



Original Article

Comparative Evaluation of Mouriquand's Cytological Grading System with Histopathological Grading in Carcinoma Breast

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ABSTRACT

Background: Cytological grading of breast carcinoma by fine needle aspiration cytology (FNAC) is an essential first-line diagnostic approach that facilitates early treatment planning, patient stratification for neoadjuvant chemotherapy, and prognostic risk assessment, particularly in resource-limited settings where excision biopsy may be delayed.

Aims: To evaluate cytological nuclear grading of breast carcinoma using Mouriquand's six-parameter scoring system and to correlate the results with the Modified Bloom Richardson Grading Score (MBRGS) as assessed on surgical histopathological specimens.

Materials and Methods: Seventy-seven consecutive patients (age range 23–80 years) presenting with a palpable breast lump and diagnosed as carcinoma breast on clinical examination were enrolled. FNAC smears were prepared using three staining techniques — May-Grünwald Giemsa (MGG), Papanicolaou (Pap), and Haematoxylin and Eosin (H&E) — and graded using Mouriquand's cytological criteria across six parameters. Corresponding histopathological specimens were graded using MBRGS (Elston–Ellis modification). Statistical concordance was assessed using Pearson's correlation coefficient, coefficient of determination, and Cohen's kappa statistic.

Results: The majority of tumours were classified as cytological grade II (61.0%) by Mouriquand's criteria, with a mean cytological grade of 2.1. On MBRGS, 42 cases (54.5%) were histopathological grade II. Overall concordance between cytological and histopathological grading was observed in 70 of 77 cases (90.9%), which was statistically significant ($p < 0.001$). The coefficient of correlation was $r = 0.75$ ($r^2 = 0.56$). Cohen's kappa was 0.879 (95% CI; SE = 0.068; $p < 0.001$), indicating near-perfect agreement. Diagnostic accuracy was 96.0%, with sensitivity of 99.1% and specificity of 82.4%. Nuclear shape, enlarged nucleoli, and cell size were the most predictive cytomorphological parameters on multiple regression analysis.

Conclusions: Mouriquand's cytological grading system demonstrates a high degree of concordance with MBRGS histopathological grading. Its routine application in FNAC practice is recommended, as it provides a reliable, cost-effective, and timely basis for neoadjuvant therapy selection and prognostication in breast carcinoma.

Keywords: breast carcinoma, FNAC, cytological grading, Mouriquand's grading system, Modified Bloom Richardson Grading Score, histopathological grading, neoadjuvant chemotherapy.

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INTRODUCTION

Breast carcinoma is the most frequently diagnosed malignancy in women worldwide and the leading cause of cancer-related mortality in females globally. Accurate grading is pivotal in guiding therapeutic decisions, predicting prognosis, and selecting candidates for neoadjuvant chemotherapy (NACT), which has emerged as the primary systemic treatment modality for locally advanced and early operable breast cancers.¹

Fine needle aspiration cytology (FNAC) remains a cost-effective, minimally invasive, and rapid diagnostic tool that permits cytomorphological grading prior to surgical intervention. Several cytological grading systems have been developed, including those by Hunt et al.,² Robinson et al.,³ Das et al.,⁴ Saha et al.,⁵ and Mouriquand et al.⁶ Among these, Mouriquand's six-parameter nuclear grading system has garnered particular interest because its scoring architecture closely parallels the three-parameter MBRGS — the widely accepted histopathological gold standard.

The Elston–Ellis modification of the Bloom–Richardson grading system (MBRGS) stratifies invasive ductal carcinoma (IDC) into three histological grades based on tubule formation, nuclear pleomorphism, and mitotic count.⁷ Correlating cytological and histopathological grades is critical because FNAC is increasingly used to guide NACT decisions before definitive surgery, and cytological grade must reliably predict the underlying histological behaviour.

Despite robust data supporting cytological grading, the most reliable cytological system that mirrors MBRGS grading has not been universally established. Recent literature indicates that Mouriquand's system consistently achieves concordance rates of 80–95% with histopathological grades.^{8,9} Other cytological grading systems have similarly demonstrated good correlation with histological grade in Indian cohorts, reinforcing the broader utility of cytomorphological grading in FNAC practice.^{10,11} The present study was therefore conducted to prospectively assess the concordance of Mouriquand's cytological grading with MBRGS in a tertiary care institutional cohort and to perform multiple regression analysis of individual cytomorphological parameters.

Aims and Objectives

- (1) To assess cytological grade in carcinoma breast using Mouriquand's six-parameter grading system on FNAC smears.
- (2) To correlate cytological grade with the corresponding histopathological grade using MBRGS (Elston–Ellis modification).
- (3) To identify the most discriminative cytomorphological parameters using multiple regression analysis.

MATERIAL AND METHODS

Study design and setting

This prospective observational study was conducted in the Department of Pathology, Christian Medical College and Hospital, Ludhiana over an eight-year period. Institutional ethics committee approval was obtained prior to commencement, and informed consent was secured from all participants.

