

International Journal of Biomedical Research

ISSN: 0976-9633 (Online); 2455-0566 (Print)

Journal DOI: <https://doi.org/10.7439/ijbr>

CODEN: IJBRFA

Original Research Article**Value of scoring system in classification of proliferative breast disease on fine needle aspiration cytology****Rajan Shah**^{*1}, Arvind Kumar Sinha¹, Anju Pradhan¹ and Rajat Kumar Agarwal²¹Department of Pathology, B.P. Koirala Institute of Health Sciences, Dharan-18, Sunsari District, 56700 Nepal²Department of Surgery, B.P. Koirala Institute of Health Sciences, Dharan-18, Sunsari District, 56700 Nepal

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***Correspondence Info:**Dr. Rajan Shah
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Dharan-18, Sunsari District, 56700 Nepal***Article History:****Received:** 02/09/2017**Revised:** 25/09/2017**Accepted:** 26/09/2017**DOI:** <https://doi.org/10.7439/ijbr.v8i9.4371>**Abstract****Background:** Fine needle aspiration cytology (FNAC) breast is generally considered as a rapid, safe and reliable diagnostic tool to distinguish benign from malignant breast lesions. Masood's Scoring Index has been proposed to categorize the breast lesions so as to help in surgical management.**Objectives:** To find out the usefulness of Modified Masood's scoring Index (MMSI) in proliferative breast diseases.**Materials and Methods:** This is a prospective study, done over period of one year 2012 to 2013, which includes fifty cases of palpable breast lesions with cytological diagnosis, followed by histological confirmation on biopsy. MMSI was applied on corresponding FNAC aspirates. Breast lesions were categorized into four groups, non proliferative breast disease, proliferative breast disease (PBD) without atypia, PBD with atypia and carcinoma breast.**Results:** Out of total 50 cases, age group ranged from 17-64 years. Modification of Masood's scoring system by shifting of score 9 and 10 from category I to category II, was found to be easily reproducible scoring method of breast lesions as it has improved the diagnostic accuracy of PBD.**Conclusion:** FNAC of breast is highly sensitive and specific modality for distinguishing benign and malignant lesions but its role in diagnosing proliferative breast lesions is debatable. MMSI can be applied on FNAC aspirates in stepwise manner after cytomorphological assessment to improve diagnostic accuracy of PBD without atypia.**Keywords:** Modified Masood's scoring, Proliferative breast disease, FNAC.**1. Introduction**

Breast lump, whether benign or malignant is a cause of anxiety to the patient and her family members. Most cases of breast lumps are benign[1] but most of these patients are in a state of heightened anxiety until they have undergone specialist assessment, the necessary investigations and eventual reassurance.[2] Simply from clinical examination, it is difficult to determine whether a suspicious lump is benign or malignant. Therefore a definitive and diagnostic procedure which can separate these breast lumps at the outpatient clinic is needed. This procedure must be accurate, easy to perform and reproducible [3].

Fine needle aspiration cytology (FNAC) can be performed as an outpatient procedure, since it requires no special equipment, causes minimal morbidity and has high patient acceptance. Factors like low cost, rapid reporting and patient compliance are better for FNAC procedure [4].

FNAC of breast lump is an accepted and established method to determine the nature of the lump and it may play an important role when it is difficult to determine the nature of breast lump by clinical examination.[3] It has been shown that FNAC can reduce the number of open breast biopsies.[5]

FNAC has been found to have sensitivity ranging from 81% to 97.5% and specificity of more than 99%. [6-8]

Proliferative disease of breast includes a number of histologic lesions. Proliferative breast disease (PBD) without atypia is characterized by proliferation of ductal-epithelium and/or stroma without cellular abnormalities suggestive of malignancy. The following entities are included in this category (1) moderate or florid epithelial hyperplasia, (2) sclerosing adenosis, (3) complex sclerosing lesions, (4) papillomas, (5) fibroadenoma with complex features. [9] Fibroadenomas that contain cysts larger than 3mm, sclerosing adenosis, epithelial calcifications, or papillary apocrine change have been called as complex fibroadenomas. [10]

Fibrocystic change reflects a spectrum of changes that range from normal physiologic alterations in the breast to proliferative changes approximating in situ carcinoma [11].

