

Evaluating The Diagnostic Accuracy of FNAC of Breast Lesions with Reference To International Academy Of Cytology (IAC) Standardized Reporting And Correlation With Histopathology Of Breast Carcinoma

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Abstract

Introduction: Breast lesions are the leading cause of morbidity and mortality in women. Fine needle aspiration cytology (FNAC) of Breast is a significant component of the “Triple approach” for pre-operative diagnosis of breast lumps. This study is undertaken to explore the utility and accuracy of FNAC in various breast pathologies.

Aim: This study aims to classify various breast lesions according to the International Academy of Cytology (IAC) grading system and grade breast carcinoma on FNAC using Robinson's grading system which is then correlated with histopathology and also to evaluate the diagnostic accuracy, sensitivity, and specificity of FNAC in diagnosing breast lesions.

Materials and methods: The study was conducted on patients with breast lump. This study was conducted by retrieving FNAC smears and were grouped under five standardized categories proposed by the IAC: Category I (Insufficient material), Category II (Benign), Category III (Atypical), Category IV (Suspicious) & Category V (Malignant) respectively. C5 cases were graded by Robinson's grading system which was then compared with the histopathological Elston Ellis modified Bloom-Richardson grading system.

Results: Category I, II, III, IV, and V accounted for 10 (12.5%), 43 (53.75%), 3 (3.75%), 5 (6.25%), and 19 (23.75%) of the 80 breast lesions reported on FNAC, respectively. Histopathology correlations were available in 59 cases. The sensitivity, specificity, positive and negative predictive value, and diagnostic accuracy were 80%, 100%, 100%, 92.10%, and 94% respectively.

Conclusion: Cytological characterization based on IAC structured reporting will enhance diagnostic clarity and comparison with histopathology establishes the diagnostic accuracy of FNAC.

Keywords: Breast lesion, Elston's modified Bloom and Richardson method, FNAC, IAC grading, Robinson's grading.

INTRODUCTION

Breast cancer is one of the most common causes of cancer death in women[1-2]. Triple assessment of breast lesions plays a significant role in the early identification and definitive management of patients with breast cancer.

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Quick Response Code:



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DOI:

10.47750/pnr.2022.13.03.124

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How to cite this article: Priyanka Prakash, Eswari V, Evaluating The Diagnostic Accuracy of FNAC of Breast Lesions With Reference To International Academy Of Cytology (IAC) Standardized Reporting And Correlation With Histopathology Of Breast Carcinoma, J PHARM NEGATIVE RESULTS 2022;13: 830-838.

Triple assessment comprises Clinical examination, radiological imaging, and breast cytopathology with or without core needle biopsy (CNB)[3]. Fine needle aspiration cytology (FNAC) of the breast is a cost-effective procedure and provides clarity in differentiating benign and malignant features[4]. The IAC (Yokohama) system provides a structured protocol for reporting breast FNAC across countries[5]. Cytological grading by Robinson et al is widely used for grading breast malignancy. It corresponds well with histological grading of breast carcinoma using the Nottingham method described by Elston and Ellis (also called Elston's modified Bloom and Richardson method)[6]. It is a widely accepted tumor grading system and has been found to have good prognostic correlations. Cytological grading of breast malignancy helps in providing prognostication, which is significant in the era of neoadjuvant therapy[7]. However histopathological grading is the gold standard method.

The purpose of this study is to classify various breast lesions using the standardized reporting approach proposed by IAC (Yokohama system) in 2016. Also, to assess the concordance of cytological and histological grading using Robinson's grading system and Elston–Ellis modified Bloom and Richardson grading systems respectively, and to evaluate the diagnostic accuracy, sensitivity, and specificity of FNAC in diagnosing breast lesions.