Study population

Seventy-seven patients presenting with a palpable breast lump and diagnosed as carcinoma breast on clinical examination were enrolled. Inclusion criteria: (i) cytological diagnosis of breast carcinoma on FNAC, and (ii) subsequent surgical excision (biopsy or mastectomy) with availability of histopathological material. Patients with prior NACT (which would alter cytomorphology) and those with insufficient FNAC material (fewer than six cellular clusters with ≥ 10 cells per cluster) were excluded.

FNAC technique and smear preparation

FNAC was performed using a 20 mL disposable syringe with a 21-gauge needle under aseptic conditions. A minimum of three smears per case were prepared and stained with May–Grünwald Giemsa (MGG), Papanicolaou (Pap), and Haematoxylin and Eosin (H&E) stains. Smear adequacy was defined as the presence of at least six cellular clusters containing ≥ 10 epithelial cells per cluster on low-power examination.¹²

Cytological grading — Mouriquand's system

Each case was scored using Mouriquand's six cytological parameters: (1) cell arrangement (isolated versus clusters); (2) cell size relative to red blood cells (RBCs); (3) nuclear shape (regular versus irregular); (4) nuclear chromasia; (5) prominence of enlarged nucleoli; and (6) presence of mitotic figures. Scores of 6–10 were assigned cytological grade I, 11–14 grade II, and 15–18 grade III.⁶

Histopathological grading — MBRGS

Haematoxylin and eosin (H&E)-stained tissue sections from surgical specimens were graded using MBRGS as described by Elston and Ellis.⁷ The three components scored were: degree of tubule formation, degree of nuclear pleomorphism, and mitotic count per 10 high-power fields. Scores of 3–5 = grade I; 6–7 = grade II; 8–9 = grade III.

Statistical analysis

Data were entered and analysed using EpiData Analysis v6.1. Concordance between cytological and histopathological grades was assessed using cross-tabulation, Cohen's kappa (κ), Pearson's coefficient of correlation (r), and coefficient of determination (r^2). Diagnostic accuracy indices (sensitivity, specificity, positive predictive value [PPV], negative predictive value [NPV]) were calculated using histopathological grade as the reference standard. Multiple linear regression analysis was performed to identify the most significant cytological and histopathological predictors of the final grade. A p -value < 0.05 was considered statistically significant.

RESULTS

Clinico-demographic profile

The study comprised 77 patients with infiltrating duct carcinoma (IDC). Age ranged from 23 to 80 years, with a mean of 53 years. Seventy-five patients (97.4%) were female and two (2.6%) were male, reflecting the expected female predominance. All patients (100%) presented with a palpable breast lump; additionally, 12 patients (15.6%) had nipple discharge and 17 patients (22.1%) had constitutional symptoms. The right breast was marginally more affected (39 cases, 50.6%) than the left (38 cases, 49.4%). The upper outer quadrant was the most frequently involved site (48 cases, 62.3%), consistent with published series.^{8,9}

Cytological grading by Mouriquand's system

On Mouriquand's scoring, the majority of tumours were classified as grade II (47 cases, 61.0%), followed by grade III (16 cases, 20.8%) and grade I (14 cases, 18.2%) (Table 1). The mean cytological grade was 2.1. Grade I cases demonstrated cells arranged in tight cohesive clusters with mild nuclear pleomorphism, indistinct nucleoli, and rare mitoses. Grade II cases showed loose cluster arrangement with moderate pleomorphism, vesicular chromatin, and prominent nucleoli. Grade III cases were characterised by predominantly isolated cells, marked pleomorphism ($>5\times$ RBC size), irregular nuclear membranes with clefting and budding, multiple pleomorphic nucleoli, and conspicuous mitotic figures.

Table 1. Grade distribution by Mouriquand's cytological grading system (n = 77)

Grade	No. of Cases	Percentage (%)
I	14	18.2
II	47	61.0
III	16	20.8
Total	77	100.0

