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Original Article

Pathology Section

Application of International Academy of Cytology Yokohama System for Reporting Breast Fine Needle Aspiration Cytology- A Retrospective Study

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ABSTRACT

Introduction: Fine Needle Aspiration Cytology (FNAC) is a rapid, minimally invasive and cost-effective procedure with a high sensitivity rate of 92-95% and high Positive Predictive Value (PPV) approaching 100% for the diagnosis of breast malignancies. International Academy of Cytology (IAC) Yokohama system for reporting breast FNACs had been established in 2016 to bring consistency and uniformity of breast cytology reporting.

Aim: To classify the breast lesions according to the IAC Yokohama system for cytological reporting of breast lesions.

Materials and Methods: This was a retrospective six years study carried out in the Department of Pathology, Karpaga Vinayaga Institute of Medical Sciences, Chinnakolambakkam, Tamil Nadu, India. All females breast FNAC cases reported during the year January 2015 to December 2020 were included in the study according to the inclusion criteria. Relevant clinical and pathological data including the FNAC reports were retrieved from the medical records of the department. Corresponding FNAC smears stained with Haematoxylin and Eosin (H&E) and Papanicolaou stains were reviewed and double-checked with the FNAC reports. All those cases were grouped according to the IAC Yokohama System. Statistical analysis was carried out using Statistical Package for the Social Sciences (SPSS) version 23.0.

Results: Of the total 381 female breast FNACs, majority (60%) of them belonged to the age group of 21-40 years. The predominant presenting symptom was palpable breast lump (73%) and Upper Outer Quadrant (UOQ) was involved in 65% of cases. Out of 381 cases, 297 (78%) were benign, 52 (13.6%) were malignant and 32 (8.4%) were inadequate for diagnosis. Total 73.8% cases belonged to "C2" category and fibroadenoma was the most prevalent lesion. Pearson Chi-square test showed highly significant association between patient's age above 40 years and the risk of having a malignant breast lesion ($p<0.0001$).

Conclusion: FNAC is an effective diagnostic modality for preoperative diagnosis of breast lesions thereby facilitating proper treatment at an early stage of the disease. Also adherence to the standardised cytological reporting system like IAC Yokohama system will ensure quality assurance across various institutions, thereby strengthening the healthcare services.

Keywords: Breast lump, Classification, Females, Quality assurance, Risk of malignancy

INTRODUCTION

Breast carcinoma is one of the common malignancies among females accounting for increased morbidity and mortality worldwide [1]. The common clinical symptoms of female breast lesions include palpable breast lump, breast pain and nipple discharge. Triple assessment of breast lesions that includes clinical, radiological and pathological evaluation (FNAC/Core needle biopsy) is a time honoured valuable approach for the management of breast lesions that can obviate the need for invasive procedures like excisional biopsy in most cases [1]. FNAC is a rapid, minimally invasive and cost-effective procedure with a high sensitivity rate of 92-95% and high PPV approaching 100% for the diagnosis of breast malignancies [2]. The need for intraoperative procedures like frozen section for detecting breast malignancy has been reduced to around 80% with the help of the more reliable FNAC [2].

Over the years several studies are being carried out worldwide for establishing a standardised reporting system for breast cytology that will aid the clinicians in the proper workup and efficient management of breast lesions. Recently in 2016, IAC Yokohama system for reporting breast FNACs had been established to bring about consistency and uniformity of breast cytology reporting across the globe, thereby ensuring proper clinical treatment [1]. This system had been developed by several experts that included cytopathologists, radiologists, oncologists and surgeons from across the globe after extensive research and review of literature. According to this system, all breast lesions are grouped into one of the five categories based on cytological examination namely: C1 (Inadequate), C2 (Benign), C3 (Atypical), C4 (Suspicious for malignancy) and C5 (Malignant). C1 category includes sparsely cellular or poorly fixed smears precluding cytomorphological diagnosis. C2 category includes smears with unequivocally benign cytological features. C3 category includes cytological smears with additional features that are not common in predominantly benign processes. C4 category includes smears with cytomorphological features of malignant lesions but with insufficient cellularity or quality to make a definitive diagnosis of malignancy. C5 category includes smears with unequivocal malignant cytomorphological features.

