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Application Of International Academy of Cytologists Yokohama System for Reporting Breast Fine Needle Aspirates and Their Histopathological Correlation.

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Abstract
Introduction: *Palpable breast lumps are the most common presentation in surgical and pathological practice.FNAC is the initial diagnostic modality in the management of the breast lumps and to prevent unnecessary intervention in benign breast disease.*
Material and Methods: *This research is a hospital-based observational study of one year beginning in October 2022 and ending in September 2023. A total of 100 cases were studied in the Central Laboratory and Histopathology Lab, SIMS, Hapur.*
Result: *There was a total of 100 cases; divided into category C1, C2, C3, C4 and C5 according to the IAC Yokohama System and subsequent histopathological examination was done.*
Conclusion: *The study revealed that although FNAC is a useful preoperative tool for diagnosis, histopathology still remains he gold standard.*
Keywords: *Breast lumps, FNAC, Histopathology, Yokohama System.*

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I. INTRODUCTION

The breast, or mammary organ, is secured by skin and subcutaneous tissue. Lumps in the breast are the most common complaint for women of all ages, particularly during the reproductive years. [1]

Breast cancer is the most common cancer that women get around the world. In developing nations, it is the leading cause of death, whereas in developed nations, it is the second most common cause of death after lung cancer. [2]

In India, the incidence rate is as high as 26 per 1,000 women, and the mortality rate is 13 per 1,000 women population.[2]

Evaluation of the breast lumps requires the use of a detailed clinical history, clinical breast examination, imaging, and tissue diagnosis. [4] Ultrasound is the first line of investigation for women under the age of 30. Ultrasound can demonstrate whether the mass is solid or cystic. It can also be used to guide for FNAC in deep-seated lesions and non-palpable masses. Special tests such as mammograms are used to detect non-palpable mass in women over 30 years of age. [1]
The triple test is a combination of physical examination, imaging, and tissue diagnosis. [1]

A final diagnosis is made by histopathological examination of the excised tissue, but this is not possible in all cases, as 80% are benign. [4]

FNAC is used to evaluate palpable breast masses and cysts as well as non-palpable mammographic abnormalities. [2]

It is simple, rapid, cost-effective, minimally invasive, and highly accurate for non-palpable masses. It has a high sensitivity rate of 90–95%. [3]FNAC has decreased the amount of open biopsies because it's really good at finding out if there's a problem or not. [6] Some of the complications of FNAC are pain and hematoma formation. [5]

The reporting system followed for categorizing fine needle aspirates of the breast is the IAC (Yokohama System). It was developed in 2016 by cytologists, radiologists, surgeons, and oncologists. The IAC Yokohama System defines five categories for breast cytology, each with a clear descriptive term for the category, a definition, a risk of malignancy, and suggested management. [7]

The biopsy of breast lesions, which are palpable, provides reliable information to clinicians for modern therapeutic strategies as part of the decision-making regarding patient treatment. [6]

This study is intended to study the correlation between categorizing the fine needle aspirates according to the IAC Yokohama system and their correlation with histopathology.

II. Materials and Methods

The present study was conducted in the central laboratory and histopathology lab, Department of Pathology, Saraswathi Institute of Medical Sciences, Hapur, Uttar Pradesh, from October 2022 to September 2023.

Study Design: A hospital-based observational study

Study Period: The study was conducted for a period of one year.

Source of Data: All the females and males with lumps in the breast and no primary diagnosis of any breast disease came to the laboratory during the study period in the central laboratory, department of pathology, Saraswathi Institute of Medical Sciences, Hapur, Uttar Pradesh.

Sample Size: A total of 250 patients underwent FNAC for palpable breast lumps, but only 100 patients had histopathology of the lump.

Selection criteria:

A) Inclusion-Criteria

All females and males with palpable breast lumps and no primary diagnosis of any breast disease of all age groups.

B) Exclusion-Criteria

The patient who underwent FNAC but did not undergo a biopsy was excluded from the study.