Figure 1. Cytological Grade I Features

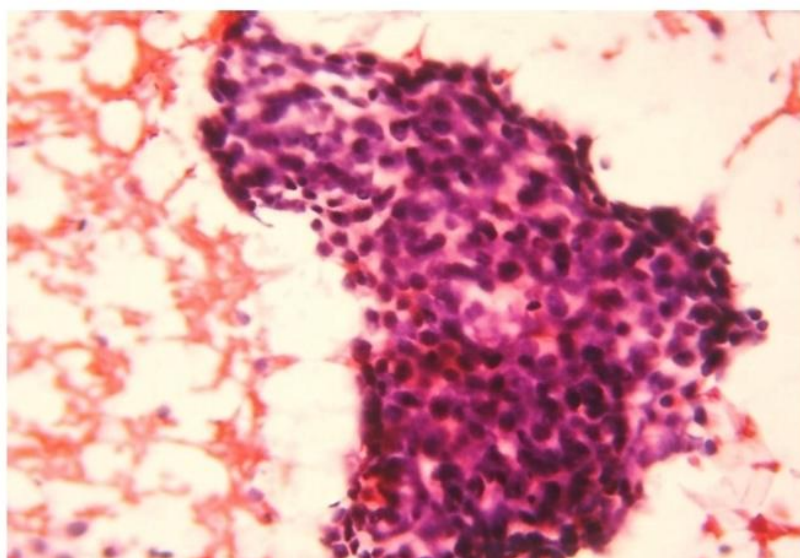


Fig. 1A: Photomicrograph showing invasive ductal carcinoma with cells in tight clusters and mild nuclear atypia. Cytological grade I, Mouriquand (Score 4), Pap, 400 $\times$.

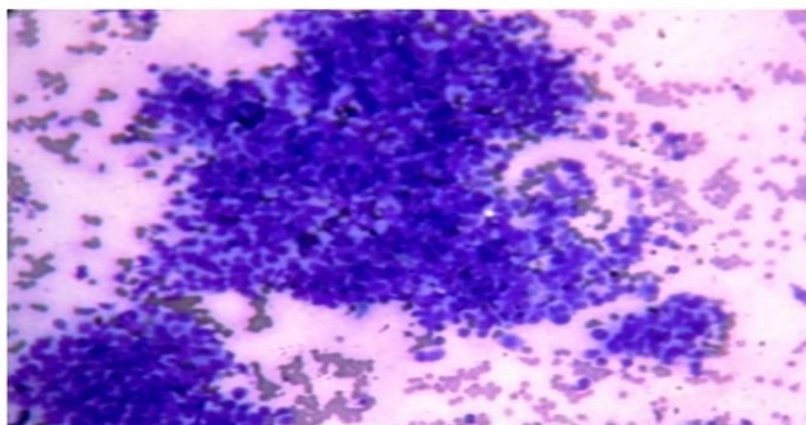


Fig. 1B: Photomicrograph showing cells displaying cellular clusters. Adequate (≥ 10 cells per cluster). Cytological grade I, MGG, 100 $\times$.

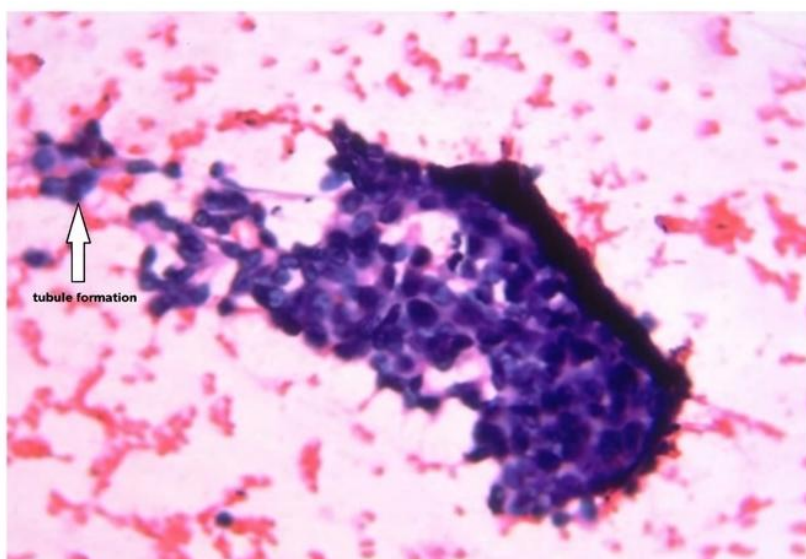


Fig. 1C: Photomicrograph with cells displaying mild pleomorphism, regular nuclear membrane and indistinct nucleoli; cells in clusters with tubule formation (arrow). Cytological grade I, H & E, 400 $\times$.