Materials and Methods:

This study was carried out in the Department of Pathology in tertiary care hospital, over 3 years (January 2019 to January 2022) after obtaining ethical clearance from the Institutional Ethical Committee. It was a retrospective and prospective study of 80 cases. It was carried out in all patients with palpable breast lumps who have undergone the FNA procedure (comprising of blind and image-guided) with the age range of 14 to 77 years after obtaining informed consent. The breast lump was palpated, fixed, cleaned with a spirit swab and FNA was performed using a 5cc and 10 cc syringe with a 22-23G needle under aseptic precautions. In cases of guided FNAC, the lump was localized using ultrasonography. Imprint smears were taken in case of discharge from the nipple or breast lesion. Axillary lymph nodes were also aspirated (if palpable) to exclude metastases. Both FNA cytology and histopathology slides were stained with hematoxylin and eosin.

IAC has categorized the breast lesion into C1 to C5 (C-Code).

C1: Insufficient material

C2: Benign

C3: Atypical

C4: Suspicious

C5: Malignant.

The clinico radiological parameters of all the patients were recorded including age, gender, laterality, clinical diagnosis, sonography, mammography, etc. To establish cyto-histopathological correlation, the corresponding histopathology report of a biopsy or excision (if conducted) was obtained in all cases. However, histopathological correlation was available in 59 of the 80 cases studied. According to IAC, 19 cases were classified as C5 and were graded cyto-histopathologically using Robinson's criteria and Elston's modified Bloom and Richardson methods, respectively.

Robinson's cytological grading includes six well-known malignant features such as cell dissociation, cell size, cell uniformity, nuclear margin, nucleoli, and nuclear chromatin, each of which is scored in the range of 1 to 3. They also developed grades from first to third grade, with scores of 6-11 for first grade, 12-14 for second grade, and 15-18 for third grade [7]. Elston's modified Bloom and Richardson approach incorporates a semiquantitative assessment of three morphological features: tubule formation percentage, nuclear pleomorphism degree, and an accurate mitotic count using a defined field area. A numerical scoring system is used and the overall grade is derived from a summation of individual scores for the three variables: three grades of differentiation are used[8].

The diagnostic accuracy, sensitivity, specificity, positive predictive value, and negative predictive value of FNAC in diagnosing breast lesions were calculated.

Prior to analysis, the data was anonymized.

Results:

This study included 80 patients, with 77 (96%) females and 3 (4%) males, ranging in age from 14 to 77 years, with breast lesions most commonly occurring in the age group 31–40 years (33.75%). Breast lesions were evenly distributed, with 35 (43.75%) in the right breast, 42 (52.5%) in the left breast, and three (4%) bilaterally. The 80 cases were classified using the IAC classification method. C1 (insufficient) was found in ten (12.5%) cases, C2 (benign) in 43 (53.75%) cases, C3 (atypical) in three (3.75%) cases, C4 (suspicious) in five (6.25%) cases, and C5 (malignant) in 19 (23.75%) cases, as shown in [Figure 1]. The C2(43) category was the most common among the 80 cases, followed by the C5 category (19). In our investigation, fibroadenoma was found in 23 (53.48 %) of the C2 lesions, followed by fibrocystic disease in 8 (18.60 %), breast abscess in 6 (13.95 %), granulomatous mastitis in 5 (11.62 %), and mastitis in

2.35 % (1). In our study, the C3 lesion included two cases of atypical ductal hyperplasia and one case as atypical. Five cases of C4 lesions was diagnosed as suspicious of malignancy. C5 lesions were the second most common entity in this study, with 19 cases being classified as positive for carcinoma. Out of 80 patients, 59 had a correlation, 13 had not been followed up on, and 8 had been medically managed, as shown in [Table 1]. Histopathological correlation was available in 9 of the ten C1 cases, including 6 benign breast lesions (1 fibroadenoma, 1 fibrocystic breast disease, 1 fibroadenoma with moderate ductal hyperplasia, 1 fibroadenoma with florid epithelial hyperplasia, 1 Granulomatous mastitis, 1 benign breast disease) and 3 cases of invasive ductal carcinoma (one patient was lost to follow-up). Cases reported as granulomatous mastitis (5 cases), breast abscess (2 cases), and mastitis (1 case) among the C2 lesions were treated medically, while the remaining 35 cases exhibited histological association. All 35 cases had benign breast disease, as shown in [Table 2], which included fibroadenoma (18 cases), fibrocystic breast disease (7 cases), fibroadenoma with usual ductal hyperplasia (4 cases), fibroadenoma with fibroadenosis (2 cases), and breast abscess (4 cases). Histopathological correlation was known for two of the three C3 cases, including one invasive ductal carcinoma, one invasive lobular carcinoma, and one patient was lost to follow-up. Only one of the five C4 patients had histological correlation, which revealed invasive ductal carcinoma, and the other four were not followed up on, as seen in [Table 3].