PBD without atypia has slightly increased risk 1.5-2.0 times for subsequent development of carcinoma. [12-15]

Non proliferative breast disease (NPBD) has 1.0 relative risk for developing into invasive carcinoma. [9,13,14] Pathologic lesions included under NPBD are (1) duct ectasia, (2) cysts, (3) apocrine changes, (4) mild hyperplasia, (5) adenosis and (6) fibroadenoma without complex features. [9]

Proliferative disease with atypia includes atypical ductal hyperplasia (ADH) and atypical lobular hyperplasia (ALH). ADH and ALH have morphological features identical to ductal carcinoma *in situ* (DCIS) and lobular carcinoma in situ respectively (LCIS). [9] FNAC has limited role in separating these breast lesion. PBD with atypia has 4.0-5.0 times risk for developing into invasive carcinoma. [12-15]

Breast cancer is the most common non skin malignancy in women. Carcinoma breast are divided into (1) in situ carcinoma comprising of DCIS and LCIS, (2) invasive carcinoma comprising of ductal carcinoma, lobular carcinoma, cribriform carcinoma, mucinous carcinoma, medullary carcinoma, papillary carcinoma and metaplastic carcinoma. [9] The relative risk for carcinoma in situ is 8.0 - 10.0 times progression into invasive carcinoma. [12-15]

Though FNAC of breast is a highly sensitive and specific modality for distinguishing benign and malignant lesions, its role in delineation of proliferative lesions of

breast is debatable. One approach to resolve the diagnostic difficulties posed by PBD on FNAC has been to apply an objective scoring system. [16]

A number of articles have been published on cytology of PBD taking cytological and nuclear features into consideration. The objective scoring system proposed by Masood *et al* [17] is most widely tested of the scoring systems although not all the authors have found it to be useful. This study was undertaken to test the usefulness of Modified Masood scoring system versus cytomorphologic diagnosis in cases with PBD .

1.1 Aims and objectives

To find out the usefulness of Modified Masood's Scoring Index (MMSI) in proliferative breast diseases.

2. Materials and methods

This prospective study was done within period of one year (2012 to 2013) in the Department of Pathology (Cytopathology and Histopathology) at B.P Koirala Institute of Health Sciences, Dharan, Nepal.

Fifty (50) cases of palpable breast lesions with cytological diagnosis, followed by histological confirmation on biopsy were included in the study. All cases were females with palpable breast lumps and in the age range of 17 – 64 years. The palpable breast lumps were fixed between thumb and finger and 22 gauge needle attached to 10 ml syringe was inserted into lump. Suction pressure was applied by withdrawing the syringe plunger to 2ml mark. Three to four passes were made into the substance of lump, keeping the needle within breast all the times. The needle was withdrawn; aspirate expressed out and was thinly spread on four to five glass slides.

PAP stains were used for the slides which were fixed in 95% ethyl alcohol. Air dried smear was stained with May-Grunwald Giemsa stain. Criteria for adequacy are the presence of four to five clusters of ductal epithelial cells, each cluster made up of five to six cells with presence of a few bare nuclei in the background.

Scoring system proposed by Masood *et al* [17] was applied to FNAC aspirates smears without knowledge of cytomorphologic diagnosis. Briefly in this system score 1 to 4 was given for each of the following parameters: cellular arrangement, cellular pleomorphism, anisonucleosis, and presence of myoepithelial cells, nucleoli and clumped chromatin (Table 1).

Table 1: Masood Scoring Index.

