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VALIDATION OF THE IAC YOKOHAMA SYSTEM FOR REPORTING BREAST FINE NEEDLE ASPIRATION CYTOLOGY AND HISTOPATHOLOGICAL CORELATION OF BREAST LESIONS IN VINDHYA REGION POPULATION

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ABSTRACT: Background: Breast cancer is commonest malignancy of women globally. A palpable breast lump is common diagnostic dilemma to surgeons. In 2016, International Academy of Cytology (IAC) established a standardized approach for reporting Breast FNAC by categorizing the lesions in five tier system from C1 to C5 to standardize reporting, which will enhance Breast FNAB cytology performance, interpretation, and reporting and its histopathological correlation to improve diagnostic accuracy. Aims and Objectives: To categorize FNAC cases according to The IAC Yokohama System and correlate histopathologically (wherever possible) and evaluate the diagnostic ability of FNAC. Material and Methods: The current prospective analytical study was carried out in the Department of Pathology, Shyam Shah Medical College, Rewa, Madhya Pradesh, for a period of 15 months. The results were analysed based on cytological and histopathological reporting. **Results:** The highest number of cases were from the age group of 21- 30 years with 29% (n=29). The maximum number of cases, 69% (n=69) of the total, were found to be categorized under the category C2 (benign) which was followed by Category C5 (Malignant) seen in 13% (n=13). In the present study (2022) the sensitivity, specificity, PPV, NPV and accuracy of FNAC were 95%, 100%, 100%, 98.60% and 98.90% respectively (excluding premalignant cases). Conclusion: FNAC using IAC Yokohama system is a rapid and effective method for the primary categorization of palpable breast lumps and provides better clarity to the clinicians in the management of the patient and can reduce unnecessary surgeries.

INTRODUCTION: Breast cancer accounts for most common female malignancies in all cities across India and is now the most common cancer in Indian women, having recently overtaken cervical cancer. The incidence of breast carcinoma over worldwide is 10.4%, developed countries have a higher incidence ¹. A woman with a breast lump is one of the most prevalent presentations in the

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outpatient department with increasing public awareness of breast pathologies ². It's crucial for surgical pathologists to distinguish between benign and malignant breast lesions because a palpable breast lump presents with a diagnostic conundrum to surgeons ¹.

FNAB offers significant benefits as a diagnostic test with its rapidity of diagnosis, low cost, high rate of acceptance by patients, low complication rates, virtually no contra-indications and high accuracy. However, nowadays usage of core needle biopsy has gained popularity as it allows evaluation of histological grade as well as hormonal status [estrogen receptor (ER)/ progesterone receptor (PR)/ human epidermal growth factor receptor

(Her2)]. In the diagnosis of breast cancer, FNAC offers a high sensitivity of 90%-99% and a high positive predictive value of 100% and a high degree of accuracy that is up to 96.2%³.

The lack of a standardised reporting system has led to pathologists using various terminologies and diagnostic standards, which has confused clinicians when interpreting the cytopathology report and preventing definitive ultimately clinical management. In 2016, the IAC Yokohama Breast FNA Reporting System has been developed by a group of experts in cytopathology assisted by oncologists, radiologists surgeons and Standardizing reporting is the aim of this global system, which will improve the interpretation, performance, and reporting of Breast FNAB cytology. Additionally, it will facilitate better communication between cytopathologists and clinicians by integrating suggested management options with the reporting system.

Categories in Yokohama System of Reporting With Their Risk of Malignancy ⁶⁻⁷:

- 1. Insufficient/Inadequate-2.6-4.8%
- 2. Benign -1.4-2.3%
- 3. Atypia- 13-15.7%
- 4. Suspicious- 84.6-97.1%
- 5. Malignancy -99-100%

Histological diagnosis, which was considered the gold standard. The present study was undertaken to validate IAC Yokohama system and categorise FNAC diagnosis and corelate histopathology wherever possible in the above-mentioned system to improve communication between cytopathologists and clinicians by connecting the reporting system with recommended management options.

