Abstract

Context: Cytological assessment using various morphological parameters helps segregate breast lesions in fine-needle aspiration cytology (FNAC) into different categories. The prognosis and the line of management of each category differ accordingly. Aims: This study aims at assessing the validity of Modified Masood’s Scoring Index (MMSI) by the evaluation of cytomorphological features of various breast lesions compared with histopathological findings. Settings and Design: This is a cross-sectional study done in 65 female patients with palpable or nonpalpable breast lesions, undergoing FNAC and biopsy over a period of 18 months from December 1, 2012, to May 31, 2014. Materials and Methods: MMSI categorizes breast lesions, based on six cytological parameters into different categories such as nonproliferative breast disease (NPBD), proliferative breast disease (PBD) without atypia, PBD with atypia, and malignancy. The findings are compared with gold standard histopathological diagnosis. Statistical Analysis Used: Percentage of agreement, Kappa statistics, and Chi-square test. Results: Of the total 65 cases, all cases in MMSI category I and IV showed good histopathological correlation. The agreement between MMSI and histopathology was 93.8% which is more when compared with 72.3% agreement between cytology without scoring and histopathology. MMSI has increased the diagnostic accuracy of FNAC to 93.8% from 80%. Conclusion: The scoring system is easily reproducible, simple, and reliable. MMSI proved good histopathological correlation in category I and IV. This scoring technique has clearly demarcated those cases requiring surgical management. It is applicable for palpable and nonpalpable cases.

Key words: Breast lesions, fine-needle aspiration cytology, Modified Masood’s Scoring Index

Introduction

Fine-needle aspiration cytology (FNAC) technique presently has gained wide recognition, as a simple diagnostic procedure. It has largely replaced open biopsy and frozen section techniques for primary diagnosis of breast masses. Therefore, in many cases, definitive treatment can be planned in advance, preoperatively.

FNAC of breast lesions began as a screening procedure to distinguish benign from malignant conditions. For a breast FNA to be successful, it is important that the rates of equivocal and inadequate cytological diagnoses are low. The “gray zone” in breast FNAC includes a broad spectrum ranging from proliferative fibrocystic disease to sclerosing adenosis to malignancy.[1] Previous studies reported a gray zone incidence of 6.9%–20%.[2] All equivocal cases undergo excision biopsy, hence diagnosing a gray zone pathology by FNAC as atypical causes no delay in the treatment.

Cytological assessment helps segregate those cases where excision biopsy and detailed histological study are indicated. It avoids unnecessary biopsy in a majority of cases. A single morphological feature cannot be relied upon to distinguish malignant cells from benign, be it at any site.[1] So Masood introduced a Scoring Index that categorizes breast lesions, based on six various cytological parameters, into different groups such as category I – nonproliferative breast disease (NPBD), category II – proliferative breast disease (PBD) without atypia, category III – proliferative breast disease (PBD) without atypia, category IV – malignancy.[3] This Masood’s Scoring Index has a role in

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the diagnosis of palpable breast lesions in the initial method of pathological assessment.

Nandini et al.\(^4\) made an attempt to modify it, by rearranging scores of category I and II allowing more precise diagnosis, as the prognosis of both the categories differs significantly. This modified scoring system is named as Modified Masood’s Scoring Index (MMSI).

This study aims at assessing the validity of MMSI by the evaluation of cytomorphological features of various breast lesions compared with histopathological findings. It is presumed that this scoring will increase diagnostic accuracy in palpable and nonpalpable cases. Fast and accurate preoperative diagnosis is essential as the treatment strategies and prognosis of individual patients can be decided accordingly.

**MATERIALS AND METHODS**

This is a cross-sectional study done over a period of 18 months from December 1, 2012, to May 31, 2014, in the cytology and radiology departments of the institute. All patients who underwent FNAC for palpable or nonpalpable breast lumps, followed by biopsy (either trucut or excisional surgery, depending on the diagnosis at aspiration cytology) and those aspirates with adequate material were included in this study; based on inclusion and exclusion criteria.

