

A study to classify the fine needle aspirates of breast lumps as per the IAC Yokohama system for reporting breast cytopathology along with histopathological correlation

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ABSTRACT

Introduction: The burden of breast cancer is growing all over the world. Fine Needle Aspiration Cytology is an important diagnostic test in the early diagnosis of breast lesions. The IAC Yokohama classification for reporting breast cytopathology cases have five standard categories namely Insufficient (C1), Benign (C2), Atypical (C3), Suspicious of malignancy (C4) and Malignant (C5).

Aims and Objectives: To classify the breast cytopathology cases as per the IAC Yokohama system of reporting breast cytopathology and to calculate the Risk of Malignancy, Sensitivity, Specificity, Positive Predictive Value, Negative Predictive Value.

Materials and Methods: The cytopathological diagnoses of breast lesions were categorized as per the IAC Yokohama system for reporting breast cytopathology. With histopathology as gold standard, Sensitivity, Specificity, Positive Predictive Value (PPV), Negative predictive value (NPV), Risk of malignancy (ROM) and diagnostic accuracy were also calculated using standard formulae.

Results: A total of 223 cases of FNACs of breast lesions were done in this study of which 105 had histopathological correlation. The number of cases in each IAC Yokohama category are C1 (6), C2 (174), C3(13), C4(8), C5(22). The ROM malignancy in each of these categories was C1(0%), C2 (3.84%), C3(55.55%), C4(100%), C5(100%).

Conclusion: FNAC will continue to play an important role in early diagnosis of breast cancers. The IAC Yokohama system of breast cytopathology reporting helps in standardizing the reports of these cases.

Keywords: cancer, cytology, breast lumps, risk of malignancy

INTRODUCTION

Breast cancer is the second most common cancer globally, second only to lung cancers and thereby poses a huge public health challenge. It also ranks as the fourth common cancer -causing mortality worldwide. Nearly 47.3% of the mortality due to breast cancers occur in the Asia [1].

While the breast cancer five -year survival rate exceeds 90% in high income countries, in India it is at a devastatingly low 66% leading to a large number of patients dying prematurely. It is also projected that by the year 2040, 60% of the new cases and 70% of the breast cancer deaths will be in the low and middle income countries [2]. It has been predicted that approximately 2,30,000 cases of breast cancer will be reported on an annual basis by the year 2025 in India and most of these would be in women below 45 years of age [3]. The Global Breast Cancer Initiative, a unique global strategic collaboration, aims at health promotion, early, rapid diagnosis and comprehensive cancer treatment to reduce the burden of breast cancer mortality [2].

Fine Needle Aspiration Cytology (FNAC) is an effective, rapid and cost- effective technique for diagnosing breast lumps [4]. It is an important part of the “triple assessment” approach that includes clinical, radiological and pathological assessment in that order [5].

There are many systems for standardizing reporting in cytopathology such as the Bethesda system for thyroid and cervix cytology and Milan system for salivary gland cytology. The International Academy of cytology met in 2016 and came up with a set of new guidelines with the purpose of improving and standardizing reports in breast cytology. This is called “The International Academy of Cytology Yokohama System for Reporting Breast Cytopathology”. Each diagnostic category in this system comes with “Risk Of Malignancy” (ROM) based on recent studies and also recommendations for management approach [6, 7].

This study has been conducted with the aim of classifying cytological diagnoses of breast FNAC as per “The IAC Yokohama classification system for reporting breast cytopathology”.

OBJECTIVES

- To determine the age- wise distribution of breast lumps as per various diagnostic categories of “The IAC Yokohama classification system for reporting

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breast cytopathology”.

- To calculate the Sensitivity, Specificity, Positive Predictive Value (PPV), Negative Predictive Value (NPV), ROM of the benign and malignant categories of IAC Yokohama system with histopathology as gold standard.

MATERIAL AND METHODS

The present study is a cross-sectional, observational study done over a period of 18 months between July 2022 and January 2024 at the Department of Pathology, Apollo Institute of Medical sciences and Research Chittoor. The study was conducted after due clearance from the Institutional Ethics Committee and the IEC clearance number No. FR012/IEC/AIMSR/2022 was allotted.