PROCEDURE:

- A full, detailed clinical history of the patients was taken, followed by a clinical examination of the lump.
- The procedure was explained to the patient, and informed consent was obtained from all the patients.
- The lesion was fixed, and a 24-gauge needle along with a 10-ml syringe were inserted into the lump. A resistance is felt, negative pressure is applied by pulling the piston, and the needle is moved in all directions in the lump. The negative pressure is released, and the needle is taken out. The material aspirated is pushed onto the labelled glass slides, and a few slides were immediately fixed in ethanol for the Papanicolaou method, and the remaining slides were air dried for the Giemsa staining method.
- The FNAC diagnosis was given according to the IAC Yokohama System under the following categories: 1. Unsatisfactory/non-diagnostic, 2. Benign, 3. Atypia of Undetermined Significance, 4. suspicious of malignancy; 5. malignant.
- The biopsy specimens were fixed in 10% formalin for 24 hours. Gross examination and cut-section findings were noted. The tissue section was processed and paraffin embedded. 3–4-micron-thick sections were stained with hematoxylin and eosin and studied under light microscopy.

III. RESULT

A total of 100 cases were included in the study. There were 97 females and 3 male patients (the male-to-female ratio is 0.30:1). The age of the patients in the study varied from 12 years to 70 years. The majority of the cases were between the age groups of 21 and 30 (39%).

The cytological analysis of the cases was categorized as C1 inadequate, C2 benign, C3 atypia of undetermined significance, C4 suspicious of malignancy, and C5 malignant. There were a total of 75 benign cases (75%), 13% malignant cases (12 malignant and 1 suspicious of malignancy), 5 proliferative lesions with atypia cases (5%), and 6 cases were inadequate (6%).

The most common cytological diagnosis was fibroadenoma of the breast (48%), followed by carcinoma of the breast (12%). The rest of the cases included benign epithelial proliferative disease (1%), fibrocystic disease (8%), suspicion of malignancy (1%), granulomatous mastitis (2%), gynecomastia (3%), breast abscess (9%), galactocele and lactating adenoma (2%, 1% each), and fat necrosis (2%), and 6 cases were inadequate for evaluation (6%).

The histopathological diagnosis of all 100 cases was collected and analyzed. Table 3 shows the correlation between cytological diagnosis and histopathological diagnosis.

Six cases diagnosed as inadequate in cytology were diagnosed as normal breast tissue in histopathology. Out of 75 cases in the benign category, 48 cases were diagnosed as fibroadenoma in cytology, which corresponded to a histopathological diagnosis of fibroadenoma. One case was diagnosed as benign epithelial proliferative disease in cytology, which turned out to be usual ductal hyperplasia in histopathology. Three cases were given an accessory breast tissue diagnosis in cytology, which in histopathology was confirmed as gynecomastia. 2 cases diagnosed as granulomatous mastitis in cytology were diagnosed as granulomatous mastitis in one case and as chronic mastitis in another. 9 cases were given as breast abscesses in cytology, which

were diagnosed as chronic mastitis in 6 cases, breast abscesses in 1 case, lymphocytic mastitis in 1 case, and chronic granulation tissue in 1 case in histopathology. Fibrocystic disease was diagnosed in 8 cases in cytology, whereas in histopathology, 1 case was given as duct ectasia, and the remaining 7 cases were diagnosed as fibroadenoma with fibrocystic disease. Two cases were diagnosed as fat necrosis in cytology and confirmed on histopathology as fat necrosis. 1 case of galactocele, which was the same in cytology and histopathology. 1 case as lactating adenoma in cytology, which was confirmed on histopathology.

Four cases were diagnosed as proliferative disease with atypia, and one case of fibroadenoma with atypia was diagnosed in category 3 of the Yokohama system. 4 cases of proliferative atypia turned out to be 2 cases of usual ductal hyperplasia; 1 case was diagnosed as invasive ductal carcinoma, whereas 1 case was diagnosed as fibroadenoma. One case of fibroadenoma with atypia was diagnosed as complex fibroadenoma on histopathology.