An informed and written consent was obtained from all the study subjects. FNAC was performed by following standard technique from all palpable lesions, using 23-G needle, fixed to a 10-mL syringe. For nonpalpable lesions, FNA was performed with ultrasound (USG) guidance, in conjunction with expertise of radiologists. The aspirate was expressed on two to three clean dry glass slides and smeared using a coverslip.

Smears were immediately fixed in 80% isopropyl alcohol (fixative) in a coplin jar. “Toluidine blue” stain was used to confirm the adequacy of the sample. FNAC was repeated one more time, if smears were inadequate. The slides were subsequently stained with Papanicolaou (Pap) stain as routine.

Criteria for adequacy were the presence of four or five clusters of ductal epithelial cells, each made up of five to six cells with presence of bare nuclei in the background.

The smears were scored based on MMSI which includes six different cytological parameters, namely, cellular arrangement, cellular pleomorphism, presence of myoepithelial cells, nucleoli, anisonucleosis, and pattern of chromatin. The values ranging from 1 to 4 were assigned to each of the parameters and lesions were scored by adding up the values. Based on the scores, breast lesions were grouped into four categories as given in Table 1. The minimum score is 6; score ranging from 6 to 8 is given a cytologic diagnosis of NPBD; proliferative disease without atypia is diagnosed with a total score ranging from 9 to 14; proliferative breast disease with atypia is reported when the total score ranges from 15 to 18; a cytologic diagnosis of malignancy is made when the total score ranges from 19 to 24.

**Statistical analysis**

The data were entered in Microsoft Excel programme and analyzed. The categorical data were analyzed and presented as frequencies and percentages. Age and total score were presented as mean and standard deviation (SD). The findings of MMSI, cytology, and histopathology were compared using percentage of agreement, Kappa statistics, and Chi-square test. The findings of MMSI, cytology, and histopathology were grouped as malignant versus non-malignant. The sensitivity, specificity, predictive values, and diagnostic accuracy were found for MMSI and cytology using histopathological diagnosis as gold standard.

**RESULTS**

A total number of 136 patients underwent FNAC during the study period of 18 months. A total of 65 cases eligible according to the inclusion and exclusion criteria were selected for the study.

The study subjects were females in the age range of 16–93 years with a mean age of 47.91 years (SD = 17.535). The maximum number of cases (35%) were in the age group of 41–60 years. The majority of the patients presented with a palpable lump in the breast.

### Table 1: Modified Masood’s Scoring Index

| Cellular arrangement  | Cellular pleomorphism | Myoepithelial cells | Anisonucleosis | Nucleoli | Chromatin clumping | Score |
|-----------------------|-----------------------|---------------------|----------------|----------|-------------------|-------|
| Monolayer             | Absent                | Many                | Absent         | Absent   | Absent            | 1     |
| Nuclear overlapping   | Mild                  | Moderate            | Mild           | Micronucleoli | Rare             | 2     |
| Clustering            | Moderate              | Few                 | Moderate       | Micro and/or rare macronucleoli | Occasional | 3     |
| Loss of cohesion      | Conspicuous           | Absent              | Conspicuous    | Predominantly macronucleoli | Frequent   | 4     |

| MMSI category                  | Total score |
|---------------------------------|-------------|
| I Nonproliferative breast disease | 6-8         |
| II Proliferative breast disease without atypia | 9-14        |
| III Proliferative breast disease with atypia | 15-18       |
| IV Carcinoma in situ and invasive cancer | 19-24       |
Most of the breast lumps were right-sided (58.6%). A unilateral breast lump was noted in a majority of the cases (93.8%). Only 9.2% of patients presented with multiple breast lumps. Irrespective of the side, the maximum number of lumps palpated in one particular quadrant was in superior lateral quadrant (49.3%). The majority of the breast lumps requested for FNAC were <3 cm in size (72.3%), non-tender (92.3%), and were firm in consistency (69.2%). About 7.7% of cases included in the study were USG-guided.

MMSI was done for all the cytology cases based on six parameters. A total score ranging from 6 to 23 was obtained during the study with a mean of 13.06 (SD = 6.100).

