%		
Specificity$_1$	96.97%		
Overall sensitivity and specificity (test A + test B)			
Malignant	39	6	45
Benign	3	32	35
Total	42	38	36
Overall sensitivity	92.8%		
Overall specificity	84.2%		

Table 7: Measure of agreement between FNAC and mammogram.

Measure of agreement	Value	SE	T value	P value
Kappa	0.875	0.054	7.891	<0.001

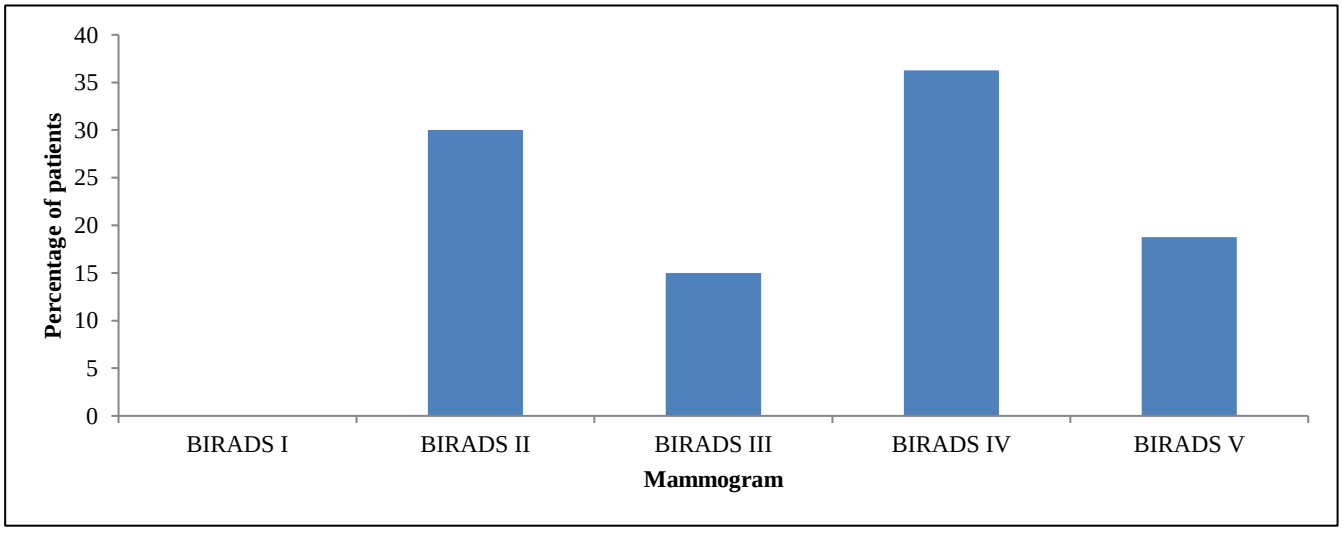

Figure 1: Distribution of patients according to mammogram findings.

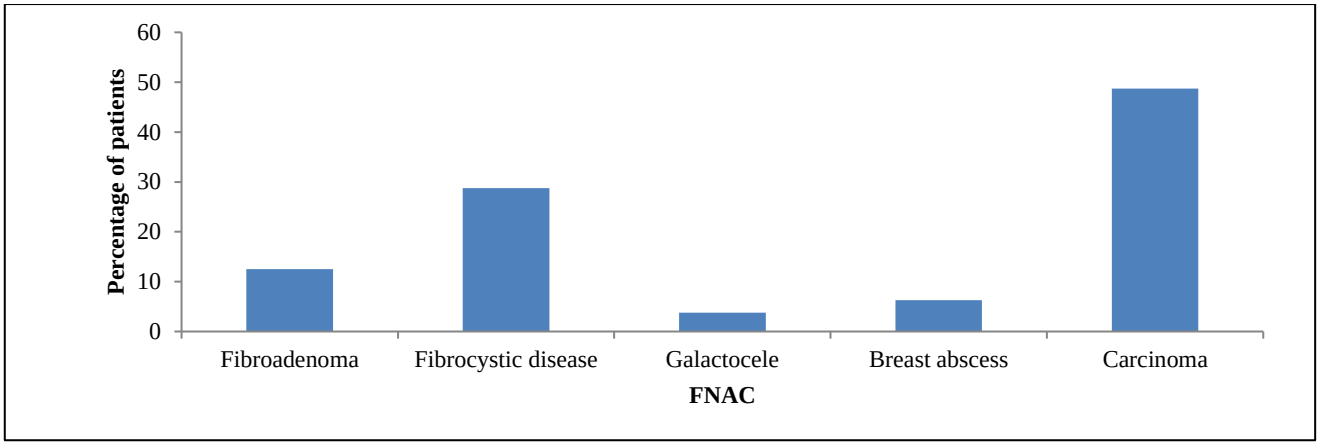

Figure 2: Distribution of patients according to FNAC findings.

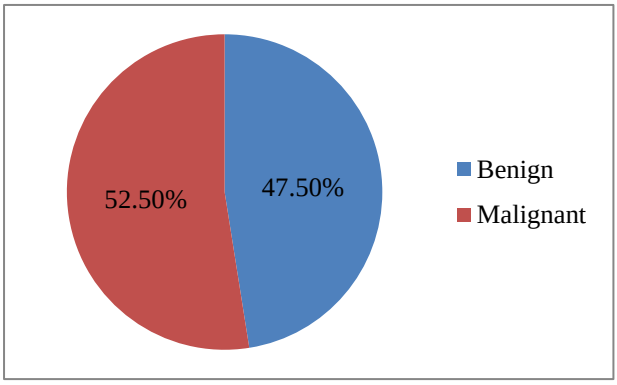

Figure 3: Histopathology findings in the study group.