Figure 2. Comparative Cytological Analyses of Grade II Cell Clusters

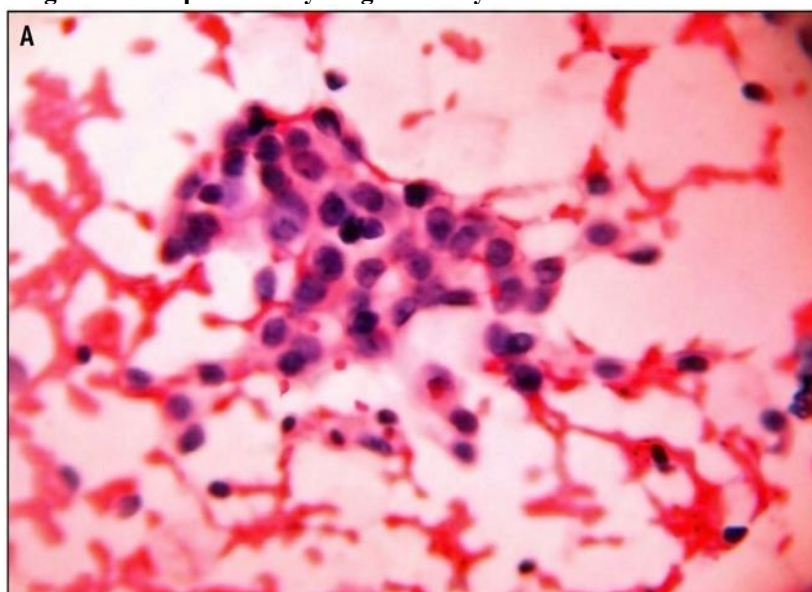


Fig. 2A: Photomicrograph showing loose clusters of moderately pleomorphic cells, 3–4 $\times$ RBC size with vesicular chromatin and red nucleoli. Cytological grade II, Mouriquand (Score 8), Pap, 400 $\times$.

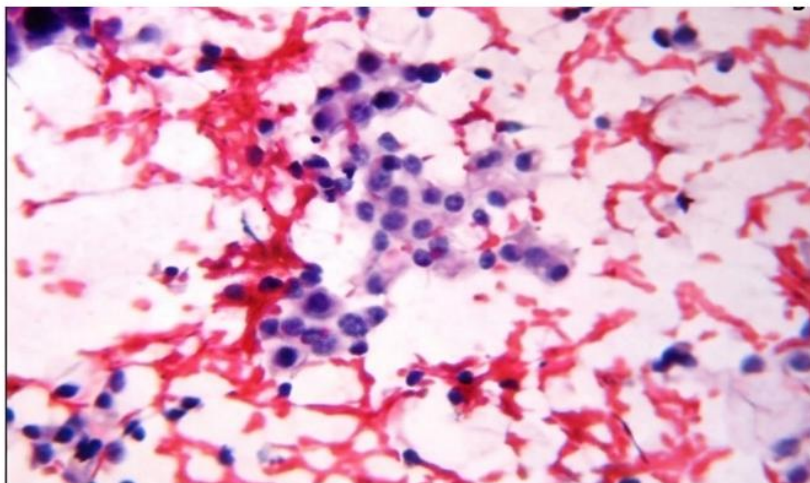


Fig. 2B: Photomicrograph showing cells in loose clusters with moderate pleomorphism. Cytological grade II, H & E, 400×.

Figure 3. Cytological Grade II Features — Adequacy and Morphology

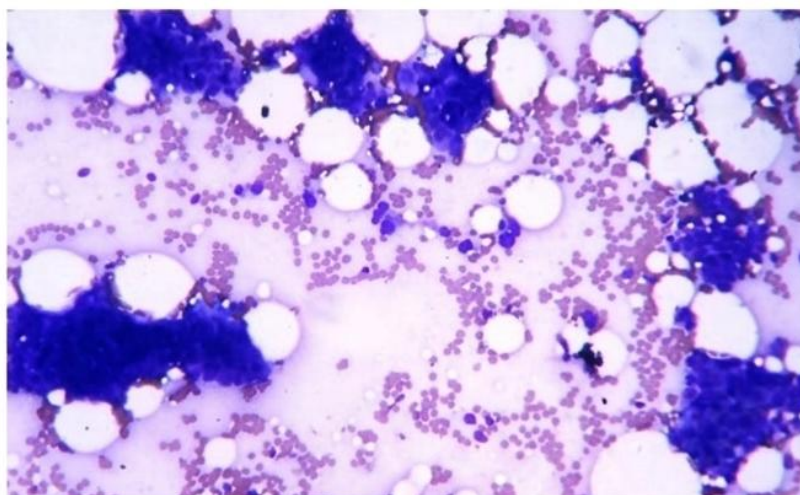


Fig. 3A: Photomicrograph in low power view showing cells 1–2× RBC with moderate pleomorphism, occasional tubule formation. Adequate smear (>6 clusters, ≥10 cells/cluster). Cytological grade II, MGG, 100×.

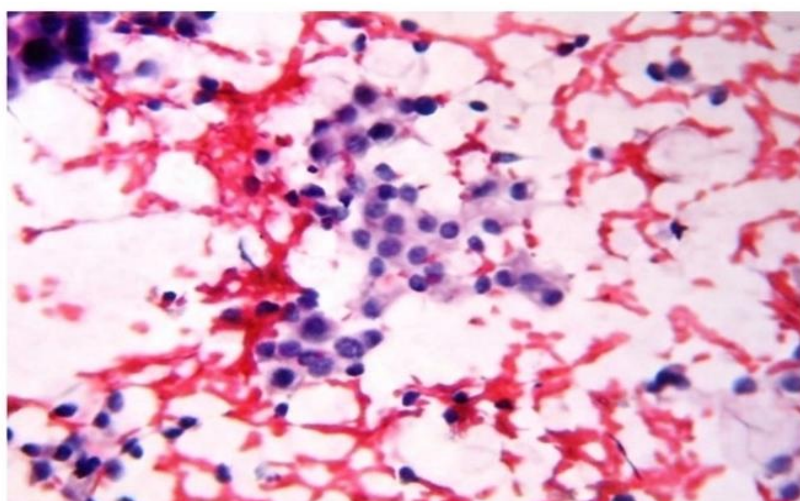


Fig. 3B: Photomicrograph showing cells in loose clusters and moderate pleomorphism. Cytological grade II, H & E, 400×.

