ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 15, Issue 7, 2022

Online - 2455-3891
Print - 0974-2441

Research Article

COMPARATIVE EVALUATION OF CYTOLOGICAL AND HISTOPATHOLOGICAL GRADING IN INVASIVE DUCTAL CARCINOMA BREAST: A CROSS-SECTIONAL STUDY

SHIV KUMAR[1], NINDER KUMAR[1]*, RAMESH KUMAR[1], HARNAM SINGH REKHI[2]

[1]Department of Pathology, Government Medical College, Patiala, Punjab, India. [2]Department of Surgery, Government Medical College, Patiala, Punjab, India. Email: drninder@gmail.com

Received: 04 April 2022, Revised and Accepted: 10 May 2022

ABSTRACT

Objectives: Carcinoma breast is most commonly diagnosed cancer in women. Fine-needle aspiration cytology (FNAC) and histopathology play very important role in diagnosing breast cancer. Main objective of this study is to compare the cytological and histopathological grading in invasive ductal carcinoma of breast.

Methods: The study was conducted in the Department of Pathology, Government Medical College, Patiala. Fifty patients with palpable breast lump were selected. The age of whom varied from 30 to 86 years. FNAC was done, smears were prepared and stained with Romanowsky and Papanicolaou stains. Cytological grading was done according to Robinson's method. After surgery, the results were compared with histological grading according to Nottingham's Modification of Bloom–Richardson method.

Results: On cytological grading of 50 cases, 25 (50%) cases were graded as Grade II, 21 (42%) as Grade I, and 4 (8%) as Grade III. Whereas on histological grading, Grades I, II and III tumors were 17 (34%), 22 (44%), and 11 (22%), respectively. Overall concordance of cytological grading with histological grading was 76% with a kappa value of 0.605 and $p<0.001$.

Conclusion: The study showed that the cytological grade correlates well with the histological grade. Cytological grade can be of great value in evaluating the aggressiveness of tumor, neoadjuvant chemotherapy and can be used as a prognostic factor for better management of patients.

Keywords: Carcinoma breast, Robinson's grading, Nottingham's modified Bloom–Richardson grading, Fine-needle aspiration cytology (FNAC).

 DOI: http://dx.doi.org/10.22159/ajpcr.2022v15i7.44839. Journal homepage: https://innovareacademics.in/journals/index.php/ajpcr

INTRODUCTION

Breast cancer is the leading cause of death worldwide. It accounts around 24% of all female cancers and 11.6% of malignancies in both the sexes together [1]. A recent data from Globocan 2020 (India) shows that a total of 178,361 new cases of breast cancer were diagnosed in 2020, which is the highest number than any other type of cancer diagnosed in India in 2020 [2]. There were 90,408 deaths due to breast cancer which is again the highest number of deaths as compared to the deaths due to any other cancer in India in 2020 [2]. The incidence of breast cancer is 4–7 times higher in the United States and Europe than in other countries, but rates are rising worldwide [3].

Invasive ductal carcinoma is a group of malignant tumors of breast that have tendency to invade adjacent normal breast tissues and also metastasize to distant organs. These lesions can be classified into the various histological types. Out of these, invasive ductal carcinoma, not otherwise specified (NOS), is most common type. Many terms have been used to describe these tumors, including invasive carcinoma of no special type (NST) or ductal carcinoma, NOS. Nowadays, preferred term accepted by the WHO is invasive ductal carcinoma, no special type. This occupies about 75–80% of all breast carcinomas [4].

Several parameters such as histological grading and hormone receptor markers have been used to measure special prognostic groups and to predict the response to treatment protocols. FNAC is valuable tool in work up of all breast abnormalities including the palpable and non-palpable lumps. FNAC has very high sensitivity and specificity. The idea of cytological grading was to assess tumor before surgery so that most suitable treatment can be selected as soon as possible and morbidity associated with over treatment of low-grade lesion can be avoided. The essential aspect of the oncologic pathology has been the morphological appearance of tumors and can be correlated with the grade of malignancy [5]. Histological grading describes the microscopic growth pattern of the invasive ductal carcinoma as well as cytological characteristics of differentiation extent. Grading of the breast cancer has been shown to be of high prognostic significance by the various studies. If the histological grading correlates well with the cytological grading, it can be of great value in pre-operative prognostication and management of breast cancer. If grading is incorporated in cytology reports, it adds to objectivity, great reproducibility, and high authenticity to the report [6].