The Risk of Malignancy (ROM) and the suggested management options for each of the five categories have also been incorporated in this system that provide better information to the clinicians and help them in effective management of the patients with breast lump. The ROM according to this system is 2.6-4.8% for C1; 1.4-2.3% for C2; 13-15.7% for C3; 84.6-97.1% for C4 and 99.0-100% for C5 category of breast lesions [1]. The aim of this study was to classify the breast lesions according to the IAC Yokohama system for cytological reporting of breast lesions.

MATERIALS AND METHODS

This was a retrospective six years observational study carried out in the Department of Pathology Karpaga Vinayaga Institute of Medical

Sciences and Research Centre, Tamil Nadu, India, from January 2015 to December 2020, The analysis of the study was done from January 2021 to December 2021 after approval by the Institutional Ethics Committee (IEC) (IEC Ref. No: KIMS/SUG/2019/58).

Sample size: Purposive sampling technique was used for selection of desired samples according to the inclusion criteria.

Inclusion criteria: All female patients of all age group who presented with breast lump for FNAC with informed consent were included for the study. Female patients with recurrent breast lump and lactating females with breast lump were also considered in the study.

Exclusion criteria: Patients with only nipple discharge and cytological examination carried out on direct smear preparation of the nipple discharge. Male patients with breast lesions. Patients with co-morbidities and unable to tolerate the minimally invasive FNAC procedure were excluded from the study.

Data Collection

Relevant clinical and pathological data including the FNAC reports were retrieved from the medical records of the Department of Pathology. Corresponding FNAC smears stained with H&E and Papanicolaou stains which were stored for 10 years in the Department of Pathology were retrieved from filing section, reviewed, confirmed and double-checked with the FNAC reports in the medical records. All the clinical and pathological data retrieved were tabulated for further analysis.

All those breast cytology cases were grouped into five categories (C1-Inadequate; C2-Benign; C3-Atypical; C4-Suspicious for malignancy and C5-Malignant) according to the International Academy of Cytology (IAC) Yokohama System for Cytological reporting of breast lesions [1]. Thus the IAC categories C1(Inadequate), C2 (Benign) and C3 (Atypical) fall under Low Risk for Malignancy (LRM) group while the IAC categories C4 (Suspicious for malignancy) and C5 (Malignant) fall under High Risk for Malignancy (HRM) group [1]. Hence in this study, the five IAC categories were further sub-categorised into a two-tier system (Low Risk for Malignancy-LRM and High Risk for Malignancy-HRM) depending on the magnitude of risk of malignancy in order to statistically evaluate the association between patients' age group and the sub-category (LRM and HRM).

STATISTICAL ANALYSIS

Statistical analysis was carried out using SPSS 23.0. Pearson Chi-square test was used to investigate the association between patients' age group and the sub-category (HRM and LRM) of breast lesion. A p-value of <0.05 was considered to be statistically significant.

RESULTS

Of the total 381 female breast FNACs, majority (60%) of them belonged to the age group of 21-40 years. Out of 381 cases, 297 (78%) were benign, 52 (13.6%) were malignant and 32 (8.4%) were inadequate for diagnosis [Table/Fig-1]. Majority of benign lesions were observed in females less than 40 years of age while more number of malignancies occurred in females more than 40 years of age.

Age (years)	Benign	Malignant	Non diagnostic	Total cases	Percentage
≤10	0	0	0	0	0
11-20	47	0	0	47	12.3
21-30	91	0	8	99	26
31-40	107	12	10	129	34
41-50	37	15	12	64	16.7
51-60	11	16	1	28	7.3
61-70	3	6	1	10	2.6
71-80	0	3	0	3	0.8
81-90	1	0	0	1	0.3
Total	297	52	32	381	100

[Table/Fig-1]: Age-wise distribution of breast lesions.

The predominant presenting symptom was palpable breast lump (73%) followed by breast lump associated with pain in 14.2% of cases. The other symptoms were breast pain, breast lump with nipple discharge and breast lump with nipple retraction [Table/Fig-2].

S. No.	Clinical presentation	Total cases	Percentage
1	Palpable breast lump	278	73
2	Pain in breast	32	8.3
3	Breast lump with pain	54	14.2
4	Breast lump with nipple discharge	06	1.6
5	Breast lump with nipple retraction	11	2.9
	Total	381	100

[Table/Fig-2]: Clinical presentation of breast lesions.