Figure 4. Cytological Grade III Features

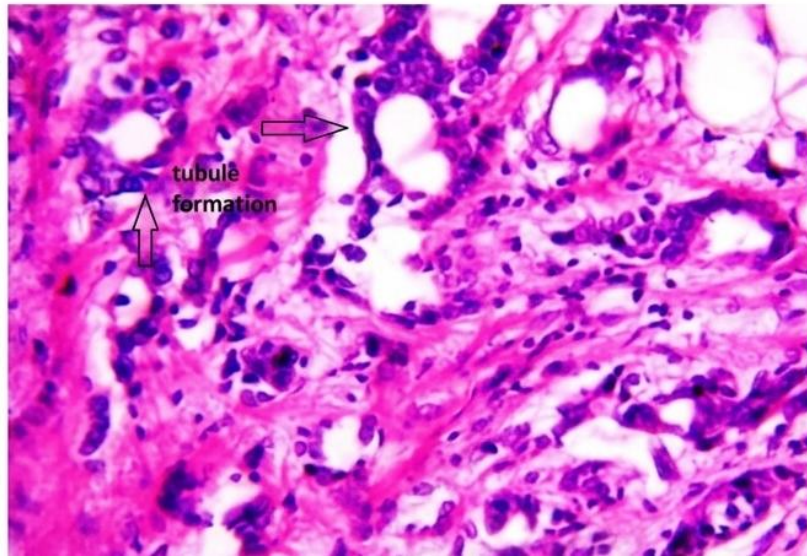


Fig. 4A: Photomicrograph showing markedly pleomorphic cells and nuclei with prominent enlarged 2–3 nucleoli (arrow) and clumped chromatin. Cyto grade III, Pap, 400×.

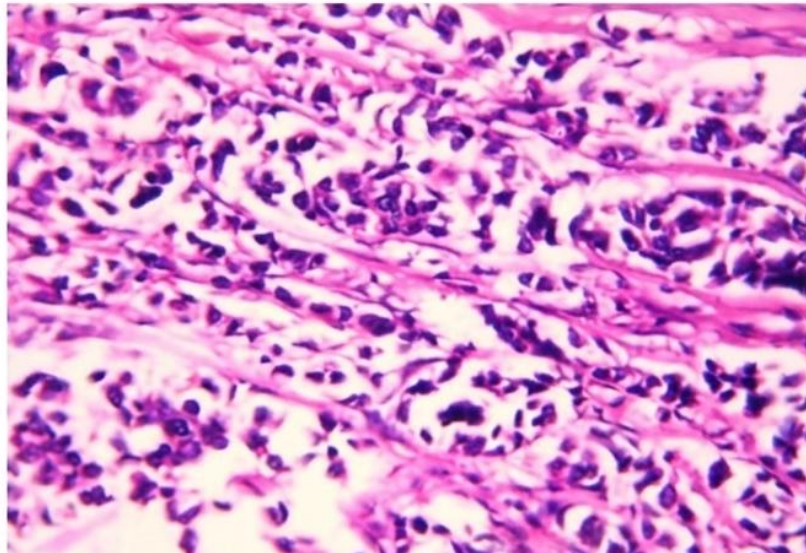


Fig. 4B: Photomicrograph showing markedly pleomorphic isolated cells with enlarged nucleoli and mitotic figure (arrow). Cyto grade III, Mouriquand (Score 14), Pap, 400×.