C5 cases were mostly seen in the fifth decade of life. Cytologically 19 C5 cases were grouped under 3 grades based on Robinson's criteria as follows: 4(21%) cases were well differentiated(Grade I), 9(47%) cases were moderately differentiated (Grade II), 6(32%) of cases were poorly differentiated(Grade III) as indicated in the graph [Figure 2]. All 19 cases were cytologically scored using Robinson's criteria, which revealed that 78.9% of the cases had highly pleomorphic cells (cell uniformity) and 63.15 % have clumped and cleared chromatin (nuclear chromatin), yielding a maximum score of 3. Following that, 47.3 % had increased cell size (3-4 times RBC size), 42.1 % had cells

grouped in clusters and singles giving the highest score of 2. The greatest score of 2 as well as 3 were achieved by 73.6 %, which had an equal proportion of cells with nuclear folds and nuclear clefts & buds. However, in 42.1 %, the nucleoli were indistinct, resulting in a score of 1, as illustrated in [Figure 3]. The histology correlation for 12 of the 19 C5 cases was available, and 7 patients were lost to follow-up. The 12 cases includes 9 invasive ductal carcinoma, 2 medullary carcinoma of the breast, and 1 metaplastic carcinoma, as shown in [Table 3]. Elston's modified Bloom and Richardson approach was accessible for ten cases, including one (10%) case that was well-differentiated (Grade 1), three (30%) cases that were moderately differentiated (Grade II), and six (60%) cases that were poorly differentiated (Grade III), as shown in [Figure 4]. This approach could not grade the remaining two medullary carcinomas. The concordance of cytological and histopathological grading were assessed, and two cases out of ten were found to be discordant, with cytologically diagnosed grade I being diagnosed as grade III on histopathology and cytologically diagnosed grade III being diagnosed as grade I in histopathology, as shown in [Table 4]. The statistical tests used in the interpretation of the results obtained in our study were sensitivity of FNAC as a diagnostic procedure for the entire study, Specificity of FNAC in relation to the malignant lesions, Positive predictive value of FNAC as a diagnostic procedure for the entire study and Negative predictive value in relation to the malignant lesions.

After excluding cytologically insufficient cases, non-follow-up patients, and medically managed patients from our study, we had 50 cases to analyze statistically. For the entire trial, FNAC had a sensitivity of 80% and a positive predictive value of 100%. Only patients having a lump in their breast were included in our study. As a result, there were no normal people in a statistical sense. Hence, the ability of Fine-Needle Aspiration Cytology as a diagnostic test to correctly identify those individuals without disease (i.e., true negatives) could not be assessed because FNAC would yield some result in every patient in our study[12]. In relation to malignant lesions, the specificity and negative predictive value (NPV) of FNAC were 100% and 92.10 %, respectively.

Table 1: Correlation between IAC grading and histopathology

Histopathology(59)	FNAC(80)				
	C1(10)	C2(43)	C3(3)	C4(5)	C5(19)
Benign (41)	6	35			-
Malignant (18)	3	-	2	1	12
No follow up (13)	1	-	1	4	7
Medical management (8)	-	8			-

Table 2: Correlation between IAC grading and histopathology(C1 & C2 cases)