Aims and Objectives: The aim of present study is to differentiate and categorize the palpable breast lumps and to study the correlation, accuracy of FNAC with Histopathology of palpable breast lumps presenting at SSMC and SGMH, Rewa.

MATERIALS AND METHOD: The current prospective analytical study was carried out in the

Inclusion Criteria:

- 1. Females with palpable breast lump/swellings.
- **2.** Patients should be cooperative to the procedure and subsequent followups.

Exclusion Criteria:

- **1.** Patients not willing (written informed consent taken).
- **2.** Patients in past or presently undergoing chemotherapeutic treatment for breast cancer.
- **3.** Patients with bleeding diathesis.
- 4. Patients without palpable breast lump.
- **5.** Male patients with breast lumps.

In the present study, patient falling under inclusion criteria were studied. A total of 100 cases presenting with breast lump were included after taken a written informed consent. Fine needle aspiration cytology procedure was performed under all aseptic conditions, stained using H&E, Giemsa and Papanicoloaustains and reported. The slides were reported and categorized as per IAC Yokohama system for reporting Breast cytology from category 1 to category 5 $^{6-7}$. The patients were followed up under proper coordination from Department of Surgery. If the patient was planned for a surgical procedure the specimen submitted for biopsy was obtained, processed and findings recorded. Chi-square test for categorical data was used for calculation of p-value to assess statistical significance.

RESULTS: In the present study, highest number of cases were from the age group of 21- 30 years with 29% (n=29), followed by 60 years with 5% of the cases (n=5). The youngest female with breast lump was of 15 years of age and the oldest one was 77 years old.

AGE	IAC Yokohama Classification								Total		
(completed age in	(C1		C2	(C 3		C4		C5	
years)	Ν	%	Ν	%	Ν	%	Ν	%	Ν	%	Ν
<20	2	50	22	31.88	0	0	0	0	0	0	24
21-30	1	25	27	39.13	1	20	0	0	0	0	29
31-40	1	25	17	24.64	3	60	2	22.22	1	7.69	24
41-50	0	0	2	2.9	0	0	2	22.22	7	53.85	11
51-60	0	0	1	1.45	1	20	3	33.33	2	15.38	7
>60	0	0	0	0	0	0	2	22.22	3	23.08	5
Total	4	4	69	69	5	5	9	9	13	13	100

TABLE 1: AGE-WISE CATEGORIZATION OF BREAST LUMP CASES (N=100)

The most common age group with category (C1) unsatisfactory was younger females (<20 years), whereas the categorization for benign and atypical probably benign lesions (C2) and (C3) were highest among 21-30 years of age group and 31-40 years age group respectively **Table 1.** In the present study upper and outer quadrant of the breast alone was the most frequently involved quadrant by breast lumps with 49% (n=49) of the total cases followed by lower and outer quadrant 19% (n=19) of the cases.

In present study, the maximum number of cases, 69% (n=69) of the total, were found to be categorized under the category C2 (benign) which was followed by Category C5 (Malignant) **Fig. 1C** seen in 13% (n=13). 9% (n=9) of the total cases were categorized as Suspicious of Malignancy (C4) **Fig. 1B.** Atypical Lesion (C3) **Fig. 1A** and Unsatisfactory Lesions (C1) were categorized in 5% (n=5) and 4% (n=4) of the total cases respectively **Table 2.**

TABLE 2: CYTOLOGICAL CATEGORIZATION AS PER YOKOHAMA SYSTEM (N=100)

Yokohama category	F	requency
	Numbers (n)	Percent (%)
C 1	4	4%
C 2	69	69%
C 3	5	5%
C 4	9	9%
C 5	13	13%
Total	100	100%

Chi square = 100.00; p<0.0001. p-value < 0.05 is considered as significant. In the present study p- value obtained was 0.0001 which is very significant.

