



COMPARISON OF TWO CYTOLOGICAL GRADING SYSTEMS FOR BREAST CARCINOMA ON FNAC AND THEIR HISTOLOGICAL CORRELATION

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ABSTRACT **Introduction:** Carcinoma of the breast is one of the most common malignancy in women. Fine needle aspiration (FNA) is increasingly being used to determine various prognostic parameters in patients with breast mass. Cytological grading should be part of all FNA reports of breast carcinoma so that preoperative prognostication could be done. This study was undertaken to compare results of two cytological grading methods to see which corresponded better with the histological grade. **Materials and Methods:** The present study was conducted in the Department of Pathology, Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly for a period of two years. Breast lumps, diagnosed as infiltrating ductal carcinoma on FNAC and histopathology were assessed with regard to age, laterality, quadrant involved, size of the tumor, presenting symptoms, distribution of cases according to Robinson, Mouriquand and Nottingham grading. **Results and Conclusion:** This study included a total of 80 cases of infiltrating ductal carcinoma of the breast. Robinson's cytological grade II was most common grade in the present study comprising 50 cases (62.50%). In the present study grade II was observed in maximum number of cases in Mouriquand's cytological grading constituting 45 cases (56.25%). The concordance between Robinson's cytological grading and Nottingham modification of Bloom Richardson histological grading was 87.50%. The sensitivity of Robinson's cytological grade was 90.40% and Mouriquand's cytological grade was 94.23% respectively

KEYWORDS : BREAST CARCINOMA, FNAC, ROBINSON'S, MOURIQUAND'S

1. Introduction

In India, Breast cancer is generally diagnosed at a relatively advanced stage, because of lack of awareness, general indifference towards the health of females in the Indian society, lack of national breast cancer screening program and paucity of diagnostic aids, majority of the breast cancers are diagnosed at a relatively advanced stage.^{1,3}

FNAC is reliable method to diagnose any palpable masses of the breast. Cytological grading has been observed to hold concordance of 66-76% with histological grading. It is cheaper, fast, minimally invasive, multiple sampling of the lesion simultaneously, yield good result on same day as compared with core needle biopsy of breast.^{2,6}

The histological grading proposed by Nottingham modification of Bloom-Richardson (BR) method for breast carcinoma is widely accepted tumor grading system and it is useful, sensitive guide for selecting neoadjuvant therapy and has been found to have a good prognostic correlation.^{3,7}

In this study we evaluate cytological grading systems and correlated with BR method to determine best cytological grading scheme correspond to the histologic grading of breast carcinoma and its role in prognosis of therapy. Of the different cytological grading methods corresponding to Nottingham modification of Bloom Richardson histologic grading, the method described by Robinson et al was found to be useful in grading breast carcinoma in FNA.⁹ Mouriquand's grading method¹⁰ also corresponded to Nottingham modification of Bloom Richardson's grading system and shown to have good prognostic correlation.⁸

The present study is conducted to grade breast carcinomas in FNA smears by two cytological grading methods mentioned above to determine which of these two methods are more accurate to predict histological grade (gold standard) in infiltrating ductal carcinoma of breast.⁴

2. Materials and Methods

80 cases of breast lumps diagnosed as infiltrating ductal carcinoma of breast in department of pathology, SRMS IMS on FNAC and histopathology were retrospectively reviewed from December 2020 to August 2022. Representative smears from breast lumps are stained with MGG and PAP. Submitted sections for histopathology were stained with H & E. The pathological features assessed with regard to age, laterality, quadrant involved, size of the tumor, presenting symptoms, distribution of cases according to Robinson, Mouriquand

and Nottingham grading. Cytological grading of tumors was done based on Robinson and Mouriquand grading systems. Histopathological grading of tumors was done using Nottingham modification of Bloom Richardson's grading system.

INCLUSION CRITERIA:

1. Female patients with palpable breast mass who undergone FNAC and diagnosed as invasive ductal carcinoma and subsequently underwent surgical resection were included in the study.
2. Patients who have confirmed diagnosis of invasive ductal carcinoma in cytological and histological specimens.