Upper Outer Quadrant (UOQ) of breast was involved in 65% of cases. There was no striking difference in the involvement of right (50% cases) and left breasts (45% cases) with only 20 cases (5%) being bilateral [Table/Fig-3,4].

According to IAC Yokohama system of reporting breast FNAC, 73.8% of cases belonged to "C2" category [Table/Fig-5].

S. No.	Breast quadrant	Total cases	Percentage
1	Upper outer quadrant	248	65
2	Upper inner quadrant	86	22.6
3	Lower outer quadrant	20	5.3
4	Lower inner quadrant	14	3.7
5	Central quadrant	13	3.4
	Total	381	100

[Table/Fig-3]: Breast quadrant involvement of breast lesions.

Side of breast involved	Total cases	n (%)
Right	Benign-152	190 (50)
	Malignant-28	
	Non diagnostic-10	
Left	Benign-126	171 (45%)
	Malignant-24	
	Non diagnostic-21	
Bilateral	Benign-19	20 (5)
	Non diagnostic-1	

[Table/Fig-4]: Distribution of breast lesions based on side of involvement.

IAC category	Type of breast lesions	n (%)
C1 (Insufficient/Inadequate)	-	32 (8.4)
C2 (Benign)	Fibroadenoma-158	281 (73.8)
	Fibrocystic disease-46	
	Fibroadenosis-31	
	Abscess-19	
	Granulomatous mastitis-16	
	Fat necrosis-5	
	Lactational adenoma-4	
	Phyllodes tumor-2	
C3 (Atypia-Probably benign)	Papillary lesion with atypia-16	16 (4.2)
C4 (Suspicious for Malignancy)	Ductal carcinoma-10	10 (2.6)
C5 (Malignant)	Ductal carcinoma-34	42 (11)
	Mucinous carcinoma-6	
	Apocrine carcinoma-2	

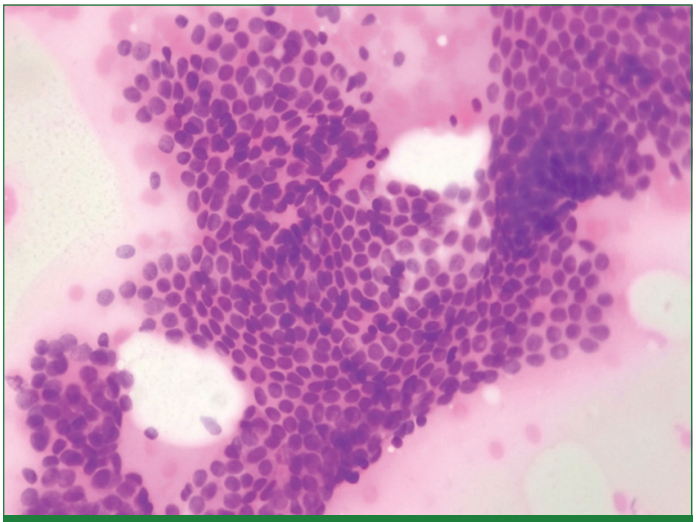
[Table/Fig-5]: Distribution of breast lesions according to IAC Yokohama system.

Fibroadenoma was the most prevalent lesion accounting for 41% of total cases. Around 94.3% of patients diagnosed with fibroadenoma were in the reproductive age group and less than 40 years of age. Pearson Chi-square test showed highly significant association between patient's age above 40 years and the risk of having a malignant breast lesion (p<0.0000001) [Table/Fig-6].

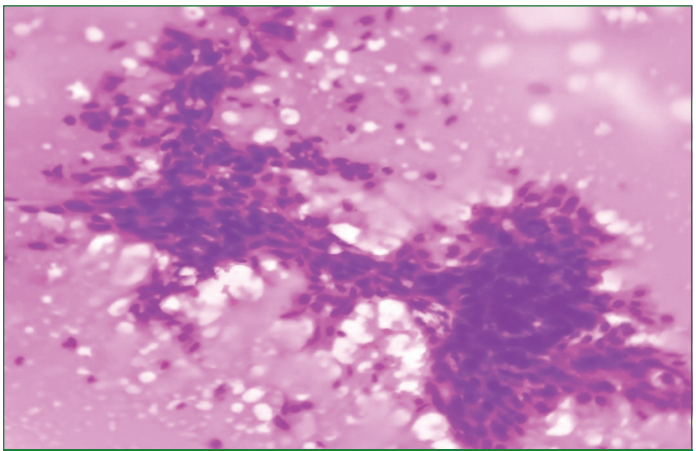
Patients age	Number of cases	High risk for malignancy (C4,C5)	Low risk for malignancy (C1,C2,C3)	Chi-square value	p-value
≤40 years	275	12	263	72.3	<0.0001 (Highly significant)
>40 years	106	40	66		
Total	381	52	329		