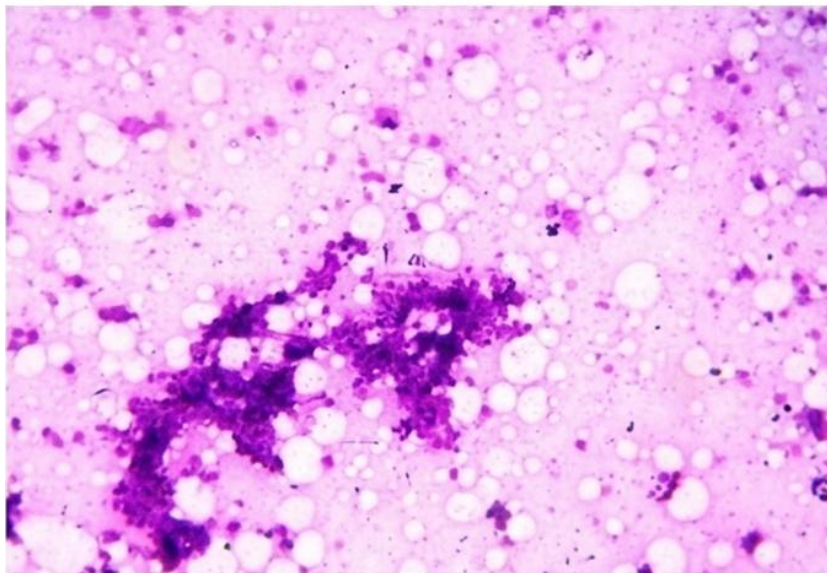


Fig. 4C: Composite image — upper: marked pleomorphism, $>5\times$ RBC, irregular nuclear membrane with clefting and budding, multiple pleomorphic nucleoli (H & E, 400 $\times$); lower: pleomorphic cells lying mostly singly and in loose clusters with mitosis (MGG, 100 $\times$). Cyto grade III.

Histopathological grading — MBRGS

On MBRGS, the maximum number of cases (42, 54.5%) were assigned histopathological grade II (Table 2). Grades I and III had nearly equal representation (17 cases [22.1%] and 18 cases [23.4%], respectively). The mean histopathological grade was 2.1, identical to the mean cytological grade, further underscoring the concordance between the two systems.

Figure 5. Histopathological Features — MBRGS Grades I and II

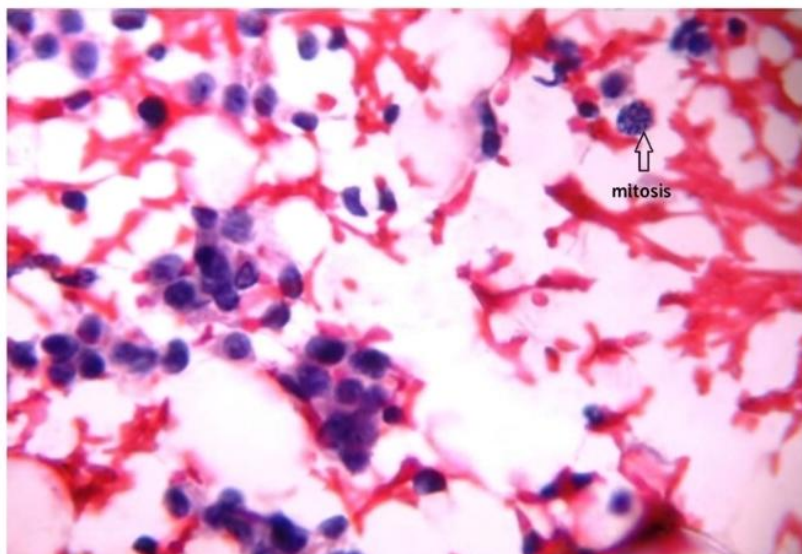


Fig. 5A: Photomicrograph showing well-differentiated invasive ductal carcinoma, grade I, Elston's modification of BR, Score 4 with tumour cells displaying mild pleomorphism and tubule formation (arrows). H & E, 400 $\times$.

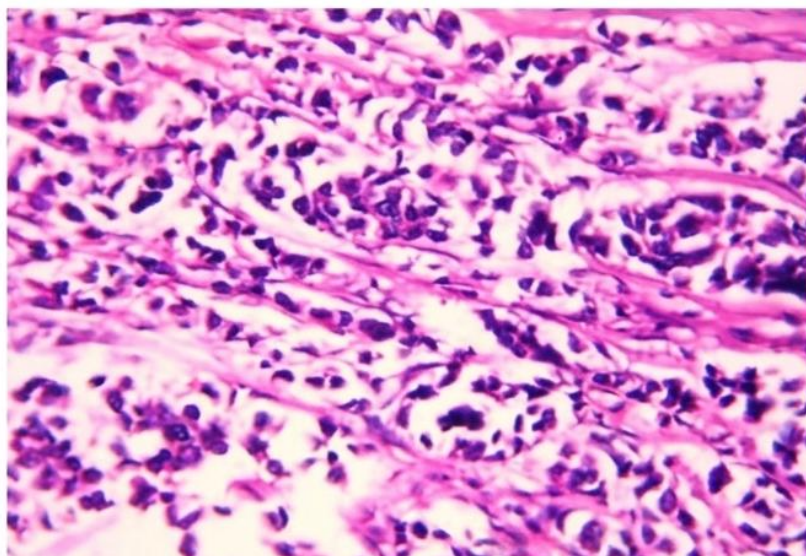


Fig. 5B: Photomicrograph showing moderately differentiated invasive ductal carcinoma, grade II (Score 6). H & E, 400×.

