



APPLICATION OF YOKOHAMA SYSTEM FOR BREAST FNAC WITH ASSESSMENT OF RISK OF MALIGNANCY.

Pathology

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ABSTRACT

Introduction: This study is based on application of recently proposed International Academy of cytology (IAC) Yokohama system of Breast cytology. **Aim:** The main objective of the study was to categorise the Breast Fine Needle Aspiration Cytology (FNAC) samples according to this new system of reporting and to assess the Risk of malignancy (ROM) for each category as well as the diagnostic yield of the Breast FNAC. **Materials and Methods:** Total of 191 FNAC cytology smears from July 2021 to June 2022 were obtained. Microscopy was done and classification was done according to newly proposed IAC Yokohama system of reporting. The ROM was obtained. The sensitivity, specificity, Predictive Value (PPV), Negative Predictive Value (NPV) and accuracy of Breast FNAC were calculated accordingly. **Results:** The Breast FNAB samples were distributed as follows: insufficient material 6.29%, benign 63.87 %, Atypical probably benign 3.14%, suspicious for malignancy 4.71% and malignant 21.98%. Of the 191 FNAC cases, 44 cases had histopathological correlation. The respective ROM for each category was 00% for category 1 (insufficient), 00% for category 2 (benign), 33.3% for category 3 (atypical), 100% for category 4 (suspicious for malignancy) and 100% for category 5 (Malignant). The sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy were respectively 100%, 92.3%, 89.47% 100% and 95.35% when malignant, suspicious of malignancy and atypical categories were considered positive. **Conclusion:** Categorisation of the Breast FNAC cytology according to IAC Yokohama system of reporting helps pathologist in the diagnostic clarity and guides clinician in the appropriate patient management. IAC Yokohama system of reporting breast cytopathology serves as a common language to pathologist and clinician.

KEYWORDS

Breast FNAC, Fibroadenoma, Mammary Carcinoma.

INTRODUCTION

Breast carcinoma is the most common malignancy in women worldwide, which is the most frequent cause of death in women in developing countries like India and second most common cause of cancer death in most of the developed regions (1).

Fine needle aspiration cytology (FNAC) is a simple, quick, minimally invasive, reliable, and affordable procedure. One of the major goals of FNAC is to differentiate between benign and malignant lesions (2). Sometimes this differentiation is quite difficult by using FNAC alone and at that time, Triple breast assessment i.e. 1. Clinical assessment, 2. Radiological assessment (Mammography / USG), 3. FNAC which actually cause minimal physical and physiological discomfort becomes highly acceptable by patients as well as clinicians. Use of this triple assessment varies greatly between hospitals and cities and between developed and developing countries (2).

The International Academy of Cytology (IAC) gathered a group of cytopathologists who are expert in breast cytology and developed the IAC Yokohama system for reporting Breast Fine Needle Aspiration cytology (FNAC) in 2016. This system has five categories for reporting Breast cytology: C1-Insufficient/Inadequate, C2- Benign, C3-Atypical, C4-Suspicious of malignancy and C5-Malignant. Each category has a clear definition, a risk of malignancy (ROM) and a suggested management algorithm (3).

This categorization by Yokohama system helps in improving communication between the cytopathologist and clinician and also helps to decide further investigations like excisional biopsy judiciously (4).

The present study aimed at classifying the breast FNAs according to the IAC Yokohama system and evaluating the risk of malignancy and diagnostic accuracy of different categories. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy were also assessed.

MATERIALS AND METHODS

A retrospective evaluation of all breast lesions came for FNAC was done between July 2021 and June 2022 at the Government Medical

College, Vadodara in Department of Pathology. FNAC of breast lesions were carried out with written consent of patient. Aseptic precautions were taken. Procedure was performed by a disposable 10 ml syringe and a 22-gauge needle. Regular smears were made and fixed in methanol. Staining was done with Papanicolaou, Giemsa and haematoxylin and eosin stain. Recently proposed IAC, Yokohama reporting method of breast cytology was applied to each smear results. We received 191 breast FNAs, and 44 out of 191 cases had histopathological correlations.

The IAC Yokohama System divides patients into five groups based on their risk of malignancy (ROM).

SR NO.	Category	Explanation
1	C1	Insufficient/inadequate
2	C2	Benign
3	C3	Atypical
4	C4	Suspicious of malignancy
5	C5	Malignant

Previously, C1 was termed as unsatisfactory, but that is now been replaced as insufficient or inadequate, which is the more appropriate term. Also, C3 was previously termed as suspicious, probably benign. As it creates confusion for clinicians between categories C3 and C4; thus, C3 is now termed as atypical.

