ORIGINAL ARTICLE

Evaluation of Robinson's Cytological Grading of Breast Carcinoma and its Correlation with Elston-Ellis Modification of Scarff-Bloom-Richardson's Histological Grading

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Abstract:

Introduction: Fine Needle Aspirate (FNA) can serve as a valuable adjunct in cases of breast carcinoma by predicting cytological grading and guide the selection of appropriate therapy. *Aim and Objectives:* To evaluate the cytological grading in breast carcinoma cases by using Robinson's grading and correlate it with Elston-Ellis modification of Scarff-Bloom-Richardson's grading. *Material and Methods:* This study was carried out in the Department of Pathology, Bhagat Phool Singh Government Medical College for Women, Khanpur Kalan, Sonepat from 1st July 2015 to 30th June 2019. Fifty-one cases of breast carcinoma that underwent both fine needle aspiration and mastectomy were included. Robinson's grading system was used for cytological grading and results were correlated with Scarff-Bloom-Richardson's histological grading. Concordance rates, sensitivity and specificity were calculated. *Results:* The overall concordance rate between cytological and histological grading was 76.47%. Sensitivity was high in cytological Grade I tumors (83.33%) and least in cytological Grade III tumors (66.67%). Specificity was high in cytological Grade III tumors (94.29%) and least in cytological Grade II tumors (77.42%). *Conclusion:* Robinson's cytological grading is easy, reproducible and correlates well with histological grade. It can be used routinely in predicting the prognosis and better management of patients as per the grade of tumor.

Keywords: Breast carcinoma, Prognosis, Robinson's cytological grading, Scarff-Bloom-Richardson's grading.

Introduction:

Breast carcinoma is the most common malignant tumor affecting 2.1 million women each year and the leading cause of cancer related deaths in women worldwide [1]. It is the most common cancer in urban females and second to cancer cervix among rural females in India [2]. In 2018, a total of 1,62,468 new cases and 87,090 deaths were reported from breast cancer in India. Several prognostic indicators for breast carcinoma are tumor size, histological subtype, grade, axillary lymph node status, hormone receptor and human epidermal growth factor receptor status and cell Proliferation Index [3].

Histological grading of breast carcinoma using Scarff-Bloom-Richardson's histological grading described by Elston and Ellisis widely accepted and has been found to have good prognostic correlation. It is derived by scoring tubule formation, nuclear pleomorphism and mitotic frequency [4]. In carcinoma breast, clinical examination, mammography and Fine-Needle Aspiration (FNA)

forms a diagnostic triad, which has approximately 100% accuracy [5]. FNA has become widely accepted as a reliable diagnostic tool with high sensitivity and specificity with a minimal rate of complications [6]. FNA cytology is highly sensitive (65-99%) and specific (96-100%) [7].

Neoadjuvant therapy is becoming increasingly popular as first line treatment modality for aggressive breast tumors to downstage the tumors, making it operable and reducing the morbidity. Among many criteria for selection of patients for neoadjuvant therapy, one of them is high grade tumors [8-9]. Thus, it is desirable to grade the tumor preoperatively on FNA cytology so that the most optimal treatment could be selected. The purpose of the present study was to find the utility of cytological grading of breast carcinoma on using Robinson's system and compare it with histological grading based on method proposed by Scarff- Bloom-Richardson's system.

Material and Methods:

This is a cross-sectional study conducted in the Department of Pathology, Bhagat Phool Singh Government Medical College for Women, Khanpur Kalan, Sonepat, Haryana from 1st July 2015 to 30th June 2019. Sample size was calculated with help of N-master software using formula: $n=Z^2P(1-P)/d^2$. The study was approved by Institutional Ethics Committee. Fifty-one cases of breast carcinoma that underwent both fine needle aspiration and mastectomy were included in the study. Cases with history of recurrent breast carcinoma, uncooperative patients and who had received chemotherapy and radiotherapy prior to mastectomy were excluded. A written informed consent was obtained from all patients.

After taking proper history and examining the breast lump, FNA of breast lumps was performed using 22 gauge needle attached to 10 ml syringe and smears were prepared from the aspirated material. One or two smears fixed in 95% ethyl alcohol were stained with Papanicolaou stain while rest of the smears were air dried and stained with Romanowsky stain. Cytology smears stained with Papanicolaou stain were used for Robinson's cytological grading. This system takes account of six parameters namely cell dissociation, cell size, cell uniformity, nucleoli, nuclear margin and chromatin pattern. Each parameter was given a score of 1-3 and final score was obtained by adding scores of all six parameters. A score of 6-11 was labelled as Grade I, 10-12 as Grade II and 15-18 as Grade III.