FNAC(53)						
	C1(10)	C2(43)				
Histopathology(44)	C1(10)	Fibroadenoma (23)	Fibrocystic disease. (8)	Breast abscess (6)	Granulomatous mastitis(5)	Mastitis(1)
Fibroadenoma(19)	1	18				
Fibrocystic disease (8)	1		7			
Breast abscess (4)				4		
Fibroadenoma with usual ductal hyperplasia (4)		3	1			
Fibroadenoma with moderate ductal hyperplasia(1)	1					
Fibroadenoma with florid ductal hyperplasia(1)	1					
Fibroadenoma with fibroadenosis(2)		2				
Granulomatous mastitis(1)	1					
Benign breast disease(1)	1					
Invasive ductal carcinoma(3)	3					
No follow up (1)	1					
Medical management (8)				2	5	1

Table 3: Correlation between IAC grading and histopathology(C3,C4& C5 cases)

FNAC(27)			
Histopathology(15)	C3(3)	C4(5)	C5(19)
Invasive ductal carcinoma(11)	1	1	9
Medullary carcinoma(2)			2
Metaplastic carcinoma(1)			1
Invasive lobular carcinoma(1)	1		
No follow up(12)	1	4	7

Table 4: Robinsons grading system and Modified Bloom– Richardson grading system.

Grading	Robinsons grading	Modified Bloom– Richardson Grading
Grade I	2(20%)	1(10%)
Grade II	3(30%)	3(30%)
Grade III	5(50%)	6(60%)

Table 5: Comparison between the various studies done for IAC grading system

Studies	C1	C2	C3	C4	C5
Bajwa and Tariq. ^[17]	13.6	60.6	6.2	9.3	10.3
Modi et al. ^[18]	3.7	59.8	4.6	8.4	23.3
Sunita et al. ^[19]	2.9	50	3.5	6.5	37.1
Georgieva et al. ^[20]	25.6	44.3	2.2	5.3	22.5
Panwar et al. ^[21]	1.3	82.6	5.7	1.7	8.4
Present study	12.5	53.75	3.75	6.25	23.75

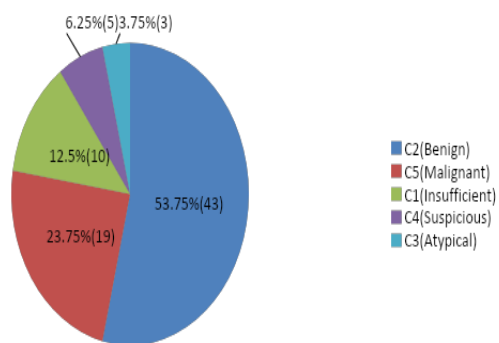
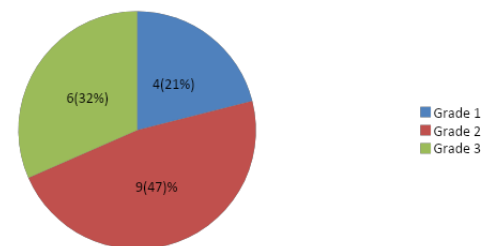
Figure 1: IAC Category wise distribution of patients

Figure 2: Robinsons grading system Number of cases(19)


Figure 1: Cytosmear shows predominantly hemorrhage with some inflammatory cells and degenerated cells(H&E, x10 & x40).C1-Insufficient.