METHODS

This cross-sectional study was carried out on 50 patients in age group of 30–86 years with breast cancer at the Department of Pathology, Government Medical College, Patiala, Punjab. Patients who diagnosed as primary ductal carcinoma breast by FNAC, irrespective of age and sex, and all histopathology specimens with cytologically proven malignant tumors were included in the study. History of the patients was taken with relative thorough clinical examination.

FNAC of breast lump was done according to standard procedure using 22–23 G needle fixed to 20ml syringe with the help of Franzen's handle. Smears were stained with May–Grunwald–Giemsa and Papanicolaou stain. Cytological grading was done by Robinson's grading method [6]. It considered six different cytological parameters, that is, cell dissociation, nuclear size, cell uniformity, nucleoli, nuclear margin, and chromatin pattern. Each parameter was given a score of 1–3. Scores were summed up to reach a final score and cytological grading was done accordingly. Score of 6–11 given Grade I, score of 12–14 given Grade II, and score of 15–18 given Grade III (Table 1).

After surgery, specimens were fixed in 10% neutral buffered formalin for 24–72 hours, and then, grossing of the specimens was done. Sections were processed and stained with Hematoxylin and Eosin

Table 1: Robinson's cytological grading system

S. No.	Features	Score 1	Score 2	Score 3
1	Cell dissociation	Mostly in cluster	Mixture of scattered singly and clusters	Mostly scattered singly
2	Nuclear Size	1–2 times the RBC size	3–4 times the RBC size	>5 times the RBC size
3	Cell uniformity	Monomorphic	Mildly pleomorphic	Pleomorphic
4	Nucleoli	Indistinct	Noticeable	Prominent
5	Nuclear Margin	Smooth	Folds	Buds/clefts
6	Chromatin pattern	Vesicular	Granular	Clumped and clearing

Table 2: Nottingham's modification of Bloom– Richardson grading system

S. No.	Feature	Score 1	Score 2	Score 3
1	Tubule formation	>75%	10–75%	<10%
2	Nuclear pleomorphism	Small, regular uniform cells	Moderate variation in shape and size	Marked nuclear pleomorphism
3	Number of Mitoses/10 HPF	0–5	6–10	≥11

stain. Confirmation of invasive ductal carcinoma, NST was done on histopathological examination. Histological grading was done according to Nottingham's modification of Bloom–Richardson's grading method [7]. It includes three parameters, that is, tubule formation, cellular pleomorphism, and mitosis per 10 HPFs. Score of 1–3 was given to each parameter, and then, scores were summed up to reach a final score. Histological grading was done accordingly. Score of 3–5 was given Grade I, score of 6–7 given Grade II, and score of 8–9 given Grade III (Table 2).

Cytological grades were compared with histological grades. Statistical testing was done by percentage analysis and kappa (k) measurement of agreement.

Ethical issues

Ethical approval was taken from the Institutional Ethic Committee of Government Medical College, Patiala, before starting the study.

RESULTS

On cytological evaluation, all 50 cases were diagnosed as ductal carcinoma and grading was done using Robinson's grading system.

The patients age ranged from 30 to 86 years with a mean age of 53 years (Table 3 and Fig. 1).

Maximum patients encountered of the 5th and 6th decades of age comprising 30 patients (60%) of total. Only one male patient aged 65 years was encountered in our study (Fig. 1).

Out of total 50 cases, 21 (42%) were reported as Grade I, 25 (50%) as Grade II, and rest 4 (8%) as Grade III tumors on cytology by Robinson's method (Table 4 and Figs. 2-4).

The cytological diagnosis of malignancy (invasive ductal carcinoma, NST) was confirmed in these 50 patients on histopathology and grading of tumors was done according to Nottingham's modification of Bloom–Richardson's grading system. Seventeen (34%) cases were assigned Grade I, 22 (44%) cases Grade II, and 11 (22%) cases were given Grade III tumor (Table 4 and Figs. 2-6).