A suspicion of malignancy was given in one case in cytology, which was diagnosed as ductal hyperplasia on histopathology. 12 cases were diagnosed as malignant aspirates on cytology, which were diagnosed as ductal carcinoma in 9 cases and invasive ductal carcinoma in 3 cases on histopathology. The cytological diagnosis was correlating with the histopathological diagnosis in most of the cases.

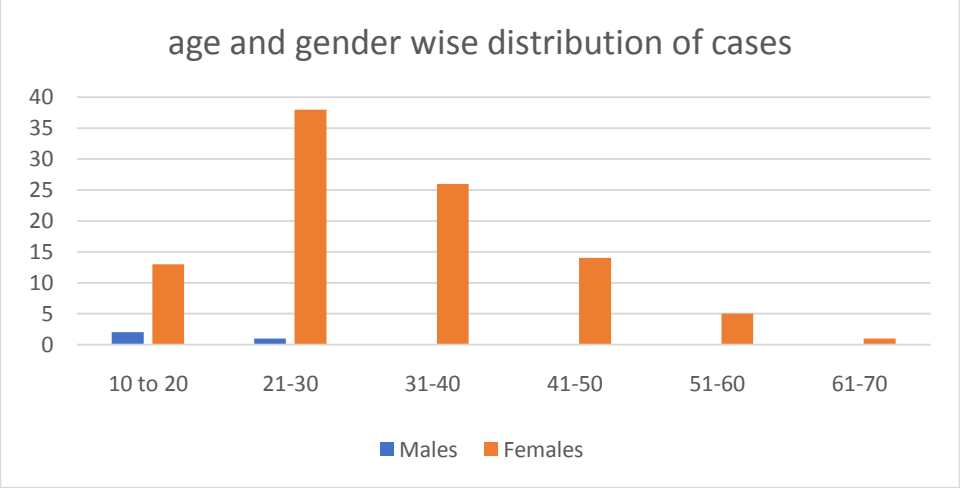

Chart no. 1 Age and Gender wise Distribution of Cases. This chart depicts the number of cases received during the duration of the study and their distribution according to age and gender.

Table no. 1 Cytological Categories of Reporting

Cytological categories	Explanation
C1	Inadequate
C2	Benign
C3	Atypia of Undertermined Significance
C4	Suspicious of Malignancy
C5	Malignant

Table no. 2 Cytological diagnosis of different breast lumps

Cytological Diagnosis	No. of Cases	Percentage
Carcinoma breast	12	12
Suspicious of Malignancy	1	1
Atypical Duct Hyperplasia	3	3
Fibroadenoma	48	48
Gynecomastia	3	3
Granulomatous Mastitis	2	2
Lactating Adenoma	1	1
Galactocele	1	1
Fibrocystic Disease	8	8
Fibroadenoma with atypia	1	1
Fat Necrosis	2	2
Breast Abscess	9	9
Inadequate for evaluation	6	6

Table no. 3 Cyto-histological diagnosis of palpable breast lump.

Cytological Category	Cytological Diagnosis	No. of cases	Histopathological diagnosis
C1	Inadequate	6	Invasive Ductal Carcinoma (1) Fibroadenoma (4) Lipoma (1)
C2	Fibroadenoma	48	Fibroadenoma (48)
	Gynecomastia	3	Gynecomastia (3)
	Benign Epithelial Proliferative disease	1	Usual Ductal Hyperplasia (1)
	Granulomatous Mastitis	2	Granulomatous Mastitis (2)
	Breast Abscess	9	Breast Abscess (1) Chronic Mastitis (6) Lymphocytic Mastitis (1) Chronic Granulation tissue (1)
	Fibrocystic Disease	8	Fibroadenoma with Fibrocystic Changes (8)
	Galactocele	1	Galactocele (1)
	Fat Necrosis	2	Fat Necrosis (2)
	Lactating Adenoma	1	Lactating Adenoma (1)
C3	Proliferative disease with atypia Fibroadenoma with Atypia	4 1	Atypical Ductal Hyperplasia (2) IDC (1) Complex Fibroadenoma (1) Fibroadenoma (1)
C4	Suspicious of Malignancy	1	Ductal Hyperplasia (1)
C5	Malignant	12	Ductal Carcinoma (9) Invasive Ductal Carcinoma (3)