Acute/chronic inflammatory diseases, Benign Phyllodes tumours, papilloma, atypical ductal hyperplasia (ADH), fibroadenomas and fibrocystic changes are all regarded as benign lesions.

All invasive mammary carcinomas, Phyllodes tumours (borderline and malignant), Ductal carcinoma in situ (DCIS), and lymphomas are categorized as malignant for statistical analysis in the present study.

Statistical Analysis

The risk of malignancy (ROM) was calculated for each category as, Risk of malignancy (ROM) = The number of malignant cases confirmed histologically/total number of cases in the diagnostic category.

Cases without a corresponding histological diagnosis were eliminated

while determining the risk of malignancy, sensitivity, and specificity.

Using gold standard histopathological diagnosis specificity, sensitivity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy were evaluated.
Sensitivity = True positive/(True positive + False negative)
Specificity = True negative/(True negative + False positive)
PPV = True positive/(True positive + False positive)
NPV = True negative/(True negative + False negative)
Diagnostic accuracy = (True positive + True negative)/All analyzed cases.

- The above ratios were calculated for the following groups–
- Group A- Only the “malignant” category was regarded as a positive report.
 - Group B- All cases in the “malignant” and “suspicious of malignancy” category were regarded as positive for malignancy.
 - Group C- All cases in the “malignant,” “suspicious of malignancy,” and “atypical” categories were regarded as positive for malignancy.

RESULT

Total 191 patient underwent for breast FNAC during the period from July 2021 to June 2022. The age group of patients ranged from 14 years to 74 years with the majority of cases belonging to the 3rd and 4th decades. Bilateral lesions were seen in 08 (4.1%) cases, whereas the remaining had unilateral lesions out of which 92(48.16%) cases have left side lesions and 91(47.64%) cases have right side lesions.

The 191 breast FNAC were categorised according to the IAC Yokohama System as following.

Table 1: Distribution Of Breast FNACs According To IAC Yokohama System.

Sr. no.	category	Total no. of cases
1	C1 (Insufficient/inadequate)	12(6.29%)
2	C2 (Benign)	122(63.87%)
3	C3 (Atypical)	06(3.14%)
4	C4 (Suspicious of malignancy)	09(4.71%)
5	C5 (Malignant)	42(21.98%)

Histopathological correlation was available in 44 cases (23.04%). The histopathological diagnoses for the breast lesions in different cytological categories were evaluated and are summarized with cyto-histological correlation as follows.

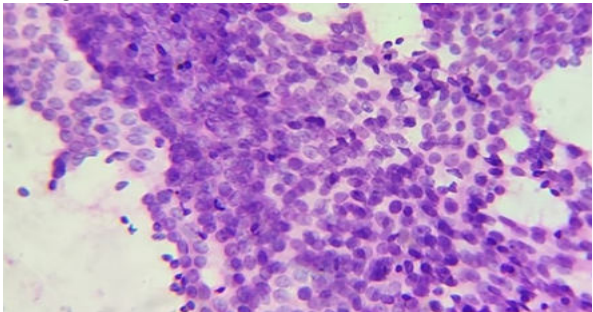


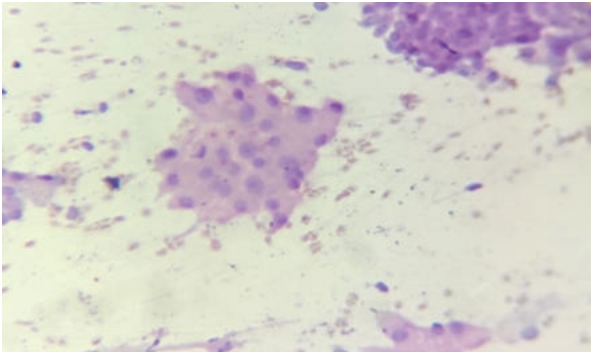
Figure 1: The cytology smear shows benign breast ductal epithelial and myoepithelial cells arranged in monolayered sheet. The ductal cells have uniform round to oval nuclei, even chromatin and some of the cell nuclei have prominent nucleoli. Myoepithelial cells have hyperchromatic nuclei. Background shows some stripped bipolar nuclei. All features are suggestive of **benign breast lesion-Fibroadenoma**.

Table 2: Distribution Of IAC Yokohama System Categories With Cyto-histological Correlation And Risk Of Malignancy (ROM).