EXCLUSION CRITERIA :

1. Known cases of invasive duct carcinoma of breast who have received chemotherapy or radiotherapy.
2. Male patients with ductal carcinoma of breast.

In the Robinson's grading system six different cytological parameters namely cell dissociation, cell size, cell uniformity, nucleolus, nuclear margin and nuclear chromatin are used to grade the tumors. A score of 1-3 will be given to each of these parameters and the tumors will be graded by adding up the scores. Cancers scored in the range of 6-11 will be graded as I, score of 12-14 will be graded as II, and score ranging from 15-18 will be graded as III.

In the Mouriquand's method, a score of 0-3 will be given to different cellular characters, nuclear features, nucleolus and mitosis. The tumors will be graded I if the combined score will be < or = 5, graded II for a score ranging from 6 to 9, and grade III if the score will be > or = 10.

Nottingham modification of Bloom Richardson histological grading, a score of 1-3 will be given to tubular formation, nuclear pleomorphism and mitosis. The tumors will be graded as: Grade I – (Well differentiated) 3-5, Grade II – (moderately differentiated) 6-7, Grade III – (poorly differentiated) 8-9.

3. RESULTS

In the present study, a total number of 80 cases of breast carcinoma were included. The tumor was typed, graded and evaluated for two cytological grading system Robinson's and Mouriquand's to histological grades of infiltrating ductal carcinoma. When malignant cells were examined within six distinct parameters (nuclear pleomorphism, presence of multiple nucleoli, mitoses, nuclear

margins, tubular formation and cellularity), we observed correlation between different cytological grading and histological grades.

A total number of 80 cases, who undergone FNAC for infiltrating ductal carcinoma and subsequently underwent surgical resection were included in the study. All of the cases were of female, no single case in male was included in study. The results of the study are as follows.

Out of 80 cases maximum cases (40%) were in the age group of 41-50 years, followed by (27.50%) of age group 31-40 years. The youngest patient was 26 years in age and the oldest was 70 years old.

Out of 80 cases infiltrating ductal carcinoma involved right side of breast in 50 cases (62.5%) and left side of breast in 30 cases (37.50%). As most common clinical presentation of breast carcinoma is palpable lump. Maximum 42 cases (52.5%) presented with only lump in breast followed by 20 cases (25.0%) presented with painful lump. 10 cases (12.50%) presented with ulcerated lump while only 8 (10%) cases presented with lump with nipple discharge.

In the present study as observed, in maximum cases 56 (70%) tumor size was 2 to 5 cm followed by more than 5 cm was in by 22 (27.50%) cases and in only 2 (2.50%) cases size was less than 2 cm.

Table 1 : Distribution of cases according to Robinson's grading

Grade	No. of cases	Percentage
Grade I	19	23.75%
Grade II	50	62.50%
Grade III	11	13.75%
Total	80	100%

Table 2 : Distribution of cases according to Mouriquand's grading

Grade	No.of cases	Percentage
Grade I	05	6.25%
Grade II	45	56.25%
Grade III	30	37.50%
Total	80	100%

By Robinson's cytological grading out of 80 cases, majority of cases belong to grade II (62.50%) with 50 cases, followed by grade I (23.75%) with 19 cases and grade III (13.75%) with 11 cases.

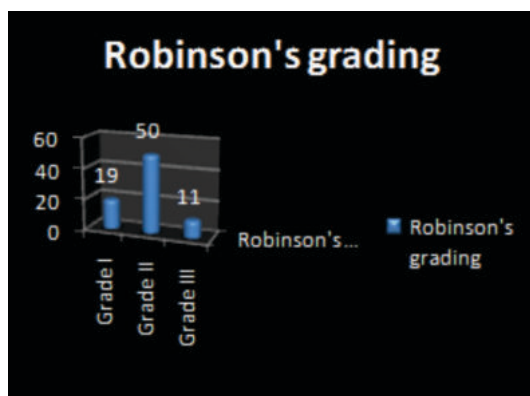


Figure 1 : Distribution of cases according to Robinson's grading

By Mouriquand's grading, out of 80 cases, 45 cases (56.25%) were grade II, 5 cases (6.25%) were grade III and 30 cases (37.50%) were grade I