The categories of MMSI were compared with histopathological diagnosis which is the gold standard and are given in Table 2.

Category I had a maximum number of cases (47.7%). All the cases were benign on follow-up biopsy. Out of 31 cases, 29 were fibroadenomas and two reported as phyllodes tumor.

Category II had three cases (4.6%). On biopsy, one was epithelial proliferative lesion and the other two were low-grade carcinomas with in situ areas. Low cellularity, cohesiveness, mild to moderate atypia, and presence of bare nuclei can be attributed to underscoring of these cases.

Category III had two cases (3.1%). Both were reported as low-grade infiltrating ductal carcinoma on histopathology.

Thus, all the cases in MMSI category I and IV showed 100% histopathology correlation which forms the major population (92.3%) in our study. The agreement between MMSI and histopathological diagnosis was 93.8%. Kappa could not be done as there was no histopathology case corresponding to category 3 of MMSI.

The agreement between MMSI and cytology was 76.9%. Kappa = 0.65 which indicates good agreement between MMSI and cytology. The cytology diagnosis without scoring was also compared with histopathology. The agreement between cytology and histopathology diagnosis was 72.3%. Kappa could not be done due to lack of category 3 case in histopathology. The percentage of agreement for cytology alone (72.3%) was less compared with MMSI (93.8%). The overall results of 65 FNAC cases included in the study are shown in Table 3. Of 33 carcinoma cases, MMSI could correctly diagnose 29 cases.

The overall sensitivity, specificity, diagnostic accuracy, positive predictive value (PPV), and negative predictive value (NPV) of MMSI were 87.9%, 100%, 93.8%, 100%, and 88.8%, respectively. For cytology diagnosis without scoring, the corresponding values were 60.6%, 100%, 80%, 100%, and 71%. The advantages of scoring include increased diagnostic accuracy and no false-positive (FP) cases of malignancy.

### Table 2: Comparison of MMSI vs histopathological diagnosis

| Groups | MMSI | Histopathological diagnosis | Total |
|--------|------|-----------------------------|-------|
|        | CA   | NPBD | PBD without atypia |       |
| 1      | 0    | 31   | 0 | 31 |
| 2      | 2    | 0    | 1 | 3  |
| 3      | 2    | 0    | 0 | 2  |
| 4      | 29   | 0    | 0 | 29 |
| Total  | 33   | 31   | 1 | 65 |

MMSI, Modified Masood’s Scoring Index; NPBD, nonproliferative breast disease; BPD, proliferative breast disease

### Table 3: Comparison of MMSI with cytological and histopathological diagnosis

| Groups | Category | MMSI | Cytology | Histopathology |
|--------|----------|------|----------|----------------|
| 1      | NPBD     | 31   | 26       | 31             |
| 2      | PBD without atypia | 3   | 18       | 1              |
| 3      | PBD with atypia | 2   | 1        | 0              |
| 4      | CA       | 29   | 20       | 33             |
| Total  | 65       | 65   | 65       | 65             |

MMSI, Modified Masood’s Scoring Index; NPBD, nonproliferative breast disease; PBD, proliferative breast disease

### Discussion

The reliability of FNAC in separating benign from malignant lesions is well established. However, there are limited data regarding its ability to demarcate proliferative lesions with and without atypia and ductal carcinoma in situ (DCIS) by morphology alone. It is reported that NPBD carries no increased risk of carcinoma breast in future. The risk is 1.5–2 fold in women with proliferative lesions without atypia, 4–5 fold in women with proliferative lesions with atypia, and 8–10 fold in women with DCIS.[8-10] Therefore, it is necessary that an accurate diagnosis should be made on cytology.

MCI[3] categorizes all breast lesions into four categories, namely, NPBD, PBD without atypia, PBD with atypia, and carcinoma. The MMSI[4] further increased the diagnostic accuracy by rearranging scores of category I and II.