In present study, 100 female patients with breast lump who underwent FNAC and were reported according to IAC Yokohama classification. The cytology reporting were further classified as benign and malignant where Yokohama category 1, category 2 and category 3 were grouped as benign. On the other side category 4 and category 5 were grouped as malignant.

Based on this categorisation, group benign had 78% of cases (n=78) and the malignant category had 22% of cases (n=22) **Table 3.**

TABLE 3: BENIGN/MALIGNANT	BASED ON CYTOI	LOGY REPORTING
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FNAC Diagnosis	Yokohama								Total		
	(Unsat	C1: isfactory	C Be	C2: C3: Benign Atypia Probably Benign		C4: Suspicious of Malignancy		C5: Malignant			
	N	%	Ν	%	Ν	%	Ν	%	Ν	%	Ν
Benign	4	100	69	100	5	100	0	0	0	0	78
Malignant	0	0	0	0	0	0	9	100	13	100	22
Total	4	4	69	69	5	5	9	9	13	13	100

The 100 patients who underwent FNAC were followed up with coordination of Department of surgery. Among 100 cases 3 were kept on

conservative treatment and 2 cases went LAMA (Leave against medical advice). Remaining 95 cases underwent required operative procedures.

Excision biopsy was performed in 63% of cases (n=63), Lumpectomy was performed in 5% of cases (n=5), MRM (modified radical mastectomy) was performed in 23% of cases (n=23), simple mastectomy was performed in 4% of cases (n=4).

The specimens were sent by department of surgery for gross and histopathological examination. The histopathological examination and reporting of 95 cases showed highest number of cases of fibroadenoma seen in 43% of cases (41/95).

TABLE 4: EFFICACY OF CYTOLOGY FOR BREAST LUMPS

			Histopathology findings				
		Positive	Negative				
Cytology findings	Positive	22(TP)	0(FP)	22			
	Negative	2 (FN)	71(TN)	73			
	Total	24	71				
Sensitivity = TP/(TP+FN) = 91.6% Specificity= TN/(TN+FP) = 100% PPV=TP/(TP+FP) = 100% NPV=TN/(TN+FN) =							
97.3%. Diagnostic Accuracy= (TP+TN)/(TP+FN+FP+TN) = 97.89%							

TABLE 5: DIAGNOSTIC PERFORMANCE OF CYTOLOGY AGAINST HISTOPATHOLOGY TEST AS GOLD STANDARD FOR DIAGNOSIS OF MALIGNANCY

	Including Prema	Excluding Premalignant ca				
Diagnostic performance of Cytology		95	% CI		95% CI	
(FNAC)		Lower	Higher		Lower	Higher
True positive	22			19		
False negative	2			1		
False positive	0			0		
True negative	71			72		
Sensitivity	91.70%	73.00%	99.00%	95.00%	75.10%	99.90%
Specificity	100.00%	94.90%	100.00%	100.00%	94.90%	100.00%
ROC area	0.96	0.9	1	0.97	0.93	1
Positive predictive value	100.00%	84.60%	100.00%	100.00%	82.40%	100.00%
Negative predictive value	97.30%	90.50%	99.70%	98.60%	92.50%	100.00%
Accuracy	97.89%	92.60%	99.74%	98.90%	94.03%	99.97%



FIG. 1: H AND E STAINED SMEARS OF BREAST LUMP. (A) ADH: A 40-YEAR-OLD FEMALE WITH BREAST LUMP SHOWING HIGHLY CELLULAR SMEAR HAVING LARGE EPITHELIAL TISSUE FRAGMENTS CONSISTING OF DUCTAL EPITHELIAL CELLS WITH MYOEPITHELIAL CELLS. (B) FIBROADENOMA (H & E 10X)- FOLLOW UP EXICISIONAL BIOPSY SHOWED STROMA COMPRESSING THE GLANDS INTO SLIT LIKE SPACES.