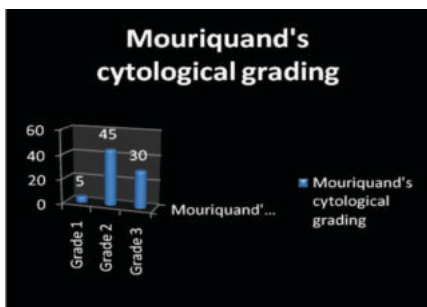


Figure 2 : Distribution of cases according to Mouriquand's grading

Table 3: Distribution of cases according to Histological grading(Nottingham's Grading)

GRADE	TOTAL SCORE	NUMBER OF CASES	PERCENTAGE
Grade 1	3-5	14	17.5%
Grade2	6-7	58	72.5%
Grade3	8-9	08	10.0%

Out of 80 cases which were graded on criteria of percentage of tubule formation, cellular pleomorphism, and mitotic count as per Nottingham's grading, 58 cases (72.5%) were of grade 2 with score 6-7 followed by 14 cases (17.5%) of grade 1 with score 3-5. Only 08 cases (10%) cases were grade 3 with score 8-9 as shown in table.

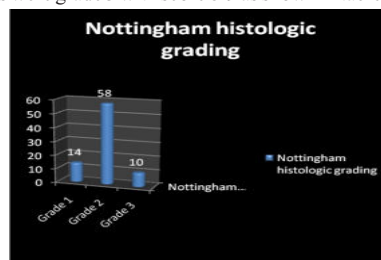


Table 4 : Comparison of cytological grading by Robinson's and Mouriquand's methods

Robinson's grading	Mouriquand's grading			Concordance	
	I	II	III		
I	19(23.75%)	05	14	00	47/80 (58.75%)
II	50 (62.50%)	0	31	19	
III	11 (13.75%)	00	00	11	
Total	80	05	45	30	

Of the 19 grade I cases by Robinson's method, only 5 were graded as grade I. Of the 11 grade III cases by Robinson's method, 11 were graded as grade III. Of the 50 grade II cases by Robinson's method, 31 were graded as grade II, whereas 19 cases were overgraded as grade III by Mouriquand's method. The concordance rate in grading by Robinson's and Mouriquand's method was obtained in 47 (58.75%) of the 80 patients as shown in table

Table 5: Correlation of Nottingham modification of Scarf-Bloom Richardson's method on histopathology with two cytological nuclear grading methods

Histopathology grade	Robinson's grading			Concordance rate(%)	Mouriquand's grading			Concordance rate (%)
	I	II	III		I	II	III	
I (n=14)	13 (92.80%)	01	-	70/80 (87.50%)	04 (26.67%)	-	10	53/80 (66.25%)
II (n=58)	06	49 (84.5%)	03		01	43 (74.13%)	14	
III (n=08)	-	-	08 (100%)		-	02	06 (75.00%)	
Total (n=80)	19	50	11		05	45	30	

Table 5 illustrate the correlation of Nottingham modification of Bloom Richardson's method on histopathology with two cytological nuclear grading methods. Out of 14 cases that had been judged histopathologically to be grade I, 13 (92.80%) cases were found to be grade I by Robinson's method contrasting only 04 (26.67%) cases by Mouriquand's method. Among the grade II tumors, the cytohistological correlation was seen in 84.50% & 74.13% cases by Robinson's & Mouriquand's methods. Best correlation was observed in grade III ;100% cases of the Robinson's and 75.00% cases of Mouriquand's methods were correlated by Nottingham modification of Bloom Richardson's grading system. In order to statistically evaluate that which of the two cytological grading methods corresponds better to histological grading system, grade I cases were considered as low grade and grade II and III together as high grade in both cytological & histological grading system.