IV. DISCUSSION

FNAC for breast aspirations was first introduced in the beginning of the 1960s by Franzen and Zajicek at the Karolinska Hospital in Stockholm. He introduced May-Grunwald Giemsa stains on air-dried smears to allow for rapid interpretation. [11] After all the success, this technique was also widely used until the 1980s. The main reasons were the fear of implantation of the tumor cells in the needle tract, a lack of confidence in the sensitivity and specificity of the procedure, and the surgeon's unwillingness to forgo the excisional biopsy procedure. [12]

Fine needle aspiration (FNAC) is the most reliable and popular tool for pre operative assessment of the breast lumps or masses as it shows high accuracy, specificity and sensitivity. It is cheap and fairly a non-complicated procedure.

FNAC was used as a preliminary investigation to differentiate between benign and malignant breast lumps. In the evaluation of breast masses, the triple assessment, which combines clinical, radiological, and pathological information through FNAC, together with a core needle biopsy, is the initial pathological investigation of choice. [8]

FNAC is an easy-to-diagnose method for all suspected breast lesions. [10] FNAC has reduced the need for an excisional biopsy in most of the cases. There are a few cases in which FNAC cannot differentiate between benign and malignant. This problem can be due to the paucity of the sample or morphological overlapping. [9] It is of advantage to patients and physicians. [10]

The reporting system used for reporting breast cytology is the Yokohama System for reporting breast cytology. IAC members who attended the Yokohama International Congress of Cytology suggested that there should be either 3 or 5 categories of reporting breast cytology. It includes five categories of reporting from C1–C5. C1 includes an inadequate degree of cellularity of the epithelial cells; this can be due to incorrect sampling, staining, or smearing. Benign lesions come under the C2 category, which mainly shows an intact glandular pattern consisting of ductal epithelial cells, myoepithelial cells, bare bipolar nuclei, and inflammatory cells. The C3 category, i.e., atypia of undetermined significance, includes smears showing cellular pleomorphism and loose clusters, which are not present in the benign category. Smears showing hypocellularity, poor preservation of cells, and some components of benign breast are included under category C4, i.e., suspicious of malignancy. Smear aspirates with strong malignant features are categorized under C5. [13] Table no. 1 shows the different cytological categories used in the reporting.

Several reports in the literature show a good correlation between FNAC and histopathological reports. In our study, the findings of 100 FNAC were correlated with the histopathology study. Table no. 2 shows cytological diagnosis of different breast lumps.

The present study showed that the maximum number of cases were present in females (n = 197), and males only had 3 cases, which is in concordance with the study conducted by Mohan et al. [21] who also showed

a female predominance. Chart no. 1 shows female predominance. The maximum number of cases in the study were in the age group 21–30 years of age, followed by 31–40 years of age, which was different from the study done by Mohan et al. [21] The malignant cases were mostly in the age group of 40–56 years of age, and the two patients were below 40 years of age.

In our study, 6% of the cases had inadequate aspiration, which was higher than the study conducted by Modi *et al.* [14]and Panwar et al. [15], who reported 1.36% and 1.3%, respectively. It was lower in comparison with the study conducted by Bajwa and Tariq et al. [16], who reported that the C1 category had 13.6% of cases. It was similar to the study conducted by Montezuma et al. [17] who reported 5.77% of cases in the C1 category. The patients who had unsatisfactory smears had a repeat cytological examination and were also advised for histopathological examination. The histopathological examination revealed that one patient had invasive ductal carcinoma, another patient had breast lipoma, and four patients were diagnosed with fibroadenoma. This discrepancy between the FNA report and histopathology can be due to FNA sampling from non-diagnostic areas.

