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Study of cytodiagnosis of breast neoplastic lesions and comparision with histopathology in tertiary care centre of South Gujarat

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Abstract
Background: Breast cancer is the most common cancer among women in the western world and second most in India after carcinoma cervix. The most common presentation of breast disease is a palpable mass with or without inflammatory lesion, nipple discharge and imaging abnormalities. Fine Needle Aspiration Cytology (FNAC) is a popular diagnostic technique as it is highly sensitive, specific, rapid, easy to perform, cost effective and can be carried out at OPD level.in the first visit without the need of anaesthesia. This technique is commonly used in combination with physical examination and mammography, so called triple-test diagnostic triad. Triple assessment of breast mass had decreased the false negative rate to less than 1%.
Aims and Objectives: The aim of this study was to find out the common causes of breast lump, to find out sensitivity and specificity of FNAC of breast lump and also to calculate statistical data like sensitivity, specificity, positive predictive value, negative predictive value and efficiency of FNAC procedure.
Materials and Methods: This study comprised of 180 cases and carried out at histopathology section of pathology department of GMERS Medical College, Valsad, a tertiary care centre in Valsad district of Gujarat state, India. The clinical case history and radiological details of the patient was recorded which includes detail history of pain, nipple discharge, ulceration of nipple and duration of lesion.
Results: Out of total 180 cases, 126 (70.0%) were benign and 54 (30.0%) were malignant. Out of total 180 cases, 95 (52.8%) were located in right sided breast, 82 (45.5%) were located in left sided breast and 03 (2.4%) were located bilaterally. Out of 121 histologically diagnosed benign cases, 101 (83.5%) were fibroadenoma. Out of total 59 histologically diagnosed malignant cases, 43 (72.9%) were intraductal carcinoma. On FNAC of breast lumps, 70% (n=126) were categorized as benign, 30% (n=54) as malignant. Subsequent histopathology of breast lumps revealed 67.2% (n=121) benign lesions and 32.8% (n=59) malignant lesions.
Conclusion: The FNAC is an essential and important test in diagnosing breast lump. It is patient-friendly, easy to perform, more reliable, repeatable, cost effective and a simple and safe test to diagnose patient presenting with lump breast. FNAC can suggest further investigation without delay if carcinoma could be diagnosed. It also help the clinicians for early diagnosis and specific management thus reducing morbidity and mortality.

Keywords: Breast lesion, fine needle aspiration cytology, histology, sensitivity, specificity, positive

Introduction
Breast cancer is the most common cancer among women in the western world and second most in India after carcinoma cervix. The incidence of the disease has shown a steep rise in women younger than 40 years of age. Only less than 50% women are alive and free of disease for 10 years after the diagnosis [1].
The most common presentation of breast disease is a palpable mass; although breast diseases can also present as inflammatory lesion, nipple secretion and imaging abnormalities [2]. Physical examination, FNAC, mammography, ultrasound, core needle biopsy and open excision biopsy are used for diagnostic workup of a palpable breast mass. Various combinations of these methods have been also used to diagnose the lesions effectively. FNAC (Fine Needle Aspiration Cytology) is a popular diagnostic technique as it can be done in the first visit without the need of anaesthesia. This technique is commonly used in combination with physical examination and mammography, so called triple-test diagnostic triad [3].

Triple assessment of breast mass had decreased the false negative rate to less than 1% [4].

Fine needle aspiration cytology (FNAC) was first described and practiced by Martin and Ellis in 1930 [5].

FNAC is highly sensitive, specific, rapid, easy to perform, cost effective and can be carried out at OPD level [6]. Molecular ancillary techniques for example progesterone receptor & estrogen receptor, proliferation antigen & DNA pattern analysis can be applied on aspirated material [7]. However, the aspiration cytology is not a substitute for conventional surgical histopathology as a definitive diagnosis is not always possible by cytology, but categorization of disease and differential diagnosis can be provided in the majority of cases [8]. The ultimate benefit of aspiration cytology; however, rests in its demonstration of malignant disease, when other diagnostic modalities are inconclusive [9]. Thus the FNAC have reduced the number of open breast biopsies. The limitations of FNAC include difficulty to differentiate ductal carcinoma in situ (DCIS), atypical ductal hyperplasia from low grade DCIS, and fibroadenoma from phyllodes tumor [10, 11].