Yokohama category (no of cases having histological diagnosis)	C1 (Insufficient/inadequate) (n=01)	C2 (Benign) (n=24)	C3 (Atypical) (n=03)	C4 (Suspicious of malignancy) (n=03)	C5 (Malignant) (n=13)
Histopathological Benign diagnosis	01	24	02	00	00

Histopathological Malignant diagnosis	00	00	01	03	13
ROM	00%	00%	33.33%	100%	100%

Among the suspicious and malignant categories, invasive ductal carcinoma was the most common histological diagnosis, whereas in the benign category, fibroadenoma was the most common. In the atypical category, majority (66.6%) of the histological diagnoses were benign (cellular fibroadenoma).



Figures 2: The cytology smear shows benign ductal epithelial cells with apocrine metaplasia. The cells have round to oval nuclei, even chromatin, prominent nucleoli and abundant granular cytoplasm. All features suggestive of **benign breast lesion with apocrine changes**.

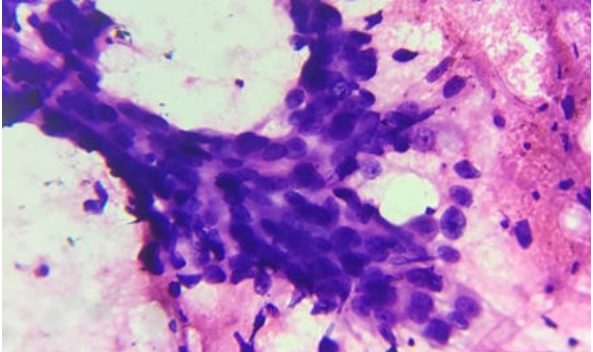


Figure 3: The cytology smear shows malignant mammary ductal epithelial cells arranged in disorganised sheet with absent myoepithelial cells. The cells have enlarged nuclei with nuclear pleomorphism and nuclear irregularity, coarse chromatin, prominent nucleoli and moderate amount of cytoplasm. All features suggestive of **mammary carcinoma**.

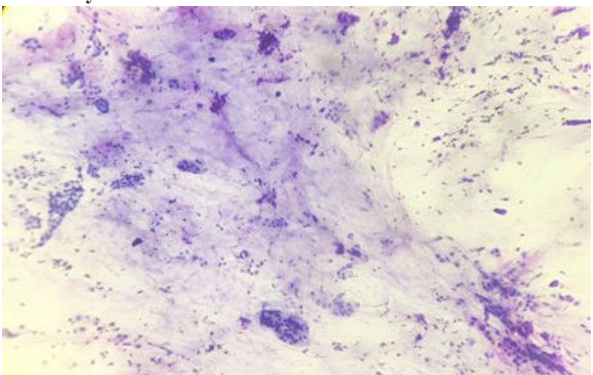


Figure 4: The cytology smear shows malignant mammary ductal epithelial cells floating into abundant extracellular mucin. The ductal cells are arranged in nests, sheets and scattered singly in mucin rich background. All features are suggestive of **mucinous mammary carcinoma**.

The sensitivity, specificity, PPV, NPV, and diagnostic accuracy of the three groups are summarized as following.

Maximum diagnostic accuracy is achieved (97.67%) when malignant and suspicious of malignant is considered positive, where as highest sensitivity is achieved (100%) when malignant, suspicious of malignant and atypical are considered positive.

Table 3: Sensitivity, Specificity, PPV, NPV, And Diagnostic Accuracy According To IAC Yokohama Of Present Study

	Group A(Category malignant considered positive)	Group B(Category malignant and suspicious of malignancy considered positive)	Group C(Category malignant, suspicious of malignancy and Atypical considered positive)
Sensitivity	76.47%	94.12%	100%
Specificity	100%	100%	92.3%
PPV	100%	100%	89.47%
NPV	86.67%	96.29%	100%
Accuracy	90.7%	97.67%	95.35%

DISCUSSION

Breast lesions are not always malignant. Most of the time they are benign and there is always a grey zone between these two. So, to differentiate among different categories, all the breast lesions should undergo triple assessment, which combines clinical, radiological and pathological parameters. These help to arrive at final diagnosis and guide management. Over the years, FNAC which also includes ultrasound guided FNAC (Fine needle aspiration cytology) and CNB (core needle biopsy) are used to aid in diagnosis.

Despite of being simple, cost effective with short TAT(turn around time), FNAC(Fine needle aspiration cytology) is less popular compare to CNB(core needle biopsy) because CNB allows the assessment of histological grade and hormonal study like ER/PR/Her2. But if we use FNAC in concordance with clinical and radiological findings, the sensitivity and specificity of FNAC is comparable to CNB and we can also perform ER/PR/Her2 on cell block. At tertiary care hospitals, FNAC has a very crucial role to play because at these centres it is not feasible to take an adequate number of CNB in each patient with breast lump due to time and cost limitations.