FNACs of 223 cases of breast lumps were done. 10 ml disposable syringes were used for FNAC procedure after taking informed consent. The cytological smears were fixed in Isopropyl alcohol and stained using Hematoxylin and Eosin stain after which they were subjected to cytopathological examination. Cytological diagnoses were classified as per the “The International Academy of Cytology Yokohama System for Reporting Breast Fine Needle Aspiration Biopsy Cytopathology”.

The various categories are as follows:

- C1- Insufficient
- C2- Benign
- C3- Atypical
- C4- Suspicious of Malignancy
- C5- Malignant

The cytological diagnoses were compared with histopathological diagnoses, which is considered as gold standard, wherever possible.

Data analysis

The data collected was entered into Microsoft excel sheet and subsequently analyzed using SPSS software version. Descriptive

statistics were done for the study.

Also, Sensitivity, Specificity, Positive Predictive Value (PPV), Negative Predictive Value (NPV), Risk of Malignancy (ROM) and diagnostic accuracy were also calculated using standard formulae, keeping histopathology as the gold standard.

These ratios were calculated by considering three scenarios:

- Scenario 1 is by considering only the C5 category as malignancy and comparing with histopathology as gold standard.
- Scenario 2 is by considering C4, C5 categories of cytology as malignancy and comparing with histopathology as gold standard.
- Scenario 3 is by considering C3, C4, C5 categories of cytology as malignancy and comparing with histopathology as gold standard.

Inclusion criteria

All patients who presented with breast lumps for FNAC during the study period, both males and females, were included in the study.

Exclusion criteria

The cases without corresponding histopathological diagnoses were not included in calculating the sensitivity, specificity, PPV, NPV, ROM and diagnostic accuracy.

RESULTS

A total of 223 FNACs of breast lumps were done during the study period and cytological diagnoses were categorized as per the “The IAC Yokohama System for Reporting Breast Fine Needle Aspiration Biopsy Cytopathology” classification into five groups. Histopathological correlation was available for 105 cases accounting to 47.09% of all cases.

The total number of male patients in the were 20 and female patients were 203. Male to female ratio is shown in the Figure 1.

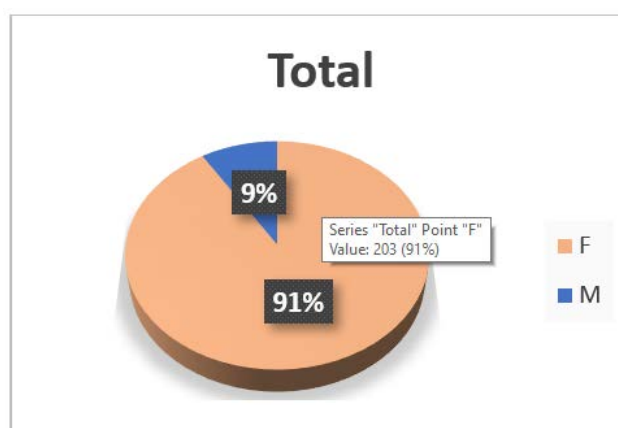


Fig. 1. Male to female ratio of the cases in the present study

The total number of cases in each IAC Yokohama category is presented in table 1.

The age of the patients in the present study ranged from 12 years to 85 years. Both the youngest and oldest were female patients. The mean age of the patients was 39.64 years.

The commonest IAC Yokohama category both was “C2 Benign” and it had 174 cases in total which was the maximum for any category. The least common category was “C1 Inadequate” which had only 6 cases. “C5 malignant” category included 22 cases. “C3 Atypia” category had 13 cases.

Tab. 1. Age-wise distribution of the cases in different IAC Yokohama categories

Age group (in years)	C1	C2	C3	C4	C5
10 to 20	1	21	0	0	0
21 to 30	1	46	1	0	1
31 to 40	2	46	5	2	3
41 to 50	1	34	5	2	7
51 to 60	1	18	1	2	2
61 to 70	0	7	1	1	6
>70	0	2	1	1	3
TOTAL	6	174	13	8	22
Percentage	2.70%	78.00%	5.80%	3.60%	9.90%

Out of the 223 cases, 105 cases had histopathological correlation. The most common benign lesion was fibroadenoma whereas Invasive ductal carcinoma, NOS was the most common histopathological diagnosis in the malignant category.

