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**ORIGINAL RESEARCH**

# Comparative Analysis of Three Cytological Grading Systems in Fine-Needle Aspiration of Breast Carcinoma

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## ABSTRACT

**Background:** Breast carcinoma is a heterogeneous disease with varying clinical and pathological characteristics. Tumor grading plays a crucial role in prognostication and therapeutic decision-making. This study evaluates the age distribution, site of lumps, and tumor grading using multiple cytological and histological grading systems to highlight their importance in clinical practice. **Methods:** This present study included patients diagnosed with breast carcinoma. The age distribution of participants was analyzed, and the location of breast lumps was documented. Tumors were graded using Robinson's, Fisher's, Howell's, and Scarff-Bloom-Richardson (SBR) systems to assess concordance and clinical significance. **Results:** The mean age of participants was 51.12 years, with a standard deviation of ±12.024 years. The majority (38.3%) were aged 51–60 years, with 23.3% aged 41–50 years. Breast lumps were most commonly located in the upper outer quadrant (81.7%), followed by the upper inner quadrant (10%). Tumor grading showed that Grade 2 tumors predominated across all systems: 55.0% in Robinson's, 51.7% in Fisher's, 56.7% in Howell's, and 55.0% in SBR grading. Grade 1 tumors ranged from 18.3% to 28.3%, while Grade 3 tumors varied between 18.3% and 26.7%. **Conclusion:** The study emphasizes the importance of tumor grading in breast carcinoma as a cost-effective and reliable prognostic tool, especially in resource-limited settings. The predominance of Grade 2 tumors across all grading systems underscores their clinical relevance in guiding treatment. The anatomical distribution of lumps and demographic patterns further support targeted screening and management strategies.

**Keywords:** Breast carcinoma**,** fine-needle aspiration (FNA)**,** cytological grading**,** grading systems**,** fine-needle aspiration cytology (FNAC)**,** breast cancer diagnosis**,** cytopathology**,** tumor grading**,** breast cancer prognosis



## INTRODUCTION

Breast carcinoma is one of the most common malignancies affecting women worldwide, and its early detection and accurate prognostic assessment are crucial for guiding therapeutic strategies and improving patient outcomes.[1] Fine-needle aspiration cytology (FNAC) is a widely utilized, minimally invasive diagnostic tool that provides rapid, reliable, and cost-effective evaluation of breast lesions. Cytological grading of breast carcinoma through FNAC not only aids in distinguishing between benign and malignant lesions but also provides valuable prognostic insights by correlating tumor grade with clinical outcomes and therapeutic response.

Several cytological grading systems have been developed to standardize and improve the accuracy of tumor assessment. Among the most commonly used methods are Robinson's Cytological Grading Method, Fisher's Modification of Black's Nuclear Grading System, and Howell's Cytological Grading System.[2] Each of these grading systems employs distinct parameters and methodologies to assess tumor differentiation, nuclear pleomorphism, and other cytological features. Robinson's method evaluates six parameters, including cell dissociation, nuclear size, cell uniformity, nuclear margin, chromatin pattern, and the presence of nucleoli, with each scored on a scale of 1 to 3.[4] The total score determines the grade as well-differentiated (Grade I), moderately differentiated (Grade II), or poorly differentiated (Grade III). In contrast, Fisher's system emphasizes nuclear characteristics, grading nuclear size, pleomorphism, and chromatin distribution to assess the degree of malignancy and predict tumor aggressiveness.[5] Although Fisher's method is valuable for identifying aggressive tumors, its reliance solely on nuclear features may overlook tumor heterogeneity. Howell's grading system takes a more

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holistic approach by incorporating both nuclear and cytoplasmic characteristics, including nuclear size, pleomorphism, cytoplasmic volume, and chromatin texture.[6] This comprehensive view makes it particularly useful in cases where nuclear features alone are insufficient for accurate grading.

The rationale for evaluating these grading systems lies in their significant role in the diagnostic and prognostic assessment of breast carcinoma. FNAC-based grading methods enable early determination of tumor aggressiveness, particularly in settings where histopathological grading is not immediately available. However, variations in methodology, inter-observer variability, and differences in clinical outcome correlations necessitate a systematic evaluation. This study aims to compare the effectiveness and reliability of these methods, assess their correlation with histopathological grading and clinical outcomes, and identify the most suitable grading system for routine FNAC practice. The findings of this study are expected to contribute to the optimization of cytological practices in breast cancer diagnosis. By systematically analyzing the parameters, ease of use, and clinical utility of each grading system, this study seeks to enhance diagnostic accuracy, provide valuable prognostic information, and aid in personalized treatment planning. Ultimately, this research will guide cytopathologists in selecting the most appropriate grading system for specific clinical scenarios, particularly in resource-limited settings.

## METHODS

The present study was conducted at the Postgraduate Department of Pathology, Government Medical College, Jammu (GMC Jammu), and its associated hospitals. The study was carried out in two phases: a retrospective data analysis from August 1, 2021, to July 31, 2023, and a prospective data analysis from August 1, 2023, to July 31, 2024. Written informed consent was obtained from all patients, and the study received approval from the Institutional Ethics Committee.The inclusion criteria encompassed all patients, regardless of age and sex, presenting with a breast lump and reporting to the Department of Pathology at GMC Jammu. Patients were excluded if they presented with nipple discharge but without a palpable breast lump, were lactating, or were non-cooperative.

For the retrospective component, cytology and histopathology requisition forms, diagnostic reports, and slides related to the specified diagnosis were retrieved from departmental archives. These data were systematically compiled and analyzed. For the prospective component, all patients with breast lumps reporting to the Department of Pathology were subjected to fine-needle aspiration cytology (FNAC). Smears obtained from FNAC were evaluated using three cytological grading systems: Robinson's Cytological Grading System, Fisher's Modification of Black's Nuclear Grading System, and Howell's Cytological Grading System. FNAC was performed using a 23-gauge disposable needle attached to a 20 mL disposable syringe mounted on a Franzen's handle. Wet smears were fixed in isopropyl alcohol for Papanicolaou staining, and air-dried smears were prepared for Giemsa staining. Clinical data, including patient history, physical examination findings, and imaging studies such as mammography, were recorded for comprehensive correlation with cytological and histological outcomes.The staining process involved standardized protocols for Papanicolaou and May-Grunwald Giemsa stains. For Papanicolaou staining, smears were fixed in alcohol and subjected to a series of steps, including hematoxylin staining, differentiation, and counterstaining with OG6 and EA50, followed by dehydration and mounting in DPX. For May-Grunwald Giemsa staining, air-dried smears were stained sequentially with May-Grunwald and Giemsa working solutions, rinsed, and examined microscopically.The stained smears were systematically reviewed and graded according to Robinson's, Fisher's, and Howell's cytological grading systems.

**Table 1: Robinson's Cytological Grading Method for Reporting Breast FNAC**

| Features | Score 1 | Score 2 | Score 3 |
|---|---|---|---|
| **Dissociation** | Cells in Cluster | Single, with Cell Clusters | Mostly Single Cells |
| **Nuclear Size** | 1-2 RBC Size | 3-4 RBC Size | ≥ 5 RBC Size |
| **Cell Uniformity** | Monomorphic | Mildly Pleomorphic | Highly Pleomorphic |
| **Nucleoli** | Indistinct | Noticeable | Prominent/Abnormal |
| **Nuclear Margins** | Smooth | Folds | Clefts/Buds |
| **Chromatin** | Vesicular | Granular | Clumped & Cleared |

Grading Scale*:, Grade 1: Total Score 6-11, Grade 2: Total Score 12-14, Grade 3: Total Score 15-18

**Table 2: Fisher's Modification of Black's Nuclear Grading System**

| Nuclear Character | Nuclear Grade 1 | Nuclear Grade 2 | Nuclear Grade 3 |
|---|---|---|---|
| **Size** | Minimal variation, resembling normal duct epithelium | Twice the size of Grade 1 nuclei | Larger than Grade 2, often threefold diameter variation |
| **Nuclear Membrane Contour** | Round, Smooth | Smooth | Irregular |

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| | | | |
|---|---|---|---|
| **Anisonucleosis** | Absent | Moderate | Marked |
| **Chromatin** | Fine | Uniform | Marked Hyperchromatism, Coarse, Clearing may be present |
| **Nucleoli** | Absent | May or may not show small nucleoli | Macro Nucleoli |

**Table 3: Howell's Cytological Grading System**

| Parameters | Score 1 | Score 2 | Score 3 |
|---|---|---|---|
| **Tubule Formation** | Present in >75% of Tumor | Present in 10-75% of Tumor | Present in <10% of Tumor |
| **Nuclear Pleomorphism** | Mild, Small, Regular & Uniform Cells | Moderate Variation in Size & Shape | Marked Variation in Size & Shape |
| **Mitotic Count (per 10 HPF)** | 0-1 | 2-4 | >5 |

Grading Scale*:Grade 1: Total Score 3-5, Grade 2: Total Score 6-7, Grade 3: Total Score 8-9

## RESULTS

In this section, the results of the study will be described:

**Table 4: Age distribution among study participants**

| Age (years) | Frequency | Percent (%) |
|---|---|---|
| **20–30** | 3 | 5.0 |
| **31–40** | 9 | 15.0 |
| **41–50** | 14 | 23.3 |
| **51–60** | 23 | 38.3 |
| **61–70** | 8 | 13.3 |
| **≥71** | 3 | 5.0 |
| **Total** | **60** | **100** |

The mean age of the participants was 51.12 years, with a standard deviation of ±12.024 years, indicating a moderately dispersed age distribution. The age distribution of the participants ranged from 20 to over 71 years, wherein the majority of participants (38.3%) were in the 51–60 years age group, followed by 23.3% in the 41–50 years age group. Participants aged 31–40 years comprised 15.0% of the study population, while 13.3% were in the 61–70 years age group. The youngest age group, 20–30 years, and the oldest group, ≥71 years, each accounted for 5.0% of the participants. Overall, the study included 60 participants, representing a wide range of age groups, with the highest frequency observed in the middle-aged cohort.

**Table 5: Frequency and percentage distribution of site of lump among participants**

| Quadrant | No. (%) |
|---|---|
| **Lower and inner** | 1 (1.7%) |
| **Lower and outer** | 3 (5.0%) |
| **Retro areolar** | 1 (1.7%) |
| **Upper and inner** | 6 (10.0%) |
| **Upper and outer** | 49 (81.7%) |
| **Total** | **60 (100%)** |

The majority of lumps were located in the upper outer quadrant, accounting for 81.7% of cases. The upper inner quadrant was the second most common site, representing 10% of the lumps. Other locations, including the lower outer quadrant (5.0%), lower inner quadrant (1.7%), and retroareolar region (1.7%), were less frequently involved. Overall, the distribution highlights the predominance of the upper outer quadrant as the most common site for breast lumps among the study population.

**Table 6: Frequency distribution of cases according to Robinson, Fishers, Howells and Scarff Bloom Richardsons Histological grading system**

| Grade | Robinson Grade | Fisher's Grade | Howell's Grade | Scarff Bloom Richardson's Grading |
|---|---|---|---|---|
| **Grade 1** | 16 (26.7%) | 17 (28.3%) | 15 (25.0%) | 11 (18.3%) |
| **Grade 2** | 33 (55.0%) | 31 (51.7%) | 34 (56.7%) | 33 (55.0%) |
| **Grade 3** | 11 (18.3%) | 12 (20.0%) | 11 (18.3%) | 16 (26.7%) |

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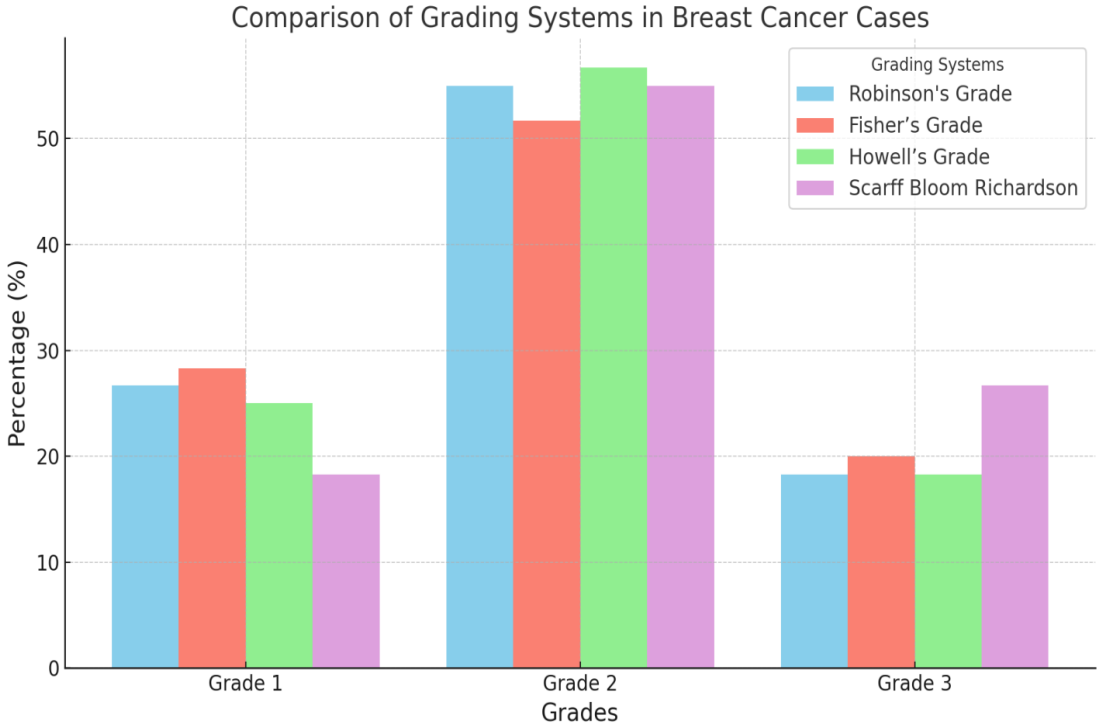
Table 6 presents the frequency distribution of cases according to the Robinson, Fisher's, Howell's, and Scarff-Bloom-Richardson (SBR) histological grading systems.For Robinson's grading, the majority of cases were categorized as Grade 2 (55.0%), followed by Grade 1 (26.7%) and Grade 3 (18.3%). Similarly, Fisher's grading showed a predominant classification in Grade 2 (51.7%), with Grade 1 and Grade 3 accounting for 28.3% and 20.0%, respectively.In the Howell's grading system, Grade 2 remained the most frequent (56.7%), while Grade 1 and Grade 3 constituted 25.0% and 18.3% of cases, respectively. Finally, the Scarff-Bloom-Richardson grading system identified 55.0% of cases as Grade 2, followed by 26.7% as Grade 3, and 18.3% as Grade 1.These findings emphasize the concordance in the predominance of Grade 2 tumors across all grading systems, with variations observed in the distribution of Grade 1 and Grade 3 tumors.




## DISCUSSION

Breast cancer remains the most commonly diagnosed malignancy and the leading cause of cancer-related mortality among women aged 20 to 59 years in the United States, as reported by Siegel RL et al. (2023).[7]The present study assessed breast carcinoma cases using four established grading systems: Robinson's cytological grading, Fisher's modification of Black's nuclear grading, Howell's cytological grading, and Scarff-Bloom-Richardson's (SBR) histological grading. These methods are integral to understanding the biological behavior of breast carcinoma and guiding therapeutic decisions. In this study, the mean age of participants was 51.12 years (±12.024), with the majority of cases occurring in the premenopausal age group (40–50 years). This age distribution aligns with findings from Heer et al. (2020) and Ferlay et al., (2011), who noted a similar pattern in their study population.[8] Comparable observations were reported by Kaur M et al. (2020), who studied 46 female patients with ductal carcinoma and found a mean age of 54 years, with ages ranging from 34 to 80 years.[9] Likewise, Patel et al. (2018) evaluated 50 cases and found that the majority of patients fell within the 40–50 years age group, with a mean age of 50.22 years.[10]Regional and global variations in age distribution of breast cancer cases have also been reported. According to Hosseini MS et al. (2013), breast cancer incidence peaks in the 50–54 age group in Iran and the 55–59 age group in Iraq, followed by a decline in older age groups.[11] This contrasts with the steady increase in incidence across all age groups observed in the United States. These variations may reflect differences in genetic predisposition, lifestyle factors, screening practices, and healthcare accessibility.The National Cancer Institute (2020) reported that American women in their 50s face a 2.4% (1 in 42) lifetime risk of developing breast cancer. While the incidence of breast cancer in women under 40 has remained stable over the past 30 years, rates in older women steadily increased until peaking in 2000, followed by a gradual decline.[13] The stabilization in younger women could be attributed to improved awareness and early detection efforts, whereas the decline in older women may be linked to changes in hormone replacement therapy use and advancements in preventive care.These findings underscore the importance of

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considering age as a critical factor in the epidemiology and management of breast cancer. The alignment of the current study's findings with existing literature reinforces the reliability of its observations and highlights the global consistency in breast cancer trends within specific age groups. Continued efforts in early detection and tailored interventions based on age-specific risk factors remain essential for improving outcomes in breast carcinoma management.

Breast cancer is a significant global health issue, affecting millions of individuals worldwide. Early detection remains a cornerstone of effective management, with the identification of breast lumps playing a pivotal role in diagnosis. While breast cancer can develop in any part of the breast, it is most frequently localized in the upper outer quadrant (UOQ)—the region higher and closer to the outer chest wall, near the axilla.In the present study, 81.7% of breast lesions were localized in the UOQ, followed by 10% in the upper inner quadrant and 5% in the lower outer quadrant. These findings corroborate with earlier studies by Hazrah P. et al. (2009), Rummel S. et al. (2015), Wu S. et al. (2014), Sarp S. et al. (2007), and Siotos C. et al. (2018), which reported UOQ prevalence ranging from 36.1% to 62%.[14-18] This high frequency of UOQ involvement is often attributed to the denser and more abundant breast tissue present in this quadrant, as suggested by Lee AH. et al. (2005).[19]However, the disproportionate occurrence of breast cancer in the UOQ cannot be entirely explained by tissue density alone. Chen JH et al. (2017) highlighted that other factors might contribute to this phenomenon.[20] For instance, Ellsworth et al. (2004) observed a higher degree of genomic instability in the outer breast quadrants compared to the inner regions, potentially predisposing the UOQ to carcinogenesis.[21]Additionally, environmental and lifestyle factors may play a role. Darbre PD. et al. (2005) proposed a link between the higher incidence of breast cancer in the UOQ and the use of cosmetic products, such as deodorants and antiperspirants, applied to the underarm and adjacent upper breast area.[22] These products may contain DNA-damaging agents or estrogen-mimicking chemicals, which could contribute to carcinogenesis in this region.The findings of the present study, combined with insights from the literature, emphasize the multifactorial nature of breast cancer development in the UOQ. While anatomical factors provide a partial explanation, genetic and environmental influences also appear to play critical roles. These observations underscore the need for further research to elucidate the interplay of these factors and to develop targeted strategies for prevention, early detection, and treatment of breast cancer.

Cytological grading (CG) of breast carcinoma serves a dual purpose: establishing diagnosis and providing critical prognostic information without imposing the additional burden of core or excision biopsy, particularly in resource-limited settings. This approach is invaluable for patients with inoperable tumors or those deemed high-risk for surgical intervention, as noted by Bansal C. et al. (2012) and Jayaram G. et al. (2005).[23,24] In this study, three widely recognized CG systems—Robinson's, Fisher's, and Howell's grading systems—were employed to evaluate the cytological smears of breast carcinoma cases, yielding results comparable to several studies in the literature.The distribution of grades using Robinson's system classified 26.7% of tumors as Grade 1, 55.0% as Grade 2, and 18.3% as Grade 3. These findings are consistent with the study by Gore C et al. (2013), which reported 28% Grade 1 cases, 56% Grade 2 cases, and 16% Grade 3 cases. Comparable results were also observed in studies by Patel. et al. (2018), Kumar S. et al. (2022), and Phukan et al. (2015).[11,26,27] Robinson's system is recognized for its simplicity and reproducibility, making it a reliable tool in cytological evaluation.When the Fisher's grading system was employed, we found that 28.3% of tumors were classified as Grade 1, 51.7% as Grade 2, and 20.0% as Grade 3. These findings align closely with the study by Choudhury M. et al. (2020), which reported 38.6% Grade 1 cases, 50.0% Grade 2 cases, and 11.4% Grade 3 cases.[28] Similar concordance was noted with the results of Susmitha MS. et al. (2017).[29] The slight variations in Grade 3 distribution across studies may reflect population-specific tumor biology or methodological differences in interpretation.The Howell's grading system classified 25.0%, 56.7%, and 18.3% of tumors as Grade 1, Grade 2, and Grade 3, respectively. These results are consistent with the findings of Choudhury M. et al. (2020), who reported 29.5% Grade 1 cases, 54.5% Grade 2 cases, and 15.9% Grade 3 cases.[28]Patil VS. et al. (2018) also observed similar grading distributions.[28] Howell's system has been praised for its ability to identify subtle nuclear changes, contributing to its widespread adoption.The consistency of findings across the three grading systems and multiple studies underscores the robustness of cytological grading as a diagnostic and prognostic tool. The predominance of Grade 2 tumors in this study and others highlights the intermediate aggressiveness typical of many breast carcinoma cases. Variations in Grade 1 and Grade 3 distribution may reflect differences in the study population, environmental factors, or observer interpretation.Cytological grading is particularly beneficial in resource-limited settings, as it provides rapid and cost-effective prognostic insights. Moreover, the use of multiple grading systems ensures that subtle variations in tumor morphology are adequately captured, enhancing diagnostic precision. Continued validation of these grading systems through comparative studies will further strengthen their role in breast cancer management, especially for patients unable to undergo surgical biopsy.

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## CONCLUSION

Tumor grading remains a cornerstone in the assessment of breast carcinoma, providing critical prognostic information and guiding therapeutic decisions. The concordance observed across Robinson's, Fisher's, Howell's, and Scarff-Bloom-Richardson grading systems highlights their utility and reliability in classifying tumors. Grade 2 tumors emerged as the most prevalent across all systems, reinforcing its clinical relevance in predicting outcomes.These findings emphasize the role of grading systems as indispensable tools in resource-limited and advanced clinical settings alike, supporting personalized management strategies while fostering consistency in cancer prognosis and treatment planning.

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