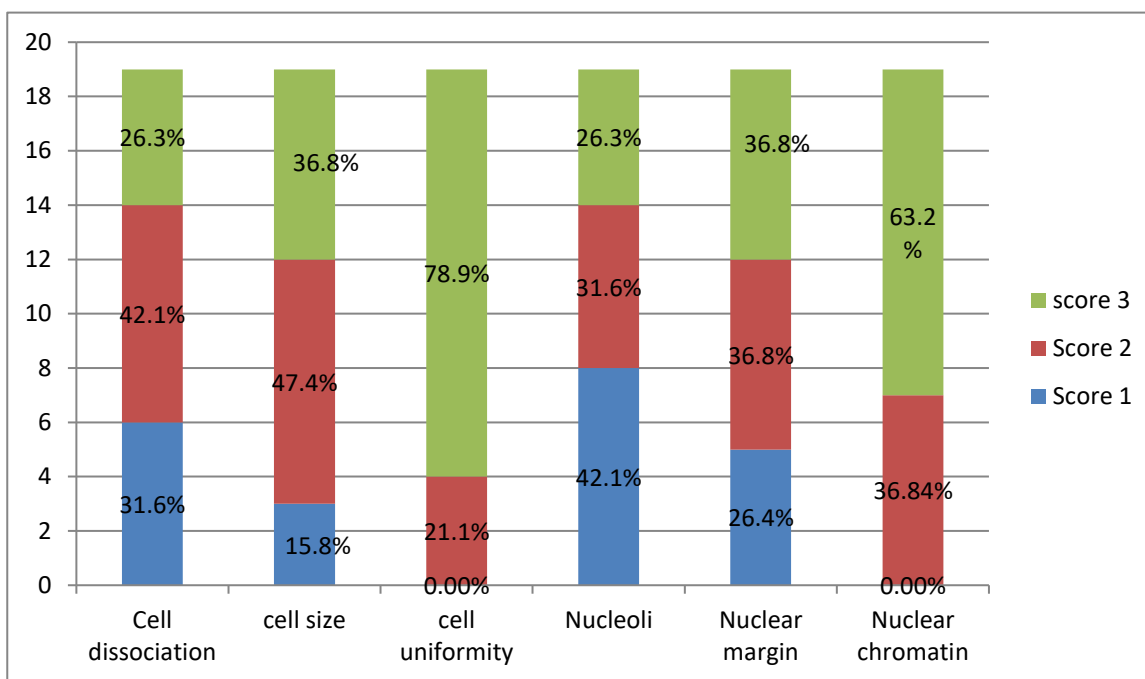


Figure 3: Cytological score of C5 cases based on Robinsons grading system

Figure 4: Histopathological grading of C5 cases by Elston - Ellis modified SBR grading system(10)

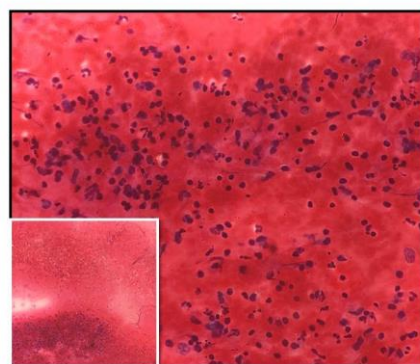
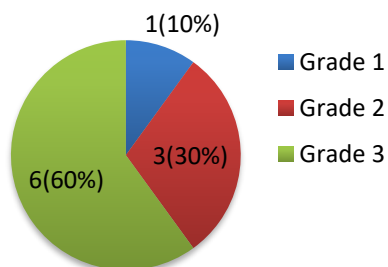


Figure 5: Cytospin shows predominantly hemorrhage with some inflammatory cells and degenerated cells(H&E, x10 & x40).C1-Insufficient.

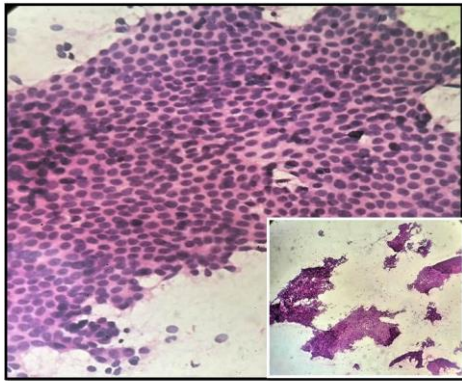


Figure 6: Cytosmears shows cohesive monolayered sheets of uniform ductal epithelial cells and myoepithelial cells (H&E, x10 & x40). C2- Benign, Fibroadenoma.

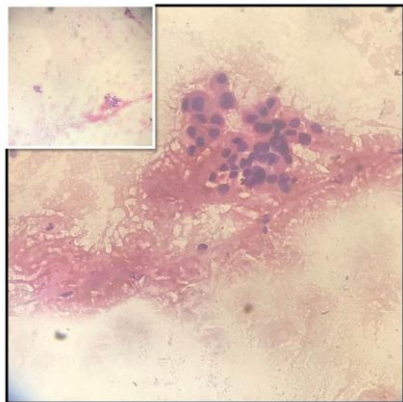


Figure 7: Cytosmears show low cellularity with cells in scattered groups and in singles. The cells have abundant eosinophilic cytoplasm with pleomorphic nuclei and coarse chromatin in a background of hemorrhage and fatty stroma. (H&E, x10 & x40). C3- Atypical.