Aims and objectives

The aim of this study was to find out the common causes of breast lump and to find out sensitivity and specificity of FNAC of breast lump in our institute. This study was initiated to correlate fine needle aspiration cytology diagnosis and histopathology diagnosis of the breast lesions also to calculate statistical data like Sensitivity, specificity, positive predictive value, negative predictive value, and efficiency FNAC procedure.

Materials and Methods

Study design: The present study was carried out at histopathology section of pathology department of GMERS Medical College, Valsad a tertiary care centre in Valsad district of Gujarat state, India during the period of April 2014 to March 2018.

Type of study: Retrospective

Inclusion criteria: All patients presenting with breast lump enlargement were included in the study.

Exclusion criteria: Those patients with aspirated material was either inadequate or smears were unsatisfactory for evaluation and known case of malignancy were excluded from this study.

Data collection procedure: In present study, we analysed all 180 cases which received for cytopathology and histopathology examination under the diagnosis of breast tuours from surgical department. The clinical case history and radiological details of the patient was recorded which includes detail history of pain, nipple discharge, ulceration of nipple and duration of lesion. The examination of breast lump was done with recording of size and site of lump, consistency, and fixation to skin and underline tissue, retraction of nipple along with regional lymph node involvement.

Technique

The skin overlying the lump was cleansed with antiseptic solution after determining the site by palpation. Local anaesthesia was not used. The tumor was gripped by one hand in position suitable for needling. Lesions were held between the index finger and thumb of one hand and were punctured. Tight fitting 10 ml plastic disposable syringes and fine 22 Gauge needles of 38 mm length were used for FNAC. When the needle had entered the tumor mass, the plunger of the syringe was retracted to create a vacuum in the system while the needle was guided in a straight line through the lesion. This was maintained with the thumb and index finger of another hand, and the needle was moved through the tumor three or four times in different directions [12]. Throughout this procedure the negative pressure was maintained by keeping the plunger retracted. When the aspiration was completed, the syringe was allowed to equalize before the needle was withdrawn.

Preparation of smears

The needle was then removed from the tumor and the syringe was disconnected from the needle. The syringe was filled with air and reconnected to the needle. The contents of the needle were then carefully expressed on clean dry slides and smears of adequate density was prepared by gentle pressure with the flat surface of another slide. Aspirate containing blood or cystic fluid were spread like that of a case of ordinary blood smears and large tissue fragments that were collected at the end of the smear, then gently squeezed with the flat pressure with the glass slide.

Fixation and staining of smears

The wet smear fixed with Ether Alcohol mixture stained with Papanicolaou Stain. Air dried smears followed by staining with May-Grunwald-Giemsa stain for Fine Needle Aspiration cytology, and alcohol (95%) fixed smears followed by staining with Haematoxylin-Eosin stain for tissue sections were used. FNAC diagnosis were given in benign and malignant categories. Surgical specimens obtained were incisional biopsy, total excisional biopsy or modified radical mastectomies. Each formalin fixed specimens received surgical specimen in Histopathology Section were examined grossly for its size, shape, weight, consistency and appearance. Tissue cut surface was also examined for the presence of hemorrhage, necrosis and cystic spaces etc. Presence or absence of any gross involvement of adjacent structure along with depth of the tumor was also noted. All these specimens were dissected by grossing followed by fixation, dehydration, clearing and impregnation in a automatic tissue processor. Paraffin blocks were made and sections were cut at 3 to 5 micron thickness and haematoxylin and eosin stain was done. Detailed histopathologic examination done to establish a diagnosis. Cytohistological correlation was done. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy of FNAC in diagnosing breast lesions was calculated using the formulas.

Results

Table 1: Distribution of cases (FNAC diagnosis) according age.

Age Group	Benign (%)	Malignant (%)	Total (%)
<20	28 (22.2)	00	28 (15.6)
21-30	51 (40.5)	00	51 (28.3)
31-40	32 (25.4)	04 (7.4)	36 (20.0)
41-50	11(8.7)	14 (25.9)	25 (13.9)
51-60	04 (3.2)	25 (46.3)	29 (16.1)
>60	00 (0.0)	11 (20.4)	11 (6.1)
Total	126 (70.0)	54 (30.0)	180 (100.0)

Out of total 180 cases, 126 (70.0%) were benign and 54 (30.0%) were malignant. Out of 126 benign lesions, 51 (40.5%) were found between 21-30 years followed by 32 (25.4%) were found between 31-40 years, 28 (22.2%) were found in <20 years. Out of 54 malignant lesions, 25 (46.3%) were found between 51-60 years followed by 14 (25.9%) were found between 41-50 years, 11 (20.4%) were found in >60 years.