In category C2, the total number of cases in the present study was 75 (75%) cases in the benign category. The most common benign lesion was fibroadenoma (48%), followed by breast abscess (9%) and fibrocystic changes (8%). This was almost similar to the study conducted by Montezuma et al. [17], who reported the number of cases to be 73.38% in the C2 category. The percentage of benign cases in the present study was higher than the study conducted by Apuroopa et al. [18], who reported 58% of cases in the C2 category. The study done by Chandanwale SS et al. [19] and Vasavada et al. [20] also showed that the most common benign lesion in their study was fibroadenoma, similar to the present study. Other benign lesions received during the study period were galactocele (1%), lactating adenoma (1%), fat necrosis (2%), benign epithelial proliferative disease (1%), gynecomastia (3%), and granulomatous mastitis (2%).

All the cases of fibroadenoma on cytological smears showed the triad, i.e., a bimodal population of ductal epithelial and myoepithelial cells, tightly packed clusters of benign ductal cells representing the staghorn pattern, and the presence of the fibromyxoid pattern as shown in Fig. A and B. On histopathological examination, all the cases of fibroadenoma were confirmed as fibroadenoma with the presence of stromal tissue and ducts present either in an intracanalicular or peri-canalicular pattern as shown in Fig. C and D. Histopathological examination of the breast abscess was correlated with the cytological examination, which showed chronic mastitis. Fibrocystic changes were reported as fibroadenoma with fibrocystic changes such as epitheliosis, adenosis and apocrine metaplasia. Benign epithelial proliferative disease given on cytology was reported as usual ductal hyperplasia on histology. Histological diagnosis of gynecomastia, granulomatous mastitis, fat necrosis, lactating adenoma, and galactocele showed concordance with the cytological diagnosis.

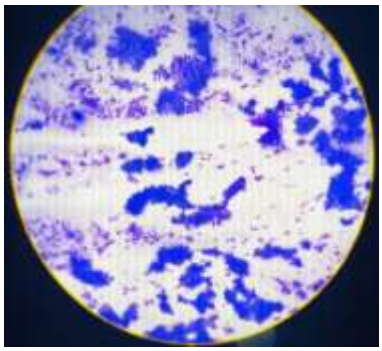

Fig. A Fibroadenoma of Breast showing moderately cellular smears and staghorn pattern. (MGG 10x)

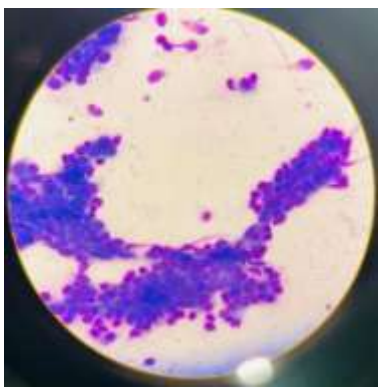

Fig. B Fibroadenoma showing sheets of ductal epithelial cells in tight cohesive clusters. (MGG 40x)

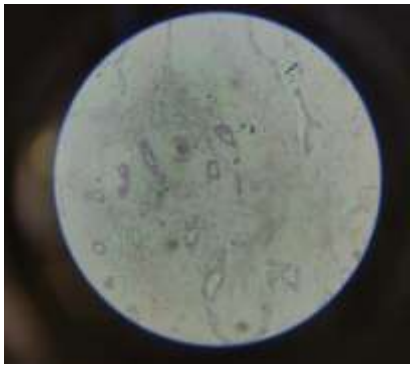

Fig C Fibroadenoma of Breast showing glands in pericanalicular pattern. (H&E, 40x)

Fig D Fibroadenoma of Breast showing glands in intracanalicular pattern. (H&E, 40x)