The risk of malignancy for each category is indicated in table 2. It was calculated by using the following formula:

Risk of malignancy = Total number of cases confirmed histologically as malignancy / Total number of cases in the diagnostic category

“C1 Inadequate” category showed 6 cases out of which all were benign on histopathology. “C2 benign” category showed a total of 78 cases out of which 3 were malignant on histological correlation. In “C3 Atypia” category, the Risk of malignancy was found to be 55.55%. All cases of C4 and C5 categories were confirmed as malignant lesions on histopathological examination. Hence, the ROM (%) for these two categories was found to be 100%.

Tab. 2. Risk of malignancy

S.No	IAC Yokohama Category	Risk of malignancy (%)
1	C1 Inadequate	0%
2	C2 Benign	3.84%
3	C3 Atypia	55.55%
4	C4 Suspicious of malignancy	100%
5	C5 Malignant	100%

Sensitivity, Specificity, Positive Predictive Value (PPV), Negative Predictive Value (NPV), and Diagnostic accuracy are given in the table 3.

Sensitivity was 86.9%, when C3, C4 and C5 categories were considered as malignant cytologically. Sensitivity was 34.8% when only “C5 Malignant” category was considered as malignant.

On the other hand, Specificity and Positive Predictive Value (PPV) were highest i.e., 100% each, in two scenarios i.e., by considering C4, C5 categories as malignant and also by only considering

ing C5 as malignant cytologically.

Common cases in histopathological spectrum of benign lesions included Fibroadenoma, Fibrocystic change, Benign Phyllodes tumor, Granulomatous mastitis, Galactocole, fat necrosis. Gynecomastia was the commonest lesion among male patients.

Malignant lesions included Duct carcinoma in situ, Invasive carcinoma NOS, Cystic papillary carcinoma, Malignant phyllodes tumor. One case of Borderline phyllodes also was diagnosed on histopathology.

Tab. 3. Sensitivity, specificity, PPV, NPV and diagnostic accuracy by considering three scenarios

S.No	Ratio	C3, C4, C5 as Malignant	C4 & C5 as malignant	Only C5 as malignant
1	Sensitivity	86.90%	65.20%	34.80%
2	Specificity	95.10%	100%	100%
3	Positive Predictive value (PPV)	83.30%	100%	100%
4	Negative predictive value (NPV)	96.30%	91.10%	84.50%
5	Diagnostic accuracy	93.30%	92.30%	85.70%

DISCUSSION

FNAC has a unique place in the diagnosis of breast lumps. Majority of breast cancers in India are diagnosed in late stages. Hence there is a need for early diagnosis to improve the outcome in patients. FNAC is a major diagnostic test in low and middle-income countries like India. It helps in differentiating benign from malignant lesions [8]. Some of the biggest advantages of FNAC include its low turn-around time, ease of the procedure and minimal risk involved. However, in situ and invasive carcinomas are not distinguished in cytological examination. Needle core biopsies of breast lumps is favored in high income countries because of the advantage of performing IHC studies of the hormone receptors and HER 2 neu receptor [6, 9].

Nevertheless, combining FNAC with radiological guidance in every case would maximize the yield as well as improvise the diagnosis.

Definitions of each category

In the study by Field AS et al, the definitions of various categories are stated clearly and are as follows [6],

- Category 1- Insufficient “Slides that are too sparsely cellular, too poorly smeared, too degenerate, or too poorly fixed to allow a cytomorphological diagnosis.”
- Category 2- Benign “A case with unequivocally benign cytological features, which may or may not be diagnostic of a specific benign lesion.”
- Category 3- Atypical “Presence of cytological features seen in benign processes or lesions, but with the addition of some features that are uncommon in benign lesions and that may be seen in malignant lesions.”
- Category 4- Suspicious of Malignancy “The presence of some cytomorphological features which are usually

found in malignant lesions but with insufficient malignant features either in number or quality to make a definite diagnosis of malignancy.”

- Category 5- Malignancy “Malignant cytological diagnosis is an unequivocal statement that the material is malignant and the type of malignancy identified should always be stated.”

In the present study, a total of 223 cases of FNAC were done out of which 105 had histopathological correlation.

The distribution of the percentage of cases in each category of the “IAC Yokohama classification” is given in table 4. “C1 Inadequate” category had only 2.7 % of all the cases. The potential reasons for inadequacy are, improper technique and fibrosis in the lesion.