Corresponding mastectomy specimens received were fixed adequately in 10% formalin. After routine processing, hematoxylin and eosinstained sections, were examined and tumor was graded using Elston-Ellis modification of Scarff-Bloom-Richardson's grading. Three parameters were taken into consideration- tubule formation, nuclear pleomorphism and mitotic count. Olympus Microscope Ch20i was used to count mitotic figures using 40× objective lens with field diameter of 0.65 mm. Each parameter was assigned a score of 1 to 3 and final sum was obtained by adding scores of all three parameters. Scores of 3-5 were reported as Grade I, 6-7 as Grade II and scores of 8-9 as Grade III.

The data were plotted on Microsoft excel and evaluated using Statistical Package for Social Sciences (SPSS) software version 22. Taking histopathology grading as gold standard, True Positive (TP), True Negative (TN), False Positive

(FP) and False Negative (FN) cases were calculated for cytological grading of breast carcinoma cases. Concordance rates, sensitivity and specificity were calculated for all three grades:

Concordance rate=Number of cytological and histological concordant cases /total cases × 100

Sensitivity= TP/ TP+FN

Specificity= TN/ TN+FP

Also, kappa value (κ) and weighted kappa was calculated to measure the degree of agreement between cytological and histological grading.

Results:

The present study comprised of total 51 female patients of carcinoma breast diagnosed initially by fine needle aspiration and later confirmed by histology. The age of the patients ranged from 21 to 70 years with maximum number of cases belonged to 40-49 years age group. All patients were females. Distribution of cases according to cytological and histological grading was recorded (Figs. 1 and 2). The concordance rate was found maximum for Grade III (85.71%) followed by Grade II (75.86%) and least for Grade I (62.50%). The overall cytological and histological correlation for all three grades was found in 39 out of 51 cases with absolute concordance rate of 76.47% (Table 1). On statistical analysis for strength of agreement between cytological and histological grading, kappa value was 0.598 which indicated moderate agreement while weighted kappa was 0.655 which showed substantial agreement (Table 2). The sensitivity of Robinson's cytological grading for breast carcinoma was 83.33%, 81.48% and 66.67% for Grade I, II and III respectively. The specificity for Grade I, II and III was found to be 93.47%, 75.86% and 94.87%. Thus, Table 3 showed that sensitivity was highest for Grade I followed by Grade II while specificity was found maximum for Grade III followed by Grade I.

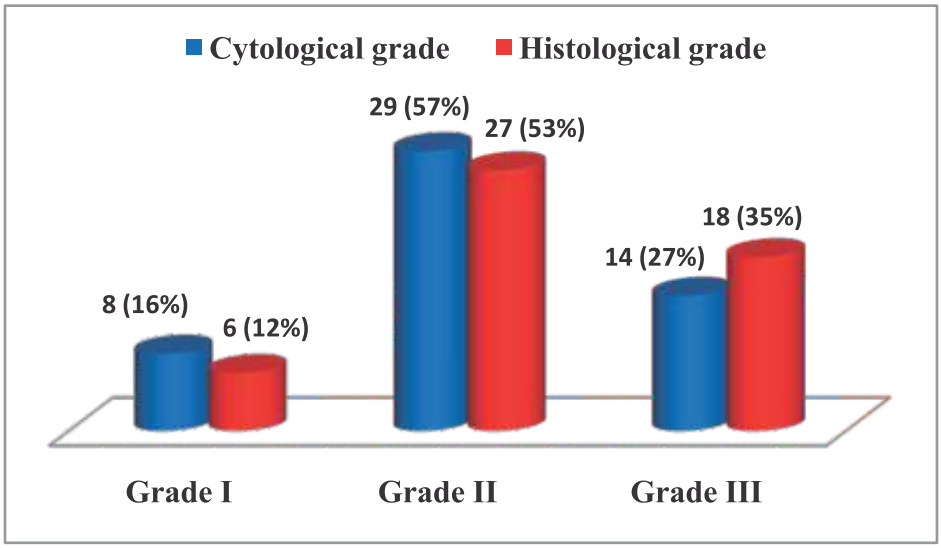

Fig. 1: Distribution of Breast Carcinoma Cases Using Cytological and Histological Grading