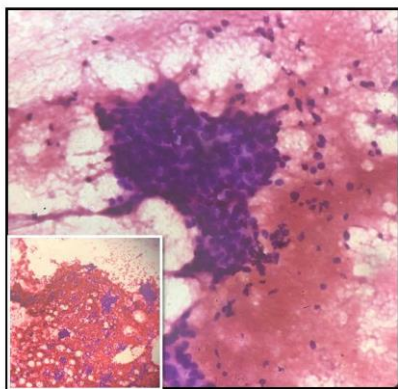


Figure 8: Cytosmears show highly cellularity with presence of atypical epithelial cells in discohesive clusters (H&E, x10 & x40). C4- Suspicious for malignancy.

and singly scattered, admixed with benign ductal epithelial and myoepithelial cells in a background of hemorrhage. Atypical epithelial cells have moderate cytoplasm, large round to oval nucleus, coarse chromatin, prominent nucleoli and mild nuclear membrane irregularity. (H&E, x10 & x40). C4- Suspicious for malignancy.

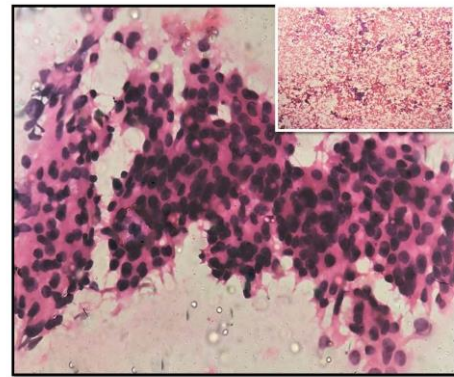
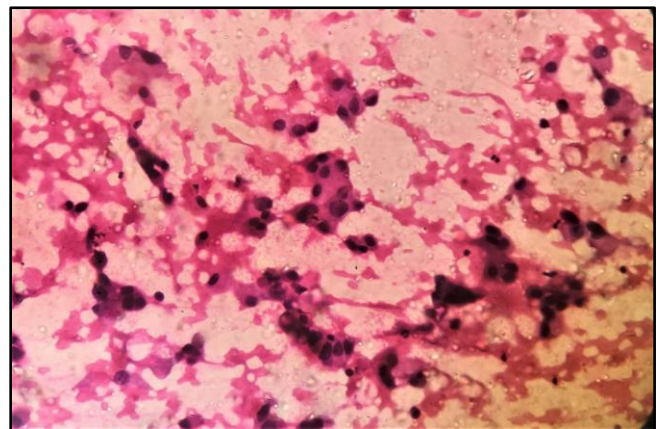


Figure 9: A) Cytosmears show highly cellularity with presence of malignant epithelial cells in discohesive clusters and singles in a background of hemorrhage. Malignant epithelial cells have abundant eosinophilic cytoplasm, pleomorphic and hyperchromatic nucleus, coarse chromatin, prominent nucleoli. (H&E, x10 & x40). B) Malignant epithelial cells in singles. C5- Malignancy.



Discussion:

Breast lumps are common in women of all ages and breast cancer is the leading cause of cancer in women worldwide. Breast cancer comprises 2.1 million new cases and 6,27,000 deaths every year [10]. Breast cancer has become the most common malignancy in Indian women, surpassing cervical cancer. An incidence of 2,05,424 new cases of breast cancer annually is projected in India, accounting ~for 29.9% of all malignancies reported in women, with 87,000 fatalities per year [9].

For tumors that are easily palpable on external examination, the FNAC technique has a wide range of applicability and utility[11]. In developed countries, the core needle procedure is preferred whereas in developing countries like India FNAC is preferred[11]. So, to improve the performance, interpretation, and reporting of breast FNA cytology, IAC has developed a standardized reporting system that will help pathologists and clinicians communicate more effectively.