Table 6 : Parameters for both grading methods

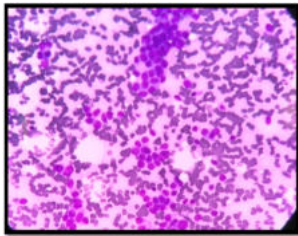
Statistical parameter	Robinson's cytological grade	Mouriquand's cytological grade
TP	57	49
FP	04	24
TN	13	04
FN	06	03
Sensitivity	90.40%	94.23%
Specificity	76.40%	14.28%
PPV	93.45%	67.12%
NPV	59.10%	57.14%
Diagnostic accuracy	85.71%	66.25%

Robinson's and Mouriquand's cytological gradings have sensitivity of 90.40% and 94.23% and specificity 76.40% and 14.28% respectively. The diagnostic accuracy for Robinson and Mouriquand's cytological grading in present study was 85.71% and 66.25% respectively.

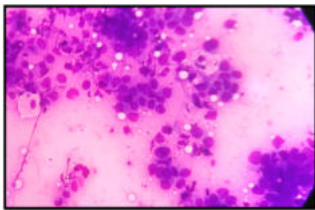
Table 7 : Kappa value for Robinson's and Mouriquand's grading

Grading system	Kappa statistics	SE of Kappa	95% of CI interval	Strength of agreement
Robinson's	0.632	0.103	0.439-0.845	Substantial
Mouriquand's	0.103	0.088	0.070-0.276	Slight

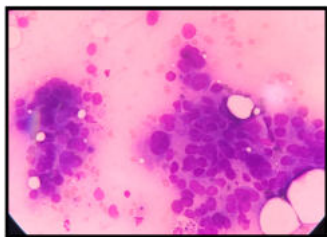
In the present study, the kappa values of agreement for Robinson's and Mouriquand's cytological gradings were $k=0.632$ (substantial) and 0.103 (slight) respectively.



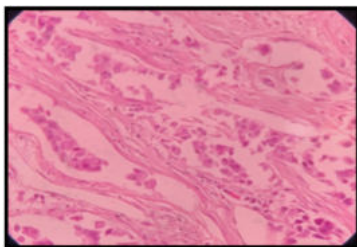
Photomicrograph 1 : Infiltrating Ductal Carcinoma, Grade I MGG (40X)



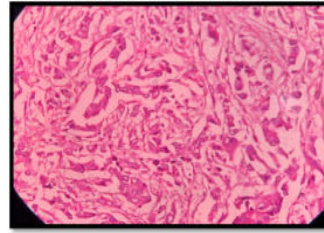
Photomicrograph 2 : Infiltrating Ductal Carcinoma, Grade II MGG (40X)



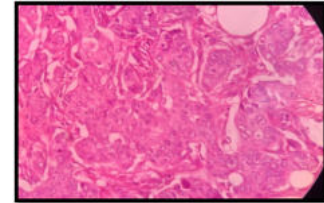
Photomicrograph 3 : Infiltrating Ductal Carcinoma, Grade III MGG (40X)



Photomicrograph 4 : Infiltrating Ductal Carcinoma, Grade I H&E (40X)



Photomicrograph 5 : Infiltrating Ductal Carcinoma, Grade II H&E (40X)



Photomicrograph 6 : Infiltrating Ductal Carcinoma, Grade III H&E (40X)

1. DISCUSSION

Breast carcinoma is no longer seen as a single disease but rather a multifaceted disease comprising of distinct biological subtypes with diverse natural history, presenting a varied spectrum of clinical, pathologic and molecular features with different prognostic and therapeutic implications.¹¹

A detectable breast lump, whether benign or malignant, is a cause of uneasiness to patient. Therefore precise pathological diagnosis is crucial for further investigation.¹²

In present study, age of the patients ranged from 26 to 70 years and maximum number of cases were between 41-50 years (40%), followed by 31-40 years (27.5%). Similar results was reported by Sheikhpour et al (44.74 ± 9.5 years)¹³ which was almost similar to present study. Majority of the patients were noticed by Bukhari et al¹⁴ that (26 cases, 34.67%) in 4th decade with the mean age being 51.61 years.

Breast lump in 50 (62.5%) cases lump were localized on right side while in 30 (37.50%) cases lump were localized on left side. This was in accordance with the study of Bukhari et al¹⁴ who showed that breast lumps were more common in the right breast (41 cases, 54.66%) compared to the left breast (34 cases, 45.33%).