Overall concordance of cytological grading with histological grading was 76% (38/50). Kappa measurement of agreement was 0.605 (k=0.605). Correlation of cytological grading with histological grading was highly significant (p<0.001).

DISCUSSION

Palpable lump of breast is a common clinical problem presented to surgeons and a multidisciplinary approach is used that based on "triple test," that is, analyzing clinical and radiological findings in combination

Table 3: Age-wise distribution of patients (n=50)

Age group (years)	Number of patients	Percentage
21–30	01	02
31–40	09	18
41–50	12	24
51–60	18	36
61–70	08	16
71–80	01	02
81–90	01	02
Total	50	100

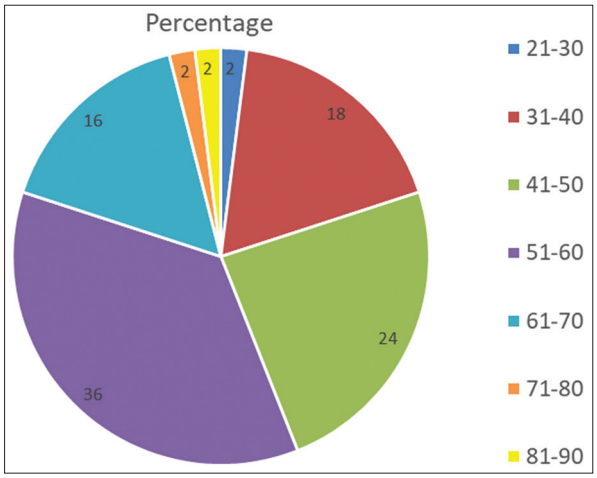

Fig. 1: Age-wise distribution of patients (n=50)

with cytological features, to diagnose the lesion and to determine the best treatment modality for the patient [8]. The importance of histopathological grading is very well established. As majority of the breast carcinoma cases diagnosed on FNAC, it is very important to perform grading on aspirates also, which can provide valuable information to the treating practitioner to plan the best management.

In our study, the age of 50 patients with carcinoma breast ranged from 30 to 86 years with mean age being 53 years. Majority of the patients (60%) were in the 5th and 6th decades of life, as also reported in various Indian studies and studies from various Asian countries. Mean age of the breast cancer patients in six hospital-based cancer registries (NCRP, 1994–1998) had been reported to be 50–53 years [9]. Hospital-based studies on carcinoma breast carried out at Delhi and Jaipur in the year 2002 also reported mean age to be 49 years and 48.8 years respectively [10].

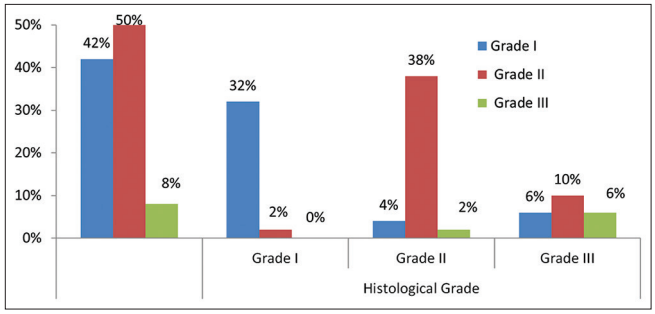

Fig. 2: Bar chart showing distribution of cases according to cytological and histological grading along with comparison between two grading systems (n=50)

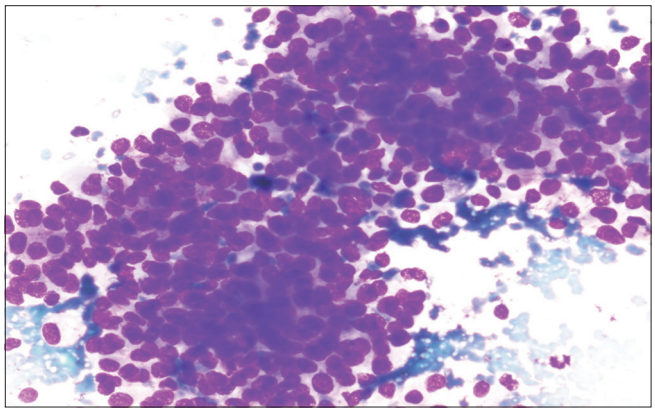

Fig. 3: Infiltrating ductal carcinoma breast, Grade II (MGG ×400)