Rapid Onsite Evaluation (ROSE) would help to reduce the number of cases classified into C1. ROSE can be carried out by staining the slides for adequacy by using 1% toluidine blue stain [10].

Maximum number of cases were in the “C2 Benign” category which is in concordance with all the studies mentioned below. The present study showed 78% of cases in this category which is very similar to that in Panwar H et al (82.6%) [11]. The study by Tejeswini V et al showed a slightly lower number i.e., 41.59% [12]. The second most common diagnostic category in the present study was “C 5 Malignant” which showed 9.9% of cases. This finding once again resonates with the finding in other studies. In the study by Panwar H et al, it was 8.4% while in the studies by Ahuja S et al and Agarwal N et al, it was 18.2% and 18.7% respectively. The study by Tejeswini V et al is in slight discordance and reported higher number of cases (32.3%) in the malignant category [10-13].

Makker I et al, have raised an issue regarding overlap between the definitions of C3 and C4 category and have proposed to merge these two categories in order to avoid confusion [14].

S.No	Name of the study	C1 Inadequate	C2 Benign	C3 Atypical	C4 Suspicious of malignancy	C5 Malignancy
1	Panwar H et al [11] (2019)	1.30%	82.60%	5.70%	1.70%	8.40%
2	Ahuja S et al [13] (2021)	3.60%	69.50%	6.30%	2.30%	18.20%
3	Tejeswini V et al [12] (2021)	3.98%	41.59%	8.41	13.72%	32.30%
4	Agarwal N et al [10] (2021)	4.90%	65.30%	7.80%	3.30%	18.70%
5	Present study (2024)	2.70%	78.00%	5.80%	3.60%	9.90%

The Risk of Malignancy (ROM) of each category is given in table 5. In the present study, the ROM of “C3 Category” is high (55.55%) which is in slight disagreement with other studies, where the values are lower. One reason could be that the degree of atypia of the cells in the area sampled was not convincing enough to classify the lesions into C4 or C5 categories. The inexperience

of the cytopathologist could be another possibility.

Agarwal N et al, Tejeswini V et al and Ahuja S et al, and showed ROM of 23.3%, 26.31% and 17.4%, respectively [10,12,13].

The ROM for C4 and C5 categories was 100% each in the present study which is in concordance with the study by Tejeswini V et al [12].

S. No	Name of the study	C1 Inadequate	C2 Benign	C3 Atypical	C4 Suspicious of Malignancy	C5 Malignancy
1	Panwar H et al [11] (2019)	0%	0%	0%	75%	100%
2	Ahuja S et al [13] (2021)	5%	1.50%	17.40%	81.80%	100%
3	Tejeswini V et al [12] (2021)	22.22%	5.32%	26.31%	100%	100%
4	Agarwal N et al [10] (2021)	16%	0.70%	23.30%	94.10%	100%
5	Present study (2024)	0%	3.84%	55.55%	100%	100%

In the present study, Sensitivity was highest (86.9%) when C3, C4, C5 categories were considered malignant (positive) when compared to other two scenarios. Similar finding was observed in the study by Ahuja S et al, where the sensitivity was found to be 97.2% [13].

In the study by Agarwal N et al, when “C5 malignant” category was considered as positive, the sensitivity was 80.5%. Specificity in the above study was 99.7% which is comparable to the present study. In that same study, when C4 and C5 categories were considered cytologically malignant (positive), the sensitivity improved to 99.1% and specificity was 99.3% [10]

On the contrary, in the present study, when category C5 was alone considered positive, the sensitivity was low (34.8%) but specificity was 100% in this scenario.

CONCLUSION

The use of “The IAC Yokohama system for reporting breast cytopathology” will help in the standardization of breast cytopathology reporting.

Sensitivity is maximum when C3, C4 and C5 categories are considered positive.

Radiological guidance should be used for every case possible to improve the diagnostic yield.

FNAC would continue to be a popular early diagnostic method in breast lesions in countries like India where Needle core biopsies are not regularly done in many centers.

LIMITATIONS OF THE STUDY

- Rapid Onsite evaluation (ROSE) was not done in this study. ROSE would have helped in increasing the cellular yield.
- Only a few FNACs were done under radiological guidance.

CONFLICT OF INTEREST

Nil

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