Cellular arrangement	Pleomorphism	Presence of myoepithelial cells	Anisonucleosis	Nucleoli	Clumped chromatin	Score
Monolayer	Absent	Many	Absent	Absent	Absent	1
Nuclear overriding	Mild	Moderate	Mild	Rare micro nucleoli	Rare	2
Clustering	Moderate	Few	Moderate	Frequent micro nucleoli	Occasional	3
Loss of cell cohesion	Conspicuous	Absent.	Conspicuous	Predominant macronucleoli	Frequent	4
Total score.						
Non proliferative breast disease 6-10						
Proliferative breast disease without atypia 11-14						
Proliferative breast disease with atypia 15-18						
Carcinoma 19-24						

Scoring system is slightly modified. NPBD, which had score of 6-10, is modified to score of 6-8 with a shift of score 9 and 10 to PBD without atypia i.e. Score 11-14 is modified to 9-14 in MMSI. (Table 2) This is modified because of better accuracy of diagnosis and management of patient. On the basis of total score obtained in a case, the

FNAC Aspirates were evaluated and categorized into four Groups/ Category:

- Non proliferative breast disease (NPBD)
- Proliferative breast disease (PBD) without atypia,
- PBD with atypia and
- Carcinoma breast

Table 2: Modified Masood Scoring Index (MMSI)

Cellular arrangement	Pleomorphism	Presence of myoepithelial cells	Anisonucleosis	Nucleoli	Clumped chromatin	Score
Monolayer	Absent	Many	Absent	Absent	Absent	1
Nuclear overriding	Mild	Moderate	Mild	Rare micro nucleoli	Rare	2
Clustering	Moderate	Few	Moderate	Frequent micro nucleoli	Occasional	3
Loss of cell cohesion	Conspicuous	Absent	Conspicuous	Predominant macronucleoli	Frequent	4
Total score.						
Non proliferative breast disease 6-8						
Proliferative breast disease without atypia 9-14						
Proliferative breast disease with atypia 15-18						
Carcinoma 19-24						

Scoring of FNAC aspirates was done blindly and independently by two observers. Cases with discrepant scores, slides were re-evaluated on a multihead microscope and a final consensus was reached. Cytological diagnosis and scoring of FNAC aspirates was done by independent observer. After biopsy, histopathology slides were evaluated to reach confirmatory diagnosis.

2.1 Statistical Analysis

Descriptive statistics was used to describe the age, site of lesion, and distribution of cases. Percentage and

mean were calculated where ever applicable. Sensitivity, specificity, positive predictive value, negative predictive value of MMSI was calculated.

3. Result

Only the specimen of breast lesions whose biopsy was done at BPKIHS was considered in this study. All patient included in the study were females with age range of 17 to 64 years. We classified the breast lesion into four category based on cytological features (Table 3).

Table 3: Comparative results chart among cytological, Modified Masood Scoring Index and Histopathology diagnosis in breast specimen.

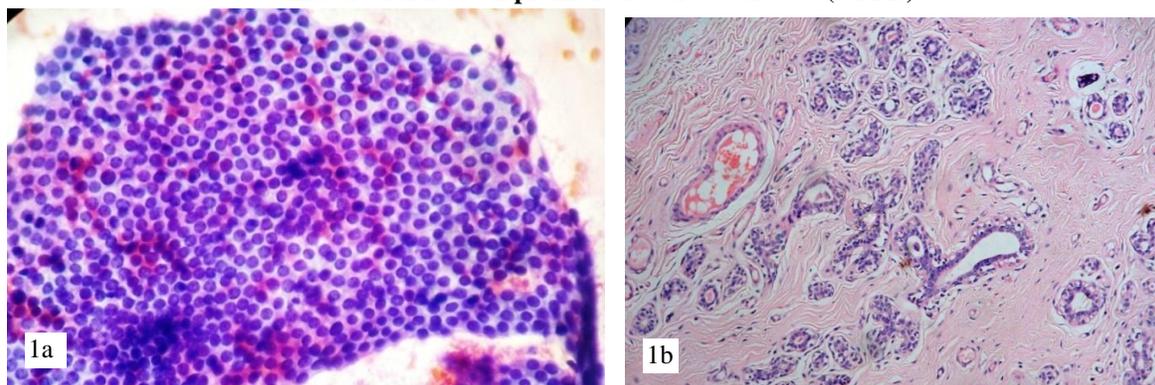
Categories	Cytological Diagnosis	Modified Masood Scoring Index	Histopathology Diagnosis (Gold Standard)
Non-Proliferative Breast Disease	20 (40.0%)	11 (22.0%)	10 (20.0%)
Proliferative Breast Disease Without Atypia	12 (24.0%)	21 (42.0%)	22(44.0%)
Proliferative Breast Disease With Atypia	2 (4.0%)	1(2.0%)	1 (2.0%)
Carcinoma	16 (32.0%)	17 (34.0%)	17 (34.0%)
Total number of valid cases	50 (100.0%)	50 (100.0%)	50 (100.0%)