Among the 71 cases excluded from the study, cytology smears are inadequate in 35 cases and 16 of them are cystic lesions. The inadequate sample rate in this study is 30%. This falls within the upper aspect of a very wide range of nondiagnostic rates (<1%–32%).[8-10]

Inadequate FNA is likely related to lesion characteristics especially low cellularity and marked fibrosis or due to technical issues. Therefore, aspirator experience, USG guidance, and immediate cytological assessment with additional repeated aspirates attempted are needed to reduce the percentage of inadequate samples. Inflammatory lesions (nine cases) are excluded from the study since nuclear atypia falsely raises the score as reported in similar previous studies.[8]
Therefore, 65 female patients who underwent FNAC for breast lumps, followed by biopsy either trucut or excisional surgery, depending on the diagnosis at aspiration cytology are included in this study based on inclusion and exclusion criteria. All the FNAC lesions included in the study are grouped into four categories based on MMSI are as follows:

**Nonproliferative breast disease (category I)**
Cytological features of this group include monolayering of uniform sized cells, absent/mild pleomorphism of cells, and presence of numerous myoepithelial cells. Nuclear features include absence of anisonucleosis, nucleoli, and chromatin clumping. This group is characterized by loss of cohesiveness, high cellularity, conspicuous nuclear pleomorphism and anisonucleosis, occasional macronucleoli, and frequent chromatin clumping [Figure 1a]. In most of the cases, fibromyxoid stroma is seen in the background.

In all, 31 cases (47.7%) in this study belong to this category. A majority of them are fibroadenomas (29 cases) and 2 reported as phyllodes tumor. Four had associated fibrocystic change. Therefore, all cases correlated with histopathological diagnosis. This confirms the accuracy of MMSI by Nandini et al.,[4] who modified the NPBD score as 6–8 instead of 6–10.

**Proliferative breast disease without atypia (category II)**
Cytological features in this group include moderate cellularity, mild cellular pleomorphism, and moderate number of myoepithelial cells [Figure 1b]. Mild nuclear overlapping with occasional micronucleoli and chromatin clumping.

Three cases (4.6%) diagnosed by scoring are included in this category, of which one is epithelial proliferative lesion and the other two are carcinomas on histopathology. This finding is in contrast to other studies by Nandini et al.,[4] and Masood et al.,[11] as no case of carcinoma is reported in this category on histopathology follow-up in their studies.

**Proliferative breast disease with atypia (category III)**
This group had the least number of cases (3.1%) and had cytomorphologic features that overlap with carcinoma. The cytological features include moderate to high cellularity, moderate degree of cellular pleomorphism and anisonucleosis, occasional macronucleoli, and frequent chromatin clumping [Figure 1c]. Both the cases are signed out as low-grade infiltrating duct carcinoma in histopathology.

Although the number of cases in this category is very few in our study, there is greater chance of them to be malignant on histopathology follow-up. Previous studies have also reported that about 30%–45% of breast FNA cases diagnosed as atypical turned out to be malignant on surgical follow-up.[12-15] Therefore, it is important to identify this category and refer them for excision biopsy.

Zhao et al.,[16] observed that 37% of the cases diagnosed cytologically as PBD with atypia turned out to be malignant on histopathology. They suggested that cytological features are not enough to be diagnosed as malignancy including low cellularity, mild atypia, and obvious myoepithelial cells in the background, as in our case.

**Carcinoma in situ and invasive cancer (category IV)**
This group is characterized by loss of cohesiveness, high cellularity, conspicuous nuclear pleomorphism, chromatin clumping with macronucleoli, and absence of myoepithelial cells. [Figure 1d].

Cases diagnosed by scoring in this category are 29 (44.6%). All the cases correlated with histopathology. The concordance rate is similar compared to a previous study by Nandini et al.,[4]

Of 14 USG-guided FNAC cases during the period, only 5 are included for analysis. A high degree of concordance is noted between MMSI scoring and histopathology in all these cases. Inadequate aspirate was obtained in six of the cases.

Inadequacy rate for USG-guided FNAC is 42.8%. This can be attributed partly to technical issues as the procedure is routinely performed in our institution by a radiologist rather than a cytopathologist. The intrinsic nature of the lump (smaller size/ slippery) also contributes. Perry[17] recommended a minimum standard of <25% as insufficient result, in image-guided FNAC procedures.