[Table/Fig-6]: Correlation between patients' age and risk of malignancy.

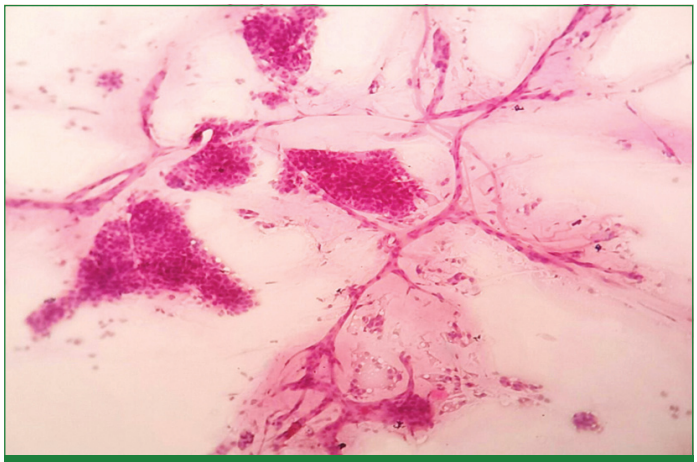
Microscopically, among the C2 category of lesions, fibroadenoma being the most common lesion showed cohesive branching clusters of benign duct epithelial cells, myoepithelial cells, fibromyxoid stroma and bare nuclei [Table/Fig-7]. In the C3 category, papillary lesion with atypia showed papillaroid clusters of benign duct epithelial cells with mild nucleomegaly, myoepithelial cells and traversing endothelial cells [Table/Fig-8]. C4 and C5 category of lesions were composed of malignant duct epithelial cells exhibiting pleomorphic hyperchromatic nuclei with the mucinous subtype showing abundant extracellular mucin and chicken wire blood vessels [Table/Fig-9] while the apocrine subtype comprising of dyscohesive clusters of malignant duct epithelial cells with abundant eosinophilic granular cytoplasm, vesicular nuclei and prominent nucleoli [Table/Fig-10]. The overall cellularity of C4 category of lesions was less compared to C5 category of lesions.



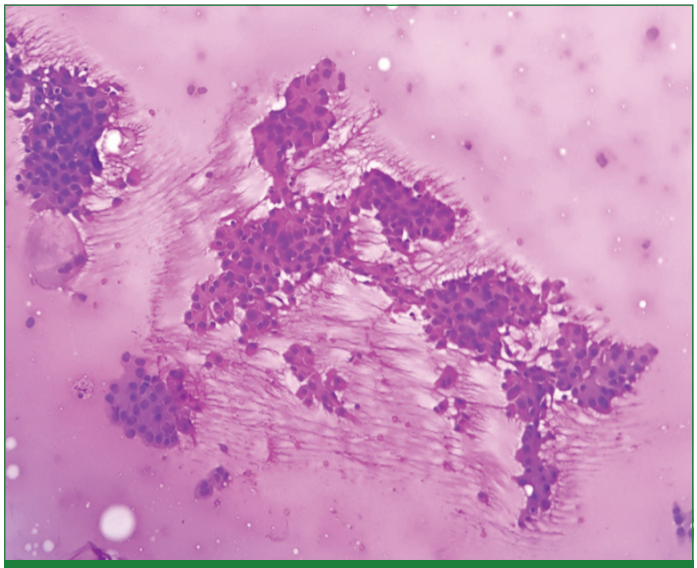
[Table/Fig-7]: 40X (H&E)- Cohesive branching clusters of benign duct epithelial cells, fibromyxoid stroma and bare nuclei (Fibroadenoma).