Table 4: Frequency distribution of score of the breast lesion

Score	Number of cases	Percentage (%)
7	2	4.0
8	9	18.0
9	5	10.0
10	3	6.0
11	1	2.0
12	8	16.0
13	4	8.0
16	1	2.0
19	1	2.0
21	2	4.0
22	9	18.0
23	5	10.0
Total	50	100.0

3.1 Non-Proliferative Breast Diseases (Category I)

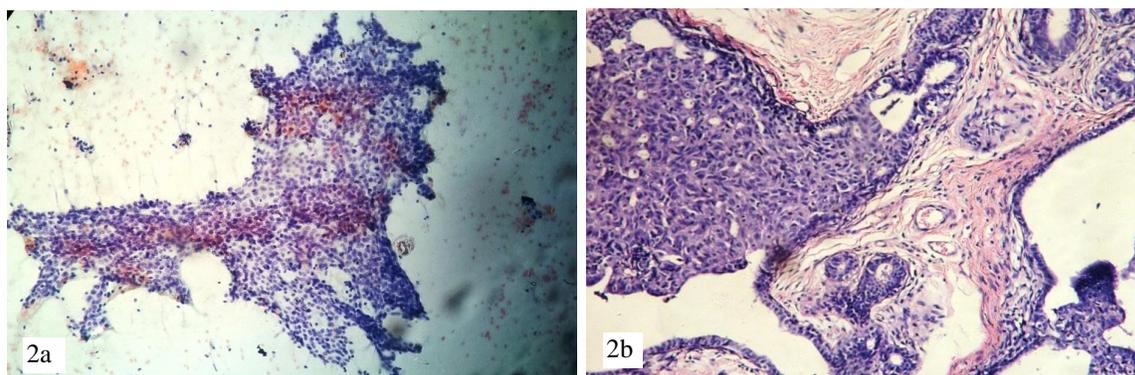
Non-proliferative breast disease (NPBD) was classified on cytology (FNAC) based on cytological features which includes monolayer sheet of uniform sized cells, monomorphic cellular arrangement and presence of myoepithelial cells. Nuclear features that include were absence of anisonucleosis, prominent nucleoli and clumped chromatin. Background shows few cases with apocrine changes and cyst macrophages (Illustration 1a).

Illustration 1: Non proliferative breast disease (NPBD)**Illustration 1(a) Monolayer arrangement of ductal epithelial cells with presence of myoepithelial cells in the sheet (400X). (1b) Corresponding histopathology section (400x)**

Based on these findings, 20/50 cases were classified as NPBD on cytology. On applying Modified Masood scoring index (MMSI) to FNAC aspirates, 11/50 cases fell under category of NPBD. Further evaluating the histopathology slides after biopsy only 10/50 cases came under category of NPBD. MMSI correctly placed 10 cases of NPBD in the category, but 1 case was under-diagnosed as NPBD which on biopsy proved to proliferative breast disease without atypia. Nine (9) cases have score 8 and two (2) cases have score 7 (Table 3 & 4).

3.2 Proliferative Breast Disease without Atypia (Category II)

Proliferative breast disease (PBD) without atypia were categorized based on cytological features including moderate to high cellularity, mild cellular pleomorphism, mild anisonucleosis with decrease in number of myoepithelial cells. Nuclear overriding, clustering with occasional micronucleoli and chromatin clumping were also included. Background shows occasional bare nuclei and apocrine cells (Illustration 2a).

Illustration 2: Proliferative breast disease (PBD) without atypia**Illustration 2(a) Smear shows ductal epithelial cells with overlapping, mild anisonucleosis. Myoepithelial cells are seen in the clusters (400x). (b) Corresponding histology section. (400x)**

Number of cases of PBD without atypia diagnosed on cytology based on above findings were 12/50. MMSI categorized 21/50 cases in this group. Ten (10) cases from NPBD were added to PDB without atypia on histopathology examination. Total cases diagnosed by histopathology to this group were 22/50. MMSI correctly diagnosed 21 cases of PDB without atypia, whereas 1 case was under-diagnosed as NPBD.