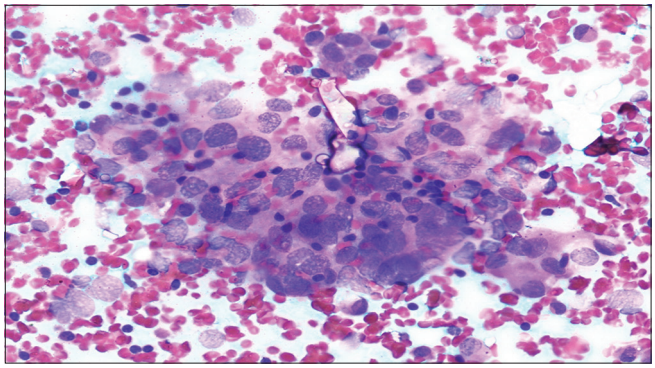

Fig. 4: Infiltrating ductal carcinoma breast, Grade III (MGG ×400)

Table 4: Distribution of cases according to cytological and histological grading along with comparison between two grading systems (n=50)

Cytological grade			Histological grade						Concordance rate
			Grade I		Grade II		Grade III		
Grade	No.	%	No.	%	No.	%	No.	%	%
I	21	42	16	32	02	04	03	06	76.2%
II	25	50	01	02	19	38	05	10	76.0%
III	04	08	00	00	01	02	03	06	75.0%
TOTAL	50	100	17	34	22	44	11	22	
Absolute concordance									76.0%
Kappa (K)									0.605
p value									<0.001

There are many cytological grading systems for carcinoma breast including Fisher's, Mouriquand's, Robinson's, Howell's, Khan's, and

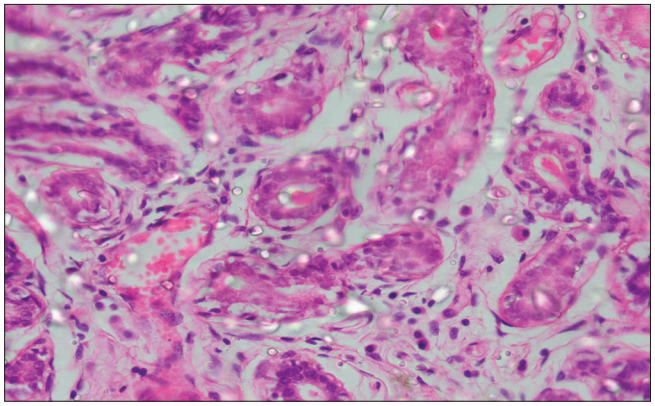

Fig. 5: Invasive ductal carcinoma, no special type, Grade I (H and E ×400)

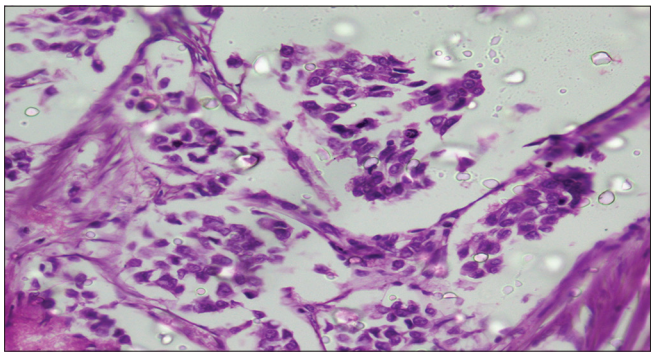

Fig. 6: Invasive ductal carcinoma, no special type, Grade II (H and E ×400)

Table 5: Comparison of concordance rate for individual grade in various studies

Authors	Year	Number of cases	Grade I	Grade II	Grade III
Bhargava *et al.* [19]	2005	18	100%	83.3%	89%
Pandya and Shah [20]	2012	59	79.2%	73.1%	66.7%
Sood *et al.* [21]	2013	116	75%	70.7%	60%
Pal and Gupta [17]	2016	50	78.6%	79.3%	71.4%
Deshmukh *et al.* [15]	2020	50	66.7%	75.0%	85.7%
Present study	2021	50	76.2%	76.0%	75%

Taniguchi's grading system. These all grading systems have good correlation with Modified Bloom–Richardson grading system. As of more simplicity, easy reproducibility, more sensitivity, and more objective set of criteria, Robinson's method was considered better than other methods [8–11].