**Diagnostic accuracy of MMSI**
Of the 33 histologically confirmed carcinoma in the study, 29 belonged to MMSI category IV, 2 cases scored as category III, and another 2 cases as category II. The overall diagnostic accuracy, sensitivity, and specificity of MMSI in diagnosing malignant breast lesions are determined to be 93.8%, 87.9%, and 100%, respectively.
Masood et al.\cite{11} evaluated MCI in fine needle biopsy (FNB) of nonpalpable breast lesions obtained by standard needle localization under mammographic guidance. Sufficient aspirated material was obtained in 91% which is superior to our technique. There is no FP diagnosis of malignancy and 3.3% of false-negative (FN) cases included carcinoma in situ. The overall diagnostic accuracy is similar to our study.

There are no FP cases in the study. Only four cases are (FN) by scoring. All of them are low-grade breast carcinomas (one case of papillary carcinoma, another case of intraductal carcinoma with mucinous differentiation, and two cases of infiltrating duct carcinoma, BRG 1). They are scored as category 2 or 3 because of low cellularity, cohesiveness, mild to moderate atypia, and bare nuclei in the background.

In papillary lesions with moderate cytological atypia, excision is advised since the findings are insufficient for a conclusive diagnosis of malignancy. Similarly, in a study comparing USG and FNAC by Takhellambam et al.,\cite{21} one case of “papillary lesion” reported by cytopathologist turned out to be DCIS with solid and micropapillary patterns on histology. In such situations, it is safer for the patient to undergo further workup by CNB, excision biopsy, or even frozen section biopsy rather than giving an FN diagnosis.

According to the UK-NHSBSP,\cite{19} the suggested thresholds for cytology performance (where therapy is partially based on FNAC) are the following: absolute sensitivity (C5 only) >70%, specificity >65%, PPV >99%, FN <4%, FP <0.5%, inadequate rate <15%, inadequate rate from cancers <5%, and suspicious rate <15%. Thus with MMSI, the sensitivity of breast FNA (87.9%) could be raised to the recommended UK NHSBSP guidelines, thereby allowing therapy based on FNAC. However, the FN rate (12.1% against <4%) and inadequacy rate (30% against <15%) are higher.

The higher percentage of malignancy on follow-up histopathology (100%) for atypical category in MMSI when compared with previous studies could be explained by the limited number of cases (3.1%) in that category.

This study showed 100% histopathology correlation in category I and IV. A 100% cyto-histopathological correlation is observed with cytology alone in other studies by Panjvani et al.,\cite{20} Qin et al.,\cite{21} Mohammad et al.,\cite{22} and Tiwari.\cite{23} In contrast, our study showed an FN rate of 12.1% for malignant cases with scoring which is comparatively less than for cytology alone (FN 39.3%). This is because of greater proportion of low-grade malignancy in our study population.

A recent study\cite{24} proposing expansion of Masood’s cytologic index (MCI) for carcinoma group into further subtypes based on selected cytological features showed 86% concordance with histopathological (Bloom–Richardson) grading. They observed that features such as anisonucleosis, nucleoli, and chromatin pattern had significant role in further grading category IV by scoring. Thus, the expanded MCI will help the cytopathologist to classify benign breast lesions into different categories and grade malignant breast lesions.

**Conclusion**

MMSI showed a diagnostic accuracy of 93.8% in comparison to cytology alone wherein 80% could only be obtained. MMSI proved 100% histopathology correlation in category I and IV. In category II and III, scoring technique has clearly demarcated the cases requiring surgical management. The study showed that nonpalpable cases can also be diagnosed with reasonable certainty by MMSI scoring.

Further subtyping of category IV similar to Modified Bloom–Richardson grading in histopathology would be done for preoperative grading of carcinoma, to decide on neoadjuvant chemotherapy, with a minimally invasive procedure.

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**Conflicts of interest**

There are no conflicts of interest.

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