Most common clinical presentation in breast carcinoma is palpable lump. Out of 80 cases maximum 42 cases (52.5%) presented with only lump in breast with ulcerated lump while only 8 (10%) cases presented with lump with nipple discharge. These findings are in accordance with the study of Raina V et al¹⁵ who also observed same concurrence as palpable lump was the main presenting symptom.

Tumor size was divided into three categories according to TNM classification system and observed that maximum cases 56 (70%) of tumor size 2 to 5 cms followed by 22 (27.50%) cases with size more than 5 cms and in only 2 (2.50%) cases size was less than 2 cms. Concurrence with the results was obtained by Neharika et al¹⁶ and Patnayak et al¹⁷ who found 53.9%, 63.9%, 67.7%, 79.6% cases of tumor size between 2-5 cm in their studies respectively.

Out of 80 cases of infiltrating breast cancer involved right upper outer quadrant of breast were 25 cases (31.25%), followed by right upper inner quadrant 14cases (17.50%), 4 cases (5.00%) were involved by right lower inner quadrant and (2.50%) cases by right lower outer quadrant. In left side breast left upper outer quadrant of breast were 15 cases (18.75%), followed by left upper inner quadrant 08 cases (10.00%), 2 cases (2.50%) were involved by left lower inner quadrant and 01 (1.25%) cases by right lower outer quadrant. Central compartment of both right and left side breast involved 5 cases (6.25%) and 4 cases (5.00%) respectively. Bukhari et al¹⁴ also observed upper outer quadrant was most commonly involved in 30% cases.

In this present study, Robinson's grading method showed the diagnostic accuracy of 85.71%, whereas 71.25% was established by Mouriquand's grading method. Pandya et al¹⁸ also observed similar

study regarding diagnostic accuracy of 90% in Robinson's grading system and 76.66% by Mouriquand's grading system.

TABLE 8 COMPARISON OF DIAGNOSTIC ACCURACY

Authors	Robinson's grading		Mouriquand's grading	
	Concordance	Discordance	Concordance	Discordance
Bukya et al	78.60%	21.40%	66.60%	33.30%
Saha et al	77.19%	22.81%	77.19%	22.18%
Pandey et al	83.33%	16.67%	66.60%	33.30%
Einstein et al	77.70%	22.30%	68.00%	32.00%
Present study	87.50%	12.50%	66.25%	33.75%

The sensitivity was 90.40% and 94.23% by Robinson's and Mouriquand's grading systems. However the specificity was low in Mouriquand's (14.28%) as compared to Robinson's method (76.40%). Pandya et al¹⁸ observed the sensitivity was 91.30% and 95.65% by both Robinson's and Mouriquand's method. The specificity by Robinson's method was 76.40% and by Mouriquand's method it was quite low 42.86%. Bukhari et al¹⁴ also reported Robinson's and Mouriquand's cytological grading system have high sensitivity of 94% and 80%, low specificity (43% and 37%)

Of the 19 grade I cases by Robinson's method, only 5 were graded as grade I by Mouriquand's method in the present study. Of the 11 grade III cases by Robinson's method, 11 were graded as grade III. Of the 50 grade II cases by Robinson's method, 31 were graded as grade II, whereas 19 cases were overgraded as grade III by Mouriquand's method. The concordance rate in grading by Robinson's and Mouriquand's methods was obtained in 47 (58.75%) of the 80 patients. The concordance observed by Bukhari et al¹⁴ observed between Robinson's and Mouriquand's cytological grading systems was 85%. Pandya et al¹⁸ and Wani et al¹⁹ reported high degree of concordance between both cytological grading systems were 76.66% and 73.25%.

5. CONCLUSION

The present study reveals that it is achievable to grade infiltrating ductal carcinoma of breast on fine needle aspiration and cytological grade correlates with histological Bloom Richardson histological grading. The Robinson's grading system had an edge over Mouriquand's grading because it is uncomplicated, simple, take little time and reproducible, depends on sample limitations, correlates exactly with Bloom Richardson histological grading method.

Mouriquand's grading	
Concordance	Discordance
66.60%	33.30%
77.19%	22.18%
66.60%	33.30%
68.00%	32.00%
66.25%	33.75%

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