[Table/Fig-8]: 40X (H&E)-Papillaroid clusters of benign duct epithelial cells, myoepithelial cells and traversing endothelial cells (Papillary Lesion).



[Table/Fig-9]: 10X(H&E)- Malignant duct epithelial cell clusters in an abundant extracellular mucin and Chicken wire blood vessels (Mucinous Carcinoma).



[Table/Fig-10]: 40X(H&E)- Dyscohesive clusters of malignant duct epithelial cells with abundant eosinophilic granular cytoplasm, vesicular nuclei and prominent nucleoli (Apocrine Carcinoma).

DISCUSSION

Around 60% of the female breast FNAC cases belonged to the age group of 21-40 years in concordance with the study of Embaye KS et al., where 56% of cases were in 21-40 years of age group [1]. The common clinical symptom in the present study was palpable breast lump similar to the findings of Embaye KS et al., Sharif A et al., and Salzman B et al., [1-3].

Jayanandhini M et al., [4] from Tamil Nadu reported maximum number of cases in the Upper Outer Quadrant (UOQ) of right breast similar to the present study. However Kamra HT et al., [5] reported more number of lesions in the left breast [5]. In the present study, benign lesions outnumbered the malignant lesions with fibroadenoma being the most common benign breast lesion reported similar to other studies by Embaye KS et al., Sharif A et al., and Jayanandhini M et al., [1,2,4].

According to the IAC Yokohama system of classification, 73.8% of cases belonged to C2 (benign) category in concordance with that of Embaye KS et al., (76% of cases) and Chauhan V et al., (73% of cases) [1,6]. In present study, 8.4% cases were placed under C1 category due to scanty insufficient cellular material while 4.2% cases belonged to C3 category. Sulaiman K et al., reported 4.8% of C1 category lesions and 3% of C3 category lesions [7]. Bajwa R and Tariq Z reported slightly higher percentage of C1 cases (13.6%) [8]. This could be related to the technical expertise of the person performing FNAC. In the present study, C4 category of lesions accounted for 2.6% of cases while C5 category accounted for 11% of cases in contrast to other studies. Sulaiman K et al., reported

5.2% of C4 lesions and 21% of C5 lesions while Ibrahim Y and Atanda AT reported 13.5% of C4 cases and 22% of C5 lesions [7,9]. In a study conducted among Indian population in the state of Haryana by Sharma U et al., 0.95% cases belonged to C4 category and 15.34% belonged to C5 category. Thus the varied results observed in the malignant category of breast lesions (C4 and C5) among the several studies could be related to the varied incidence of breast malignancy in the female population worldwide and the expertise of the reporting cytopathologists [10]. Balkrishna B Yeole and AP Kurkure studied the incidence of breast cancer among the population of various countries and reported high incidence of breast carcinoma in developed countries owing to various factors including genetic factors and changes in lifestyle [11]. Thus on comparing the present study with other related studies, C2 (Benign) was the predominant category, percentage of malignant cases (C4 and C5) varied among different population groups worldwide while the percentage of inadequate smears (C1) can be minimised by improved technical expertise of the person performing FNAC.

There was a predominance of benign lesions in females less than 40 years of age and higher incidence of malignancy in females more than 40 years of age similar to the observation of Sulaiman K et al., Chandanwale SS et al., and Almobarak AO et al., [7,12,13]. Pearson Chi-square test revealed that patients more than 40 years of age were more likely to develop HRM lesions (p-value <0.0001). Similar observation was reported by Embaye KS et al., [1].

Limitation(s)

Since this was a retrospective study based on medical laboratory records, details of family history of breast malignancies were not available in many cases and hence it was not included in this study. Future studies can incorporate the family history of breast malignancies. Also, further studies can be done by correlating the cytology findings with the histopathological impression for all the IAC category of breast lesions.

CONCLUSION(S)

Fine Needle Aspiration Cytology (FNAC) is an useful diagnostic procedure in the preoperative evaluation of breast lesions. The utilisation of FNAC as a primary investigatory procedure accompanied by a standardised reporting system is indispensable in routine clinical practice. Adopting a standardised cytological reporting system like IAC Yokohama system will bring about consistency of breast cytology reporting across various institutions and will guide the clinicians in the proper management of breast lesions.

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