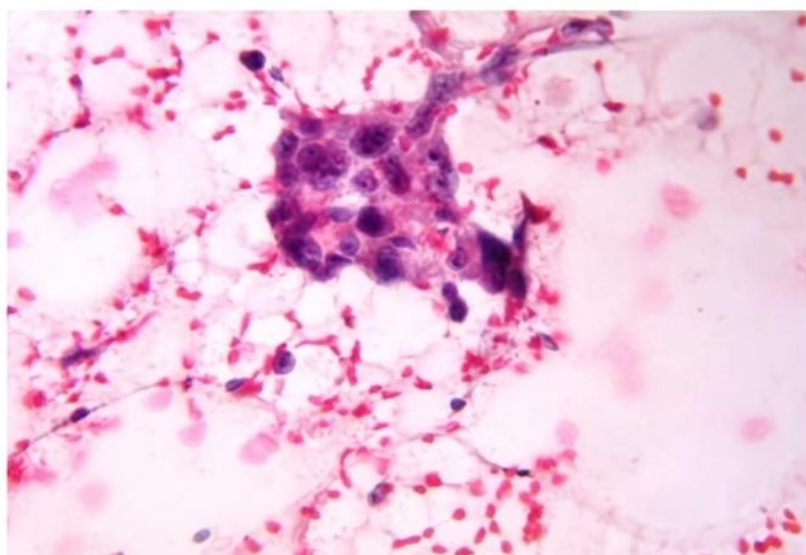


Fig. 5C: Photomicrograph with cells displaying mild pleomorphism, regular nuclear membrane, indistinct nucleoli, and tubule formation (arrow). H & E, 400×.

Table 2. Comparison of Mouriquand's cytological grading with histopathological grading (n = 77)

Mouriquand Grade	Histo Grade I n (%)	Histo Grade II n (%)	Histo Grade III n (%)	Total n (%)
I	14 (100%)	0 (0%)	0 (0%)	14 (18.2%)
II	3 (6.4%)	41 (87.2%)	3 (6.4%)	47 (61.0%)
III	0 (0%)	1 (6.3%)	15 (93.8%)	16 (20.8%)
Total	17 (22.1%)	42 (54.5%)	18 (23.4%)	77 (100%)

Concordance and statistical analysis

When Mouriquand's cytological grading was compared with histopathological grading, overall concordance was achieved in 70 of 77 cases (90.9%), which was statistically significant ($p < 0.001$). Grade I tumours demonstrated complete concordance (14/14, 100%); grade III showed 93.8% concordance (15/16); and grade II tumours showed 87.2% concordance (41/47).

Discordance was observed in seven cases, all with a single-grade difference: four cases (5.2%) were over-graded cytologically (three in grade I and one in grade II) and three cases (3.9%) were under-graded on cytology in grade II.

The coefficient of correlation between Mouriquand's cytological grade and histopathological grade was $r = 0.75$, with $r^2 = 0.56$, indicating that 56% of the variance in histopathological grade is explained by cytological grade. Cohen's kappa was 0.879 (SE = 0.068; $p < 0.001$), representing near-perfect agreement as per Landis and Koch's classification (Table 3).

Table 3. Diagnostic performance of Mouriquand's grading system relative to histopathological grading

Statistical Parameter	Value (%)
Sensitivity	99.1
Specificity	82.4
Positive Predictive Value (PPV)	95.2
Negative Predictive Value (NPV)	99.9
Diagnostic Accuracy	96.0
Coefficient of Correlation (r)	0.75
Coefficient of Determination (r^2)	0.56
Cohen's Kappa (κ)	0.879 (near-perfect)

Multiple regression analysis — cytological features

Multiple linear regression analysis of Mouriquand's six cytological parameters against histopathological grade identified nuclear shape ($\beta = 0.23$; $p < 0.001$), nuclear chromasia ($\beta = 0.23$; $p < 0.001$), enlarged nucleoli ($\beta = 0.16$; $p < 0.001$), and cell size ($\beta = 0.15$; $p < 0.001$) as the most influential predictors of histopathological grade. Cell arrangement ($\beta = 0.13$; $p < 0.001$) and mitosis ($\beta = 0.12$; $p < 0.001$) were also statistically significant. All six parameters contributed significantly to the model (Table 4).

Table 4. Multiple regression analysis of cytological features (Mouriquand's system) with histopathological grade

Cytological Feature	Regression Coefficient (β)	t-value	p-value
Nuclear shape	0.23	5.63	< 0.001
Nuclear chromasia	0.23	2.88	< 0.001
Enlarged nucleoli	0.16	4.74	< 0.001
Cell size	0.15	3.55	< 0.001
Cell arrangement	0.13	4.49	< 0.001
Mitosis	0.12	2.85	< 0.001

Multiple regression analysis — histopathological features

All three MBRGS components were highly significant predictors of histopathological grade ($p < 0.001$). Tubule formation ($\beta = 0.43$) and nuclear pleomorphism ($\beta = 0.42$) demonstrated marginally higher regression coefficients than mitotic count ($\beta = 0.41$), suggesting their relatively greater contribution to histological grade assignment (Table 5).