DISCUSSION

Breast lump is a common complaint prevailing along with anxiety regarding possibility of malignancy in the surgical out-patient department of all major hospitals.[10] A quick diagnosis of a lump in the breast along with factors like time span of getting diagnosis report, reliability of diagnosis for deciding subsequent treatment strategy, hospital stay duration and cost effectiveness play a very crucial role in successful and effective management of breast carcinoma.

Currently a combination of three tests, i.e. clinical examination, radiological imaging (mammography, USG) and FNAC (pathology) together called as triple assessment is used to accurately diagnose all palpable breast lumps.[13-18] The triple assessment is taken positive if any of the three components is positive for malignancy and negative only if all of its components are negative for malignancy. In the present study 80 female patients with breast lumps were included to investigate and compare the efficacy of mammography and FNAC in predicting positive histopathological report in breast carcinoma. In current study earlier presentation of patients suspecting breast carcinoma can be attributed to location of hospital in a metropolitan city with a large urban population having awareness of necessity of earliest possible medical consultation in breast carcinoma. Present investigation was conducted on 80 female patients with a palpable breast lump each of whom underwent a fine-needle aspiration cytology and mammography of the lump followed by excisional surgery either in the form of a lumpectomy or a definitive surgical procedure like a mastectomy. The findings were then matched with the final histology report to see as to how accurate FNAC and mammography was as compared to the histopathology. Though many aspects observed in current investigation relating to the patient profile were tabulated and compared with earlier published study reports, main objective of current investigation was focused on cytohistological correlations.

Maximum patients included in the current study were observed to be in the age range of thirty to thirty-nine years. It was also observed through current study findings that maximum of female patients attained menarche after 12 years of age and most of the included female patients exhibited premenopausal menstrual status. Majority of female patients of the current study group exhibited menopause >50 years, were married and were multiparous.

Positive family history of carcinoma was observed in only 12.5% of study participants. It was observed through current study findings that the upper and outer quadrant was the commonest site of the breast lump with almost equal probability of benign or malignancy whereas central zone of breast was found to be the least involved zone of breast lump occurrence in current study patients. Histopathology findings of current study revealed that majority of patients diagnosed to have benign lesions of the breast were in the age group of thirty to thirty-nine years whereas majority of patients with malignant lesions were in the age group above 50 years which substantiates the fact that as the age group increases the breast lesions occurring tends to be more malignant.

FNAC diagnosis revealed carcinoma as the most common indication among patients followed by fibrocystic disease, fibroadenoma, galactocele and breast abscess.

Mammogram diagnosis indicated BIRADS IV to be most prevalent followed by BIRADS II, BIRADS V and BIRADS III. Current study findings revealed that mammography diagnosis has 90% accuracy, 92.857% sensitivity, 86.842% specificity, 88.636% positive predictive value and 91.667% negative predictive value.

Results of current study were in agreement with the results published literatue by Shetty et al who reported sensitivity for a combined mammographic and sonographic assessment to be 100% and specificity to be 80.1%.[21] Martelli et al reported sensitivity of mammography to be 73%.[22] Kaufman et al reported sensitivity and specificity of mammography to be 89% and 73%, respectively.[23] Steinberg et al found that mammography had a sensitivity and specificity of 85.3% and 70.6% respectively.[24]

Yang et al reported the sensitivity of mammography to be 92%, specificity to be 94% and positive predictive value to be 84%.[25] Results of current investigation revealed that FNAC diagnosis has 96.25% accuracy, 92.857% sensitivity, 100% specificity, 100% positive predictive value and 92.683% negative predictive value. Results of current study were in agreement with reported literature by Martelli et al who sensitivity of FNAC to be 68% and specificity to be 97%.[22] Kaufman et al reported sensitivity and specificity of FNAC to be 93% and 97%, respectively.[23]

Steinberg et al reported concordance for FNAC to be 83.0%, specificity to be 99.5%, sensitivity to be 49.0% and positive predictive value to be 98%.[24] Reinikainen et al found sensitivity of FNAC to be 92% and specificity to be 83% while overall accuracy to be 88%.[26] Ariga et al observed that FNAC had a sensitivity of 99%, positive predictive value of 99% and specificity of 99%, respectively.[27] Current study findings revealed, overall sensitivity to be 92.8% and overall specificity to be 84.2%, positive predictive value 86.67% and negative predictive value to be 91.43%. Significant association between FNAC and mammography results was observed.

Limitation

Limitation of the current study was the relatively small sample size of the study population, which was not adequate to make concrete recommendations.

CONCLUSION

It was concluded from current investigation findings that FNAC has more accuracy in predicting breast cancer than mammogram. Also, it was concluded that there is a close and significant association between FNAC and mammogram diagnosis thus when combined assessment is done with mammography and FNAC, the results exhibit high sensitivity, specificity, positive and negative predictive value with minimal errors leading to reproducible and reliable diagnosis of early breast cancer. Thus, it is recommended that combined assessment should be practiced for diagnosis of early breast cancer and definitive treatment can be started from diagnosis by the combined assessment before histology.

Recommendations

Form the current study findings authors would recommend that; any patient above the age of 30 years with breast lump should go for mammography diagnosis and any form of diagnostic intervention in the breast should be preceded by mammography. Tissue diagnosis should be done before definitive treatment of carcinoma breast. For rapid diagnosis of carcinoma breast FNAC can be considered adjuvant to mammography and clinical examination and any suspicious of malignancy should be confirmed by open biopsy.

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