The use of a standardized reporting system will aid in the reproducibility of reports between different institutions and better patient care through improved communication between clinicians and pathologists. (5)

The IAC Yokohama system classifies breast cytology smears into five categories, 1-insufficient/inadequate; 2-benign; 3-atypical ;4-suspicious of malignancy and 5-malignant. The distribution of FNAC sample of present study according to Yokohama system has been compared with other studies like Sana Ahuja et al(6), Poornima V et al(7) and Montezuma D et al (8) in the table below.

Table 4: Comparison Of Distribution Of Sample According To IAC Yokohama System With Other Study.

Categories	Sana Ahuja et al(n=554)	Poornima V et al(n=470)	Montezuma D et al(n=3625)	Present study (n=191)
C1 (Insufficient/inadequate)	20(4%)	22(5%)	209(6%)	12(6.29%)
C2 (Benign)	385(70%)	332(71%)	2660(73%)	122(63.87%)
C3 (Atypical)	35(6%)	7(1%)	498(14%)	06(3.14%)
C4 (Suspicious of malignancy)	13(2%)	8(2%)	57(2%)	09(4.71%)
C5 (Malignant)	101(18%)	101(21%)	201(5%)	42(21.98%)

In present study, correlation of FNAC with gold standard histopathology was done and the risk of malignancy was calculated, which was 0% for C1, 0% for C2, 33.33% for C3, 100% for C4, and 100% for C5. These results are in concordance with the studies by Apuroopa et al(1); Poornima V et al(7) and Wong et al.(9)

Table 5: Risk Of Malignancy (ROM) Was Analysed And Compared Other Study.

Categories	Apuroopa et al(n=900)	Poornima V et al(n=179)	Wong et al(n=579)	Present study (n=191)
C1 (Insufficient/inadequate)	5%	00%	2.6%	00%
C2 (Benign)	1.2%	4%	1.7%	00%
C3 (Atypical)	12.5%	66%	15.7%	33.33%

C4 (Suspicious of malignancy)	93.65%	83%	84.6%	100%
C5 (Malignant)	100%	99%	99.5%	100%

In this study the maximum sensitivity (100%) was achieved when atypical, suspicious, and malignant cases (Group C) were considered positive test results. However, the inclusion of atypical cases in positive results resulted in decreased specificity. The highest specificity (100%) and accuracy (97.67%) were seen when malignant and suspicious of malignancy cases (Group B) were included in positive test results.

Sensitivity, specificity, PPV, NPV and accuracy of present study is comparable with other study like Wong et al.(9); Agarwal et al.(10) and Montezuma D et al.(8) as shown in following table.

Table 6: Comparison Of Diagnostic Accuracy Of Breast FNAC In Diagnosis Of Malignancy Using IAC Yokohama System In Other Study.

Categories included		Wong et al.	Agarwal et al.	Montezuma D et al.	Present study
Group A(Category malignant considered positive)	Sensitivity	75.4 %	86.7%	68.7%	76.47%
	Specificity	100 %	100%	100%	100%
	PPV	100 %	100%	100%	100%
	NPV	80.7%	71.2%	87.7%	86.67%
	Accuracy	87.9 %	90%	90.3%	90.7%
Group B(Category malignant and suspicious of malignancy considered positive)	Sensitivity	92%	96%	83.3%	94.12%
	Specificity	97.8%	91.9%	99.8%	100%
	PPV	97.6%	97.3%	99.5%	100%
	NPV	92.7%	88.3%	93%	96.29%
	Accuracy	95%	95%	94.7%	97.67%
Group C(Category malignant, suspicious of malignancy and Atypical considered positive)	Sensitivity	98.9%	98.2%	98.3%	100%
	Specificity	62.1%	69.5%	54.8%	92.3%
	PPV	71.7%	88 %	49.2%	89.47%
	NPV	98.3%	91.7%	98.6%	100%
	Accuracy	80.2%	88.6%	68.2%	95.35%

CONCLUSION.

The newly proposed IAC Yokohama System for Reporting Breast Cytopathology is a simple system that allows greater diagnostic clarity and, consequently, better communication between pathologists and attending clinicians.

Abbreviations

FNAC - Fine Needle Aspiration Cytology
IAC - International Academy of Cytology
ROM – Risk of malignancy
PPV – Positive predictive value
NPV - Negative predictive value
CNB – Core needle biopsy

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