IAC standardized reporting includes five categories from C1 to C5. C1 or Insufficient smears are defined as smears with scanty cellularity and a poorly fixed or smeared slide making the diagnosis difficult[Figure 5]. In our study, 10 cases were reported as inadequate could be due to faulty technique [13,14]. C2 or Benign breast lesions have apparent benign cytological features such as cohesive monolayered sheets of uniform ductal epithelial cells, myoepithelial cells with perfect ovoid nuclei, fine even chromatin and indistinct nucleoli, bare bipolar nuclei, apocrine sheets, foamy histiocytes, epithelioid granuloma, multinucleated giant cells, and a granular proteinaceous background. There were 43 C2 cases in our study with ductal architecture, myoepithelial cells, cystic alterations, epithelioid granuloma, and inflammatory cells[Figure 6]. C3 lesions in addition to features seen in benign lesions, also show single-cell with nuclear atypia, spindled myoepithelial cells, and cribriform, micropapillary, or papillary architecture[13,16]. We found three (3.75%) C3 cases with moderate to sparse cellularity, mild pleomorphism, and discohesion[Figure 7]. Breast lesions with high cellularity, large epithelial tissue fragments, scattered cells with low to intermediate grade nuclei, prominent nucleoli and necrosis are found in malignant lesions but lacking adequate malignant features are categorized under C4 or Suspicious category[Figure 8]. We found 5 C4 cases that could be due to subjectivity [15]. C5 refers to aspirates with low to high cellularity, widely dispersed single cells, high-grade nuclear characteristics, and no myoepithelial cells or bare bipolar nuclei [16]. We described 19 C5 cases with a high level of cellularity, discohesive cells, and a mild to the extremely pleomorphic nucleus[Figure 9].

In our analysis, 12.5 percent of cases had insufficient aspirate and were classified as C1 which was in concordance with studies done by Bajwa and Tariq (13.6%) which was higher compared to Modi et al.(3.7%) and Sunita et al(2.9%). Our study had 53.75% C2 lesions which were in concordance with Sunita et al (50%) and Modi et al(59.8%). C3 3 (3.75%) and C4 05 (6.25%) were reported in our study. Similar results were also obtained in studies done by Sunita et al and Modi et al. Our study had 23.75% C5 lesions which were in concordance with Georgia et al(22.5%).

Our findings matched the findings of other researchers which is shown in Table [5].

In our study, cytology grading showed an absolute correlation with the histological grade in 80% (n = 8) cases which were in concordance with studies done by Chandanwale et al. [22] (82.5%) and Pal and Gupta.[23] (78%). We had two discordant cases, with one case from cytologically diagnosed grade I and one case from cytologically diagnosed grade III being reported as grade III and grade I on histology. The subjective variation could be the source of discordance. The degree of tubule formation, mitosis, and nuclear pleomorphism were used to grade the histology. Because tubule formation and mitotic index were difficult to quantify by cytology, the discrepancy between the cytological and HG systems could be due to this. Nuclear properties such as nuclear size, nucleoli, nuclear membrane, and chromatin pattern were given a lot of importance in CG, whereas nuclear traits were merely one of the components of HG. This can lead to cytohistological discrepancies in breast cancer grading.

Rapid onsite evaluation (ROSE) will reduce the problem of inadequacies and costs to the system by minimizing the need for repeat procedures thus lowering the patient anxiety and waiting time while increasing the sensitivity. It can also be used to triage cases for ancillary studies. Clinical application of FNAB cytology will be enhanced by standardized use of cell blocks, immunohistochemistry, in situ hybridization, and other molecular assays of prognostic and diagnostic markers, as well as integration of cytology data to management algorithms.

Conclusion:

FNAC is a simple, reliable, and cost-effective first-line diagnostic technique for all breast masses. Given the multiple confounding factors in this procedure, breast cytopathology performance must be regularly monitored using a standardized and reproducible system to improve the diagnostic accuracy of FNAC, better communication among cytologists, surgeons, and radiologists, and interinstitutional information exchange with the long-term goal of improving patient care.

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