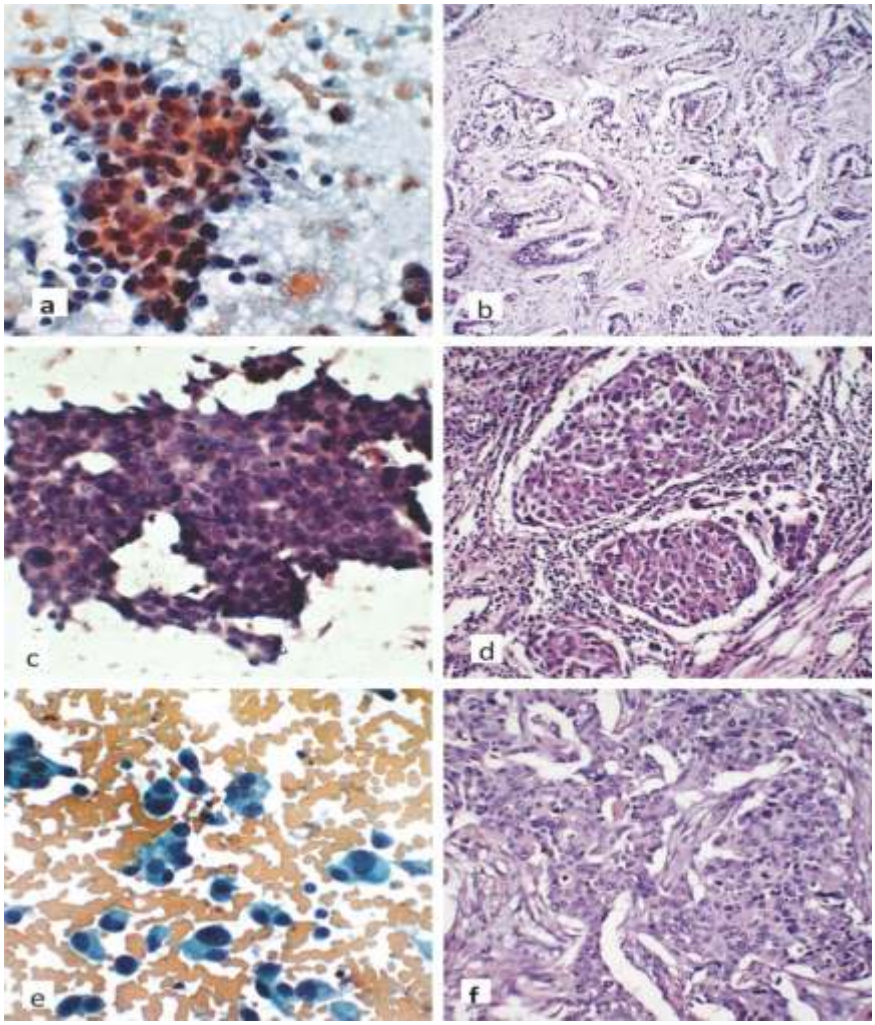

Fig. 2: Microphotographs: (a) Cytological Grade I ductal carcinoma showing tumor cells in cohesive groups, nuclei show mild pleomorphism, smooth nuclear margin and inconspicuous nucleoli (Pap,× 400), (b) Histological Grade I with tubule formation (H&E, × 200), (c) Cytological Grade II ductal carcinoma showing cells in loosely cohesive groups of moderately pleomorphic nuclei, smooth nuclear margin, granular chromatin and single prominent nucleoli (Pap, × 400), (d) Histological Grade II with clusters of moderately pleomorphic tumor cells (H&E, × 200), (e) Cytological Grade III ductal carcinoma showing predominantly dispersed cells, large pleomorphic nuclei irregular nuclear margin, granular nuclear chromatin and prominent nucleoli (Pap, × 400), (f) Histological Grade III with sheets of highly pleomorphic tumor cells with many mitotic figures (H&E, × 200).

Table 1: Comparison of Case Distribution between Cytological and Histological Grades

Cytological Grade	Total Number of Cases	Histological Grade			Concordance Rate
		I	II	III	
I	8	5	3	0	62.5%
II	29	1	22	6	75.86%
III	14	0	2	12	85.71%
Total	51	6	27	18	
Absolute Concordance Rate: 39/51= 76.47%					

Table 2: Agreement between Cytological and Histological Grading by Statistical Analysis

	Value (95% Confidence Interval)	Standard Error	Strength of Agreement
Kappa Value	0.598 (0.398-0.808)	0.107	Moderate
Weighted Kappa	0.655 (0.470-0.840)	0.094	Substantial

Table 3: Sensitivity and Specificity of Robinson's Cytological Grading

Cytological Grade	True Positive	False Positive	True Negative	False Negative	Sensitivity	Specificity
I	5	3	43	1	83.33%	93.47%
II	22	7	22	5	81.48%	75.86%
III	12	2	37	6	66.67%	94.87%