Five (5) cases have score 9 and three (3) cases have score 10. Due modification of scoring system, score 9 and 10 were kept in PDB without atypia in MMSI, so these eight

(8) cases were shifted to PDB without atypia on MMSI (Table 3 & 4).

3.3 Proliferative Breast Disease with Atypia (Category III)

Proliferative breast disease (PBD) with atypia has cytomorphological features which overlap with carcinoma. Cytological features were moderate to high degree of cellularity, moderate degree of cellular pleomorphism and anisonucleosis. The nuclear features include significant increase in the number of micronucleoli and chromatin clumping along with few myoepithelial cells and decrease in the number of bare nuclei (Illustration 3a).

Illustration 3: Proliferative breast disease (PBD) with atypia

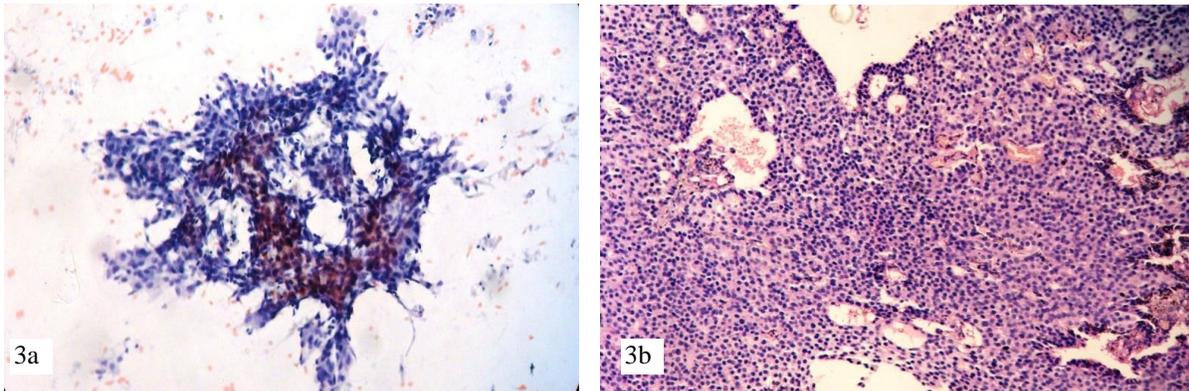


Illustration 3(a) Smear shows moderate degree of cellular pleomorphism, nuclear overlapping, anisonucleosis and occasional prominent nucleoli (400x). (b) Corresponding histopathology section. (400x)

Number of cases diagnosed as PBD with atypia on cytology was 2/50. MMSI diagnosed 1/50 case in the category. On subsequent biopsy 1/50 case turned out PBD with atypia. One case which was diagnosed as PBD with atypia on FNAC was found to be carcinoma in situ on histopathology examination (Table 3).

3.4 Carcinoma (Category IV)

Carcinoma breast were diagnosed on FNAC, based on cytological features characterized by loosely arranged

cellular pattern, high cellularity, nuclear pleomorphism, chromatin clumping with frequent macronucleoli and absence of myoepithelial cells. Background shows necrosis (Illustration 4 a). Based on these cytological features 16/50 cases were diagnosed as carcinoma breast on FNAC. MMSI categorized 17/50 cases to the group with score ranging from 19 to 24. All cases were correlated with histopathology. 17/50 cases were diagnosed as breast carcinoma on histopathology (Table 3).