Table 2: Distribution of cases (FNAC diagnosis) as per affected side of breast.

Affected Site	Benign	Malignant	Total
Right Breast	64 (50.8)	31 (57.4)	95 (52.8)
Left Breast	59 (46.8)	23 (42.6)	82 (45.5)
Both	03 (2.4)	00	03 (1.7)
Total	126 (70.0)	54 (30.0)	180 (100.0)

Out of total 180 cases, 95 (52.8%) were located in right sided breast, 82 (45.5%) were located in left sided breast and 03 (2.4%) were located bilaterally.

Table 3: Histopathological diagnosis of benign breast lesions.

HPE diagnosis	< 20	21-30	31-40	41-50	51-60	>60	Total (%)
Fibroadenoma	25	44	24	07	01	00	101 (83.5)
Fibrocystic Disease	00	03	02	00	01	00	06 (4.9)
Fibroadenosis	00	01	02	01	00	00	04 (3.3)
Phyllodes	00	01	00	01	01	00	03 (2.5)
Papilloma	02	01	00	01	00	00	04 (3.3)
Lipoma	01	00	01	00	01	00	03 (2.5)
Total	28	50	29	10	04	00	121 (100.0)

Out of total 121histologically diagnosed benign cases, 101 (83.5%) were fibroadenoma followed by 06 (4.9%) cases were fibrocystic disease, 04 (3.3%) cases each for fibroadenosis and papilloma and 03 (2.5%) cases each for phyllodes and lipoma.

Table 4: Histopathological diagnosis of malignant breast lesions.

HPE diagnosis	< 20	21-30	31-40	41-50	51-60	>60	Total
Intraductal Carcinoma	00	00	02	11	19	11	43 (72.9)
Intralobular Carcinoma	00	00	00	02	03	01	06 (10.1)
Ductal Carcinoma In situ	00	00	01	01	02	00	04 (6.8)
Intrapapillary Carcinoma	00	00	00	01	01	01	03 (5.1)
Mucinous Carcinoma	00	00	00	00	01	01	02 (3.4)
Malignant Phyllodes	00	00	01	00	00	00	01(1.7)
Total	00	00	04	15	26	14	59 (100.0)

Out of total 59 histologically diagnosed malignant cases, 43 (72.9%) were intraductal carcinoma followed by 06 (10.1%) cases were intralobular carcinoma, 04 (6.8%) cases were ductal carcinoma insitu, 03 (5.1%) cases were intrapapillary carcinoma, 02 (3.4%) cases were of mucinous carcinoma and 01(1.7%) case was of malignant phyllodes.

Table 5: Accuracy of FNAC in breast lesions.

Diagnosis	TP	TN	FP	FN	Sensitivity	Specificity	PPV	NPV	%FN	%FP
Benign	121	54	05	00	100%	91.5%	96	100	00	4.1
Malignant	54	121	00	05	91.5%	100%	100	96	9.2	00

(TP=True positive, TN=True negative, FP=False positive, FN=False negative, PPV=Positive predictive value, NPV=Negative predictive value, Sensitivity = TP X100/TP+FN, Specificity = TN X100/ TN+FP, Positive predictive value= TP X 100/TP+FP, Negative predictive value = TN X100/ TN+ FN, Efficiency= TP+TN/TP+FP+FN+TN=97.22%).

Out of total 180 breast lesions, 126 cases were diagnosed benign on cytopathology and 121 cases were diagnosed on histopathology. It shows that 05 (4.0%) cases were turned into malignant on histopathology correlation.

There was no specificity for side of breast involvement by various lumps. 52.2% (n=95) cases were with right breast involvement, 45.5% (n=82) with left breast and 1.7% (n=03) with bilateral involvement.

On FNAC of breast lumps, 70% (n=126) were categorized as benign, 30% (n=54) as malignant. Subsequent histopathology of breast lumps revealed 67.2% (n=121)

benign lesions and 32.8% (n=59) malignant lesions.