In our study on 50 patients, the majority of the tumors on cytology were Grade II (50%), followed by Grade I (42%) and Grade III (8%). In the studies done by Robinson *et al.* [6] (1994), Khan *et al.* [12] (2003), Meena *et al.* [13] (2006), Phukan *et al.* [14] (2015), and Deshmukh *et al.* [15] (2020), maximum number of cases were reported as Grade II on cytology and were comprising 46.2%, 53.0%, 51.0%, 48%, and 48%, respectively, with average of 49.2%, which is almost equal to present study, where prevalence of this grade is 50.0%.

Although several markers have been used to identify specific prognostic groups and predict response to treatment, histopathological grade still remains one of the best and cost-effective predictors of tumor behavior. The assignment of histopathological grade to all the breast carcinomas has, therefore, been recommended as standard in all surgical pathology

reports. On histopathology, Grades I, II, and III tumors were 34%, 44% and 22% respectively. In the study of Deshmukh *et al.* [15] (2020), Grades I, II, and III were 30%, 46%, and 24%, respectively, almost similar to our study.

Absolute concordance in our study was 76% which is very close to the absolute concordance in the studies of Meena *et al.* [13] (2006), Saha *et al.* [8] (2013), Handa *et al.* [16] (2014), Pal and Gupta [17] (2016), Jayasree *at al.* [18] (2020), and Deshmukh *et al.* [15] (2020), which was 79%, 77.1%, 78%, 78%, 78.2%, and 75.8%, respectively, very close to present study.

Although concordance for different grades varied in different studies in the literature, concordance of individual grades in studies of Pandya and Shah [20] (2012), Pal and Gupta [17] (2016), and Deshmukh *et al.* [15] (2020) is almost similar with the present study. In contrast to our study, individual grade concordance in study of Bhargava *et al.* [19] (2005) and Sood *et al.* [21] (2013) is different which is probably due to difference in sample size and subjective variabilities (Table 5).

Cytological grading system demonstrated highly significant correlation ($p<0.001$) and a substantial kappa value of agreement ($k=0.605$) with the histopathological grading system.

The disparity between cytological and histological observations was anticipated and the reason may be due to the inability of cytological grading system to objectively assess tubule formation and mitotic index, as being the integral part of histopathological grading system.

CONCLUSION

This study showed that the cytological grade correlates well with the histological grade. Thus, it is feasible and fairly reliable to grade breast carcinoma on aspirate smears and incorporate it in the FNAC report. This can be of great value in evaluating the aggressiveness of tumor and neoadjuvant chemotherapy and can be used as a prognostic factor for better management of patients.

AUTHORS' CONTRIBUTIONS

All the authors have contributed toward the preparation, review preparation, and editing of the manuscript. Dr. Shiv Kumar: Collection of data. Dr. Ninder Kumar: Writing of manuscript and interpretation of data. Dr. Ramesh Kumar and Dr. Harnam Singh Rekhi: Proof reading of manuscript and analysis of data.

CONFLICTS OF INTEREST

All the authors have none to declare.

AUTHORS FUNDING

No funding received for the completion and publication of the article.