Illustration 4: Carcinoma breast

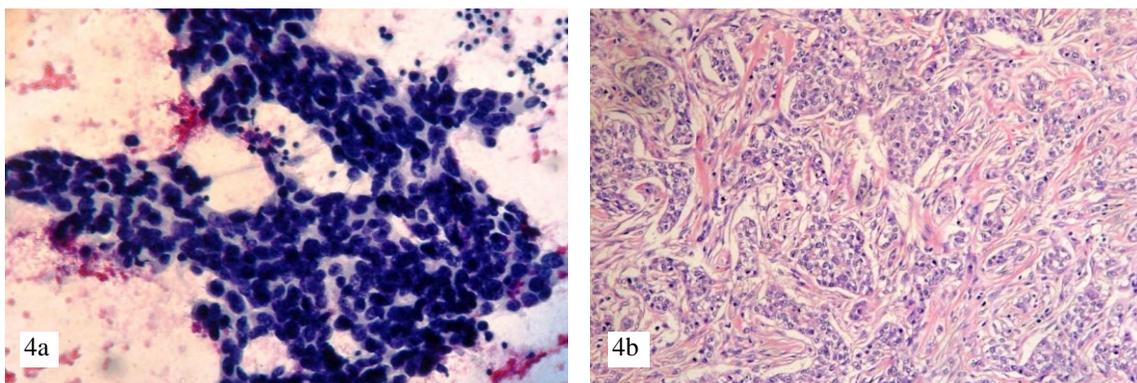


Illustration 4: (a) Sheet of highly pleomorphic cells, presence of clumped chromatin and prominent nucleoli, absence of myoepithelial cells (400x). (b) Corresponding histopathology section. (400x)

Overall, a complete concordance between histopathology diagnosis and FNAC diagnosis (cytology) was observed in 39/50 cases (78.0%). High degree of

concordance was observed when MMSI was applied. This concordance increased to 98.0% (49/50 cases) between MMSI and histopathology.

Table 4: Sensitivity, specificity, positive predictive value, negative predictive value between Modified Masood scoring index and histopathology result in breast disease

Modified Masood Scoring Index	Histopathology Diagnosis			
	Sensitivity	Specificity	PPV	NPV
Non Proliferative Breast Disease	100.0	97.5	90.9%	100.0 %
Proliferative Breast Disease Without Atypia	95.5	100.0	100.0 %	96.6%
Proliferative Breast Disease With Atypia	100.0	100.0	100.0%	100.0%
Carcinoma	100.0	100.0	100.0%	100.0%

4. Discussion

The risk of developing subsequent invasive breast carcinoma is stratified according to the degree of epithelial proliferation and atypia. [13, 14]

It is important to delineate the various proliferative breast lesions, due to differences in the risk for development of carcinoma and for managements. Proliferative breast lesions on cytology are categorized into PBD without atypia and PBD with atypia because it is not possible to delineate and classify various histologic entities on FNAC. [16]

The categorization of proliferative breast lesions by FNA remains a challenge and the cytologic criteria need to be further defined and assessed.

Decreasing the number of diagnostic categories is likely to improve the correlation between the cytologic and histologic diagnosis. [15]

A number of articles have been published on the cytology of PBD, taking cytological and nuclear features into consideration, such as those of Masood *et al*[20], Sneige *et al*[18], Frost *et al*[19], Thomas *et al*[20]. Of these, we have studied the criteria put forth by Masood *et al*. [17]

In this study, we have assessed the six cytological parameters proposed by Masood *et al*[17], which was useful for cytological scoring of breast lesions. To increase the accuracy of various category of breast lesion, the scoring index given by Masood was modified. NPBD, which had score of 6 -10, was modified to score of 6-8 with shift of score 9 and 10 to PBD without atypia, i.e. score 11-14 was modified to score of 9-14 in MMSI.

Overall, a complete concordance between histological diagnosis and diagnosis by Modified Masood Scoring Index (MMSI) was observed in 49/50 cases (98.0%). In the study done by Mridha *et al*[16], complete concordance between histopathology diagnosis and Modified Masood scoring system was observed in 47/62 cases (75.8%).

Nandini *et al*[21] observed overall concordance of 93/94 cases (98.93%) between MMSI and histopathology

diagnosis which was similar to our present study with a concordance of 49/50 cases (98.0%).

In our present study 39/50 cases (78.0%) with cytological diagnosis correctly correlated with histopathology classification which was similar to observation noticed by Nandini *et al*[21] 73/94 cases (77.65%).