Table 5. Multiple regression analysis of histopathological features with histopathological grade

Histopathological Feature	Regression Coefficient (β)	t-value	p-value
Tubule formation	0.43	9.16	< 0.001
Nuclear pleomorphism	0.42	8.06	< 0.001
Mitotic count	0.41	10.28	< 0.001

DISCUSSION

The concordance of cytological grading with histopathological grading in breast carcinoma is a subject of sustained interest given the increasing role of NACT in non-metastatic breast cancer management. The ability to reliably predict histological grade from pre-surgical FNAC material directly influences decisions regarding systemic therapy, surgical planning, and participation in neoadjuvant clinical trials.¹

In the present study, the mean age at diagnosis was 53 years. Published reports from India place the mean age of breast carcinoma diagnosis approximately a decade earlier than Western cohorts, reflecting a younger age of onset in South Asian populations.^{8,9} Female predominance (97.4%) and upper outer quadrant predilection (62.3%) were consistent with the published literature.

The grade distribution on Mouriquand's cytological scoring (grade I: 18.2%; grade II: 61.0%; grade III: 20.8%) closely mirrors histopathological grade distribution (grade I: 22.1%; grade II: 54.5%; grade III: 23.4%), with a mean grade of 2.1 in both systems. This parallel distribution has been reported by multiple investigators and lends face validity to the cytological grading approach.^{8,9}

The overall concordance rate in this study was 90.9% (70/77 cases), which compares favourably with the range of 80–95% reported in recent literature. Bukya et al.⁸ (2018) reported 88.2% concordance for Mouriquand's system, and Pandey et al.⁹ (2014) reported 84.7% with a kappa of 0.76. Similarly, Meena et al.¹¹ reported a sensitivity of 90.77% and specificity of

84.42% for cytological grading against modified Bloom–Richardson grading in an Indian cohort, while Taniguchi et al.¹³ demonstrated a positive correlation between cytologic and histologic grade that extended to associations with nodal metastasis and proliferative index.

The kappa value of 0.879 in this study indicates near-perfect agreement, which is the highest tier of the Landis–Koch scale and superior to the kappa of 0.118 reported by Bukya et al.⁸ The discrepancy is likely attributable to differences in cytologist experience, adequacy criteria, and inter-observer variability in scoring.

Grade I tumours showed the highest concordance (100%), followed by grade III (93.8%) and grade II (87.2%). Grade II remains the most heterogeneous cytological category, encompassing a wide spectrum of intermediate morphological features, which may partly explain its relatively lower concordance. Comparative studies evaluating multiple cytological grading systems side by side — including Wani et al.,¹⁴ Ohri et al.,¹⁵ Arul and Masilamani,¹⁶ and Einstein et al.¹⁷ — have consistently found that concordance with histological grade varies meaningfully depending on the specific cytological system applied, underscoring that method selection is a source of variability distinct from grade-II heterogeneity alone. The earliest systematic comparison of cytological and histological grading in needle aspirates by Kapila et al.¹⁸ similarly highlighted the importance of standardised adequacy criteria and consistent parameter scoring. Discordance in seven cases (all within one grade) is attributable to well-known limitations of FNAC: sampling-related heterogeneity, loss of architectural context (tubule formation cannot be assessed on smears), drying artefacts, and interobserver variability in parameter scoring.¹²

Multiple regression analysis confirmed that nuclear shape and chromasia ($\beta = 0.23$ each) were the most discriminating cytological features, followed by enlarged nucleoli ($\beta = 0.16$). Mitosis, although statistically significant, had the lowest regression coefficient ($\beta = 0.12$), likely because mitoses are infrequently seen per high-power field on cytological smears compared to sections. These findings suggest that nuclear morphology deserves the greatest attention during cytological grading.

The high sensitivity (99.1%) and NPV (99.9%) of Mouriquand’s system make it particularly valuable as a screening grading tool: a low Mouriquand grade reliably predicts a low histological grade, supporting conservative initial management. Specificity was lower (82.4%), indicating some grade overestimation, which may be acceptable given that clinicians generally prefer not to under-grade malignancies.

The current study is limited by its retrospective single-institution design. Inter-observer reliability of cytological parameter scoring was not independently assessed, and the male patient sub-group ($n = 2$) is too small for meaningful sub-analysis. Future multi-institutional studies incorporating digital image analysis and inter-rater reliability coefficients would strengthen the evidence base.

CONCLUSION

Mouriquand’s cytological grading system demonstrates near-perfect concordance with MBRGS histopathological grading in invasive ductal carcinoma of the breast ($\kappa = 0.879$; concordance 90.9%). Nuclear shape and chromasia are the most predictive cytomorphological parameters. Routine incorporation of Mouriquand’s grading into FNAC reporting is recommended, as it provides clinically actionable, reproducible, and timely grade information to guide neoadjuvant therapy selection and prognostication — particularly in settings where definitive histopathological assessment may be delayed.

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