FIG. 2: (C) SUSPICIOUS OF MALIGNANCY: A 44-YEAR-OLD FEMALE WITH BREAST LUMPON CYTOLOGY SHOWING MODERATE TO HIGHLY CELLULAR SMEAR SHOWS LARGE 3-D EPITHELIAL TISSUE FRAGMENTS WITH DISCOHESIVE CELLS, MINIMALLY ATYPICAL OR ENLARGED NUCLEI, PLEOMORPHIC NUCLEI. (D) INFILTRATING DUCTAL CELL CARCINOMA (H & E 40X).

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DISCUSSION: FNAC has significantly contributed to the reduction of excisional biopsies in the assessment of Breast lesions. Accurate diagnosis of Breast cancer is made in 99 % of the cases by the combination of Clinical examination, Mammography and FNAC. The present study showed similar result where highest percentage of cases were reported in benign category 69% (69/100) of all cases.

In the present study, 29(29%) cases are seen in 21-30 years of age group had the highest proportion of breast lump. Similar results were obtained by Sreedevi CH *et al*⁸ (2016) where the age group of 21-30 years had the highest proportion of breast lump accounting for 36%.

The previous studies conducted by Sankaye *et al* ⁹ (2014), Muhammed *et al* ¹⁰ (2005) and Rocha *et al* ¹¹ (1997) reported similar findings with maximum number of cases in Category (C2) benign with 58.2%, 71.3% and 76.02% of total cases respectively **Table 8**. In present study fibroadenoma was most common benign breast lesion in 47% (47/100 cases) which was in agreement with study done by Risaldar AA *et al* ¹² (2020), Ahmad F *et al* ¹³ (2016), Khanzada *et al* ¹⁴ (2009), Akhator *et al* ¹⁵ (2007) & Irabor *et al* ¹⁶ (2008).

TABLE 6: DISTRIBUTION PATTERN OF YOKOHAMA CATEGORIES IN DIFFERENT STUDIES

Study	Sankaye <i>et al</i> ⁹ (%)	Muhammed <i>et al</i> ¹⁰ (%)	Rocha <i>et al</i> ¹¹ (%)	Present Study (%)
Sample Size	225	157 809		100
Categories				
Insufficient (C1)	13(5.77)	3(1.9)	71(8.77)	4(4)
Benign (C2)	131(58.22)	112(71.3)	615(76.02)	69(69)
Atypical (C3)	8(3.55)	2(1.3)	-	6(6)
Suspicious (C4)	8(3.55)	2(1.3)	26(3.21)	8(8)
Malignant (C5)	65(28.88)	38(24.2)	97(12)	13(13)

In present study more benign cases (75%) and less malignant cases (21%) are seen histologically similar to studies by Muhammed *et al.* ¹⁰ (2005), Kim *et al* ¹⁷ (2000) and Park and Ham ¹⁸ (1997) showing 65.59%, 62.19%, 54.04% of cases respectively. This higher number of benign and lower number of malignant cases in present may be due to good follow up of the patients. In the present study (2022) the sensitivity, specificity, PPV, NPV and accuracy of FNAC were 95%, 100%, 100%, 98.60% and 98.90% respectively (excluding premalignant cases). The sensitivity of FNAC was higher in studies conducted by Patel A et al¹⁹ (2018), Khageshan AP et al²⁰ (2015), Khemka A et al²¹ (2009), Muhammed AZ et al¹⁰ (2005) which showed a sensitivity of 97.46%, 96.97%, 96%, and 90.6% respectively similar to our study.

CONCLUSION: То conclude fine-needle aspiration cytology using IAC yokohama system is a rapid and effective method for the primary categorization of palpable breast lumps. The maximum sensitivity of FNAC when reported using Yokohama system achieved was 95%, hence it can be used as a first line investigation for breast There should be no hesitation lump. in recommending surgical biopsy or frozen section for the group of smears that are atypical or suspicious

for malignancy, thus keeping the false positive rate as close to zero as possible. This ensures that patients continue to receive the benefits of FNA without the risks.

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