Table 4: Comparison of Concordance Rates Reported in Different Studies

Studies	Number of Cases	Concordance Rates (%)			
		Overall	Grade I	Grade II	Grade III
Pandey *et al.* (2012) [18]	59	74.57	79.61	73.07	66.66
Sood *et al.* (2013) [19]	116	68.97	75	70.67	60
Chandanwale *et al.* (2014) [20]	69	86.96	100	88.63	76.47
Mustaphi *et al.* (2014) [21]	44	80.1	62.5	88.9	88.9
Phukan *et al.* (2015) [13]	50	72.20	50	83.30	83.30
Pal *et al.* (2016) [15]	50	78	78.57	79.31	71.42
Sinha *et al.* (2016) [16]	150	96	89.47	100	100
Jayasree *et al.* (2020) [22]	55	78.18	60.71	100	85.71
Present study (2021)	51	76.47	62.50	75.86	85.71

Discussion:

Histological grading is considered as one of the key criterion for estimation of prognosis in cases of breast carcinoma [10]. Elston-Ellis modification of Scarff-Bloom-Richardson's grading is the most widely used system for histological grading. Nowadays, FNA cytology of breast has been an integral part of the initial diagnosis of patients with breast lumps as it is simple, cost effective, minimally invasive technique with quick and accurate results.

Fine needle aspiration is considered as reliable and rapid method for diagnosis of breast carcinoma. Prediction of grading of breast carcinoma on cytological smears will increase the utility of FNA cytology from diagnostic to prognostic purpose without any added expenses and morbidity for the patient [11]. The 'Uniform approach to report breast FNA' recommended by National Cancer Institute, Bethesda suggested that tumor grading on FNA material should be incorporated by all pathologists in their cytology reports for prognostication [12]. Cytological grading will allow in situ tumor assessment and guide appropriate treatment modality for patients depending on grade.

In the present study, cytology smears were graded using Robinson's grading and correlated with histological grading by Scarff-Bloom-Richardson's system. The concordance rate between the two was observed to be 76.47% which is comparable with many previous studies (Table 4). In the present study, the overall discordance rate of 23.53% was reported with none of the cases were upgraded or downgraded by two grades. Inability to recognize nuclear features, difference in observer's perception of cytological features while assigning

grade and variation of nuclear atypia within a tumor itself may be responsible for inability to correlate in 12 (23.53%) cases in our study.

In our study, moderate strength of agreement was found between cytological and histological grade with kappa value of 0.59 while weighted kappa indicated substantial agreement with value of 0.65 (Table 2). Majority of the discordance was observed in Grade I tumors (5/8). This can be attributed to two reasons; one is due to less number of cases observed in Grade I and second is due to the cytological variation in different parts of a tumor which may not be identified in smear examination as limited area gets aspirated in cytology as compared to histological examination of tumor [9, 11-12]. Sensitivity and specificity reported in our study was comparable with many previous studies [14-15].

Study conducted by Robinson *et al.* in 1994 concluded that all the cytological features mentioned in the grading system are accountable for final score with cell dissociation and presence of nucleoli as the most powerful predictive factors. Sinha *et al.*[16] suggested that cytological grading by Robinson is reasonably trustworthy method for pre-operative grading of breast tumors and will guide the treating doctor about neoadjuvant therapy, type of surgery and level of lymph node resection beforehand. They also concluded that presence of at least eight epithelial cell clusters in smears provide better concordance between grading systems.

Saha *et al.* [17] compared six three tier cytological grading systems and found Robinson's system as the easy, reproducible and most objective system for grading breast carcinoma on aspiration smears. Pal *et al.*[15] concluded that cytological grading precisely correlates with histological grading and should be reported universally by pathologist in their reporting to guide the surgeon regarding aggressiveness of tumor and judicious use of neoadjuvant therapy for high grade tumors.

Pandey *et al.* [18] compared Robinson's and Mouriquand's grading system with each other and with histological grading. They concluded that best comprehensive cytological grading of breast cancers is possible by Robinson's method because of well-defined and objective criteria and better reproducibility.

To conclude, high concordance was observed between histological grading by Scarff-Bloom-Richardson's system and Robinson's cytological grading system. With increasing use of neo-adjuvant chemotherapy for higher grade tumors (Grades II and III), preoperative cytological grading can prove to be beneficial tool in deciding the treatment protocol in these patients. Thus, cytological grading should be incorporated invariably in FNA reports for breast carcinoma.

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How to cite this article:

Agarwal R, Gathwal MB, Gathwal C, Rana P, Singh K, Sindhu A. Evaluation of Robinson's Cytological Grading of Breast Carcinoma and its Correlation with Elston-Ellis Modification of Scarff-Bloom-Richardson's Histological Grading. *J Krishna Inst Med Sci Univ* 2021;10(3):54-61.

Submitted: *09-Feb-2021* ***Accepted:*** *01-Jun-2021* ***Published:*** *01-Jul-2021*