Kim *et al*[22] evaluated the scoring system of Masood to diagnose the breast lesion, and to sub-classify the benign breast disease. Application of scoring system had made accurate diagnosis in the all benign cases in their study which was similar to the present study. While 37 out of 61 malignant cases were correctly diagnosed by the scoring system with sensitivity and specificity of the test were 60.6% and 100.0% respectively in the study done by Kim *et al*. [22] But in our present study MMSI correctly placed the all 17 cases of carcinoma into the category with sensitivity and specificity were 100.0% and 100.0% respectively.

In the study done by Mridha *et al*[16] found that application of scoring system in a stepwise manner after cytological assessment of proliferative breast disease without atypia and carcinoma, scoring system offers no advantage over cytomorphology. There was no need to apply a laborious scoring system to these diagnostic groups, although routine application is valuable as a training exercise. Although with above results Mirdha *et al*[16] observed that scoring system was useful in aspirates with cytological diagnosis of proliferative breast disease with atypia, as it helps in separating out a proportion of non-atypical cases, improving the diagnostic efficiency of subsequent biopsy. However in our present study Modified Masood scoring index was found to useful, easily reproducible scoring method of breast lesions as it has improved the diagnostic accuracy of non-proliferative breast disease and proliferative breast disease without atypia.

Few architectural features were consistently observed in cases of PBD. It includes three-dimensional epithelial clusters, swirling or streaming of intraluminal cells and peripheral, slit-like irregular spaces or lumens. A

few workers like Sneige and Staerke[18] compared architectural features in FNAC of ductal hyperplasia and ductal carcinoma in situ, and also applied the cytological scoring system of Masood's. Even though Sneige and Staerke[18] concluded that architectural features were more useful for diagnosis of PBD, we found in the present study cytological and nuclear features provided significant role to categorize PBD in FNAC aspirates.

There are relatively few features that reliably allow the distinction of PBD from NPBD. Frost A.R. *et al*[23] found that only the presence of swirling pattern reached statistical significance in distinguishing the proliferative breast lesions from NPBD. The identification of PBD without atypia is cytologically limited. In our present study using Modified Masood criteria there were limited cytological features which allowed us to distinguish these breast lesions.

PBD with atypia is important to identify, as it almost leads to malignancy and there are cytological features which overlap between PBD without atypia, PBD with atypia and low grade carcinoma of breast.[11,18,19] Besides cytological and architectural findings, few authors[11,19] found that six parameters of MMSI have helped in diagnosis of these cases, as it was observed in one case in the present study. The case was diagnosed as PBD with atypia on FNAC, but on MMSI and histopathology, it came out as carcinoma in situ.

Sixteen (16) cases were diagnosed as carcinoma by FNAC. So in this category application of MMSI correctly categorized 17 cases of carcinoma. Various methods of cytological and nuclear grading of breast carcinoma have been advocated by Zajdela *et al*[24], Layfield *et al*[25], Black *et al*[26] and Robinsons[27]. MMSI can be compared with Robinson's grading system as both have cellular and nuclear features for grading the breast carcinoma.

Four (4) cases were not included in our study as these cases were of inflammatory lesion of breast which falsely increases the scoring due to nuclear atypia. Limitations were observed in implementation of Masood scoring system and MMSI due to inflammation.

Sneige *et al*[18] have found poor diagnostic reproducibility of the scoring system given by Masood *et al* with frequent under-diagnosis as well as over-diagnosis of the breast lesions. This observation has been supported by the study of Sidawy *et al*[15] as well. There is only limited report where usefulness of Masood scoring system has been tested.

In our study Masood's scoring system was tested with slightly modification (MMSI) by shifting score 9 and 10 from NPBD to PBD without atypia to increase the diagnostic accuracy. Application of scoring system in our

study evaluated both the nuclear atypia as well as restored a balanced view giving emphasis to cytoarchitectural details.

5. Conclusion

FNAC of breast is highly sensitive and specific modality for distinguishing benign and malignant lesions but its role in diagnosing proliferative breast lesions is debatable. MMSI can be applied on FNAC aspirates in stepwise manner after cytomorphological assessment to improve diagnostic accuracy of PBD without atypia.

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