The gray zone, i.e., C3 category proliferative disease with atypia, showed 5% of cases in our study, which was similar to the study conducted by Panwar et al. [15] Sunita *et al.* [22], who had 3.5% in the C3 category of cases, whereas Georgieva *et al*. [23] had a lower number of cases in their study, i.e., 2.2%. However, studies done by Sneige et al. [24] reported 10.3%, which is higher compared to the present study. Lesions received in this category were proliferative disease with atypia and fibroadenoma with atypia, which on histopathology had different diagnoses. Two cases of proliferative disease with atypia showed atypical ductal hyperplasia, whereas one case was diagnosed as invasive ductal carcinoma. One case was given fibroadenoma on histopathology. Fibroadenoma with atypia on histopathological diagnosis was a complex fibroadenoma.

The C4 category of the Yokohama system is suspicious of malignancy, which was only 1% in the present study, similar to the findings observed in the study conducted by Panwar et al. [15], who also reported 1.7% cases in their study. However, it was higher in the study conducted by McHugh et al. [25], who reported 11% of cases in the C4 category. On histopathological examination, this was diagnosed as ductal hyperplasia.

The last category is C5, which is the malignant aspirate. There were 12% cases in this category of our study, which was similar to the study conducted by Apuroopa et al. [18], who also had 12.8% cases in the C5 category. A study done by De Rosa et al. [26] and Agarwal et al. [27] showed a higher number of cases in the C5 category, i.e., 28.4% and 20.4%, respectively. The malignant aspirate on cytology showed loose cohesive clusters, nuclear pleomorphism, and the presence of prominent nucleoli as shown in Fig E. On histopathological diagnosis, it was diagnosed as ductal carcinoma and invasive ductal carcinoma shown in Fig F.

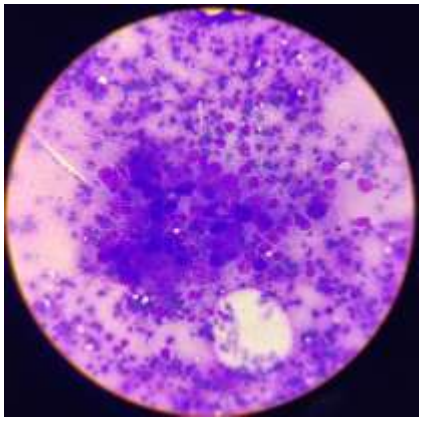

Fig E Malignant Breast Aspirate showing loose clusters ductal epithelial cells having marked pleomorphism, hyperchromatic nuclei and prominent nucleoli. (MGG,40x)

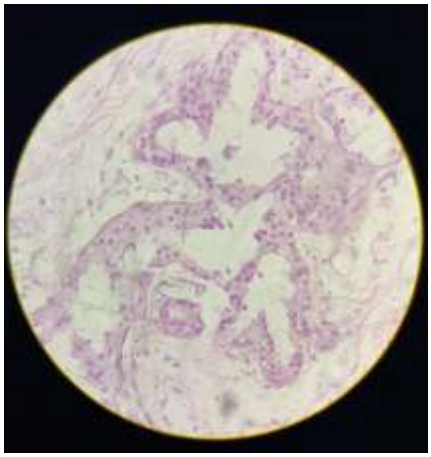

Fig F Invasive Ductal Carcinoma (H&E, 40x)

The skills of the cytopathologists performing FNAC have very much impacted the sampling yield. Unsatisfactory smears can be due to sampling error, the nature of the lesion, or a faulty FNA technique. False negative results can be due to scanty cellularity, haemorrhagic aspirate, and misinterpretation of the smear. Diagnostic efficacy of physical examination, imaging and FNAC (triple test), when combined together, are still higher.[21]

V. CONCLUSION

FNAC is a highly reliable tool for palpable breast lesions for preoperative assessment and proper surgical management of the patient. However, lesions diagnosed in FNAC that are classified in the C1, C2, C3, C4, and C5 categories need confirmation with the histopathological examination, which still remains the gold standard.

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