Discussion

In the present study, 180 cases of breast lesions were analyzed, out of which 126 cases (70.0%) cases were benign and 54 cases (30.0%) were malignant. In our study, the most common age group presenting with the breast lump was 31-40 years. Benign breast lesion occurred between 14 and 53 years of age, with peak incidence in 2nd and 3rd decade of life. Malignant breast lesion occurred between 38 and 68 years of age, with peak incidence in 6th decade of life. Alam *et al.* [13] studied that age-related incidence of carcinoma of the breast in female and resulted that benign lesions below the age 40 years and peak incidence in 2nd and 3rd decade of life, respectively, and malignant lesions above the age of 40 years and peak incidence in between 41 and 50 years. In Hebbar and Iyannn [14] study, the age incidence was ranged from 16 to 74 years (Mean age 41.68 years). The age incidence of the benign lesions ranged from 16 to 39 years (Means age 27.89 years). The incidence of the malignant lesions ranged from 34 to 74 years (Mean age 52.25 years). The most common age group for benign lesions was between 21 and 30 years and for the malignant lesion was 41 to 50 years. In the present study the most common benign lesion diagnosed was fibroadenoma and the most common malignant lesion diagnosed was intraductal carcinoma.

Table 6: Comparision of results with other studies.

Sr. No.	Study	Sensitivity%	Specificity%	PPV%	NPV%
1	Hussain *et al.* [15]	90.0	100.0	--	--
2	Alema *et al.* [16]	85.29	100.0	100.0	98.79
3	Nguansangiam *et al.* [17]	92.5	90.2	88.1	93.9
4	Ahmed *et al.* [18]	92.6	95.2	95.5	92.2
5	Yeoh and Chan [19]	79.0	98.0	92.0	94.0
6	Choi *et al.* [20]	77.7	99.2	98.4	88.0
7	`Hebbar *et al.* [21]	93.1	100.0	100.0	90.47
8	Edwin IA *et al.* [22]	100.0	93.55	95.65	100.0
9	Present study	91.5	100.0	100.0	96.0

In present study, sensitivity is 91.5% which very well comparable with study of Hussain *et al.* [15], Nguansangiam *et al.* [17], Ahmed *et al.* [18] and Hebbar *et al.* [21]. It is quite higher than Alema *et al.* [16], Yeoh and Chan [19] and Choi *et al.* [20]. It is quite lower than Edwin IA *et al,* [22].

In present study, specificity is 100% which very well comparable with study of Hussain *et al.* [15], Alema *et al.* [16] and Hebbar *et al.* [21]. It is quite higher than Nguansangiam *et al.* [17], Ahmed *et al.* [18], Yeoh and Chan [19], Choi *et al.* [20] and Edwin IA *et al,* [22].

In present study, positive predictive value is 100% which very well comparable with study of Alema *et al.* [16] and Hebbar *et al.* [21]. It is quite higher than Nguansangiam *et al.* [17], Ahmed *et al.* [18], Yeoh and Chan [19], Choi *et al.* [20] and Edwin IA *et al,* [22].

In present study, negative predictive value is 96.0% which is very well comparable with most of all study except study of Choi *et al,* [20].

Efficiency of fine needle aspiration cytology in the present study is 97.22% which is very well comparable with study of Rocha PD *et al.* [23], Waghmare RS *et al.* [24], Frable WJ *et al.* [25], Palombini *et al.* [26] and Feichter GE *et al,* [27].

Conclusion

The FNAC is an essential and important test in diagnosing and managing a patient presenting with lump breast. It is patient-friendly, easy to perform, more reliable, repeatable, cost effective and a simple and safe test to diagnose patient presenting with lump breast. FNAC can suggest further investigation without delay if carcinoma could be diagnosed. High sensitivity and high PPV shows that a patient with positive FNAC means a definite and accurate diagnosis of the concerned pathology when compared with the final histopathology report. It also help the clinicians for early diagnosis and specific management thus reducing morbidity and mortality.

Importance of this study: This is important to know the different variety of pattern of breast lesions and utility of FNAC in tertiary care hospital.

Author contribution

First author Dr. Amita Patel has collected all data and done study in his own institute. Second and corresponding author Dr. Vandana Patel has prepared the study design and drafted manuscript in presentable manner for publication.

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