

Correlation of Robinson's Cytological Grading with Elston and Ellis' Nottingham Modification of Bloom Richardson Score of Histopathology for Breast Carcinoma

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ABSTRACT

Introduction: Invasive carcinoma of the breast is one of the leading causes of death in women. In developing countries, fine needle aspiration cytology (FNAC) of the breast is used for preoperative diagnosis of breast cancer due to low cost. The grading system of breast carcinoma on FNAC is widely accepted. In the era of neoadjuvant therapy, if grading of breast carcinoma is incorporated in FNAC reports for prognostication, it will be of great help especially in patients with locally advanced disease, older patients with accompanying chronic disease and patients who reject surgery. Hence, there is much to be gained by grading a tumor on FNAC.

Materials and methods: The present study was conducted on 40 cases of cytologically diagnosed breast carcinomas. Fine needle aspiration cytology smears were graded by Robinson cytological grading system. All surgical specimens were processed and the histological grading of the resulting slides was done by the