REFERENCES

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, *et al*. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2021;71:209-49. doi: 10.3322/caac.21660
2. Available from: https://www.gco.iarc.fr/today/data/factsheets/populations/900-world-fact-sheets.pdf
3. Susan CL. The breast. In: Robbins SL, Cotran RS, Kumar V, Abbas AK, Fausto N, Aster JC, editors. Robbins and Cotran Pathologic Basis of Disease. 9th ed. Philadelphia, PA: Saunders Elsevier; 2017. p. 1053.
4. Roychowdhury M. NST (Ductal). Available from: https://www.pathologyoutlines.com/topic/breastmalignantductalNOS.html [Last accessed on 2022 Jun 12].
5. Robinson IA, McKee G, Nicholson A, D'Arcy J, Jackson PA, Cook MG, *et al*. Prognostic value of cytological grading of fine-needle aspirates from breast carcinomas. Lancet 1994;343:947-9. doi: 10.1016/s0140-6736(94)90066-3, PMID 7909010
6. Mouriquand J, Pasquier D. Fine needle aspiration of breast carcinoma: A preliminary cytoprognostic study. Acta cytol 1980;24:153-9. PMID 6245554
7. Simpson JF, Gray R, Dressler LG, Cobau CD, Falkson CI, Gilchrist KW, *et al*. Prognostic value of histologic grade and proliferative activity in axillary node-positive breast cancer: Results from the eastern cooperative oncology group companion study, EST 4189. J Clin Oncol 2000;18:2059-69. doi: 10.1200/JCO.2000.18.10.2059, PMID 10811671
8. Saha K, Raychaudhuri G, Chattopadhyay BK, Das I. Comparative evaluation of six cytological grading systems in breast carcinoma. J Cytol 2013;30:87-93. doi: 10.4103/0970-9371.112647, PMID 23833396
9. Nandakumar A. National cancer registry programme. Consolidated Report of the Population-based Cancer Registries. New Delhi, India: Indian Council of Medical Research; 1990. p. 96.
10. Gupta P, Sharma RG, Verma M. Review of breast cancer cases in Jaipur region. J Indian Med Assoc 2002;100:282-3.
11. Briffod M, Le Doussal V, Spyratos F. Cytologic nuclear grading of fine needle cytopunctures of breast carcinoma. Comparison with histologic nuclear grading and image cytometric data. Anal Quant Cytol Histol 1997;19:114-22. PMID 9113304
12. Khan MZ, Haleem A, Al Hassani H, Kfoury H. Cytopathological grading, as a predictor of histopathological grade, in ductal carcinoma (NOS) of breast, on air-dried Diff-Quik smears. Diagn Cytopathol 2003;29:185-93. doi: 10.1002/dc.10285, PMID 14506669
13. Meena SP, Hemrajani DK, Joshi N. A comparative and evaluative study of cytological and histological grading system profile in malignant neoplasm of breast--an important prognostic factor. Indian J Pathol Microbiol 2006;49:199-202. PMID 16933714
14. Phukan JP, Sinha A, Deka JP. Cytological grading of breast carcinoma on fine needle aspirates and its relation with histological grading. South Asian J Cancer 2015;4:32-4. doi: 10.4103/2278-330X.149948, PMID 25839018
15. Deshmukh SD, Khandelwal R, Khaparde SH, Shinde BB, Ayesha N, Khonde D. Robinson's cytological grading on fine needle aspirates (FNAC) of breast cancers and its correlation with histopathological grading. Int J Clin Diagn Pathol 2020;3:376-9. doi: 10.33545/pathol.2020.v3.i1f.200
16. Handa U, Kumar A, Kundu R, Dalal U, Mohan H. Evaluation of grading and hormone receptor immunostaining on fine needle aspirates in carcinoma breast. J Cytol 2015;32:1-5. doi: 10.4103/0970-9371.155222, PMID 25948935
17. Pal S, Gupta ML. Correlation between cytological and histological grading of breast cancer and its role in prognosis. J Cytol 2016;33:182-6. doi: 10.4103/0970-9371.190449, PMID 28028331
18. Jayasree KA, Mini B, Kamala VV. Cytological grading on aspirates of breast carcinoma and its correlation with histopathological grading. J Evid Based Med Healthc 2020;7:1880-3.
19. Jain M, Agarwal K, Thomas S, Singh S, Bhargava V. Critical appraisal of cytological nuclear grading in carcinoma of the breast and its correlation with ER/PR expression. J Cytol 2008;25:58. doi: 10.4103/0970-9371.42445
20. Pandya AN, Shah NP. Comparative evaluation of Robinson's cytological grading with Elston and Ellis' Nottingham modification of bloom Richardson histopathology grading for breast carcinoma. Natl J Community Med 2012;3:491-5.
21. Sood N, Nigam JS, Yadav P, Rewri S, Sharma A, Omhare A, *et al*. Comparative study of cytomorphological Robinson's grading for breast carcinoma with modified bloom-Richardson histopathological grading. Pathol Res Int 2013;2013:146542. doi: 10.1155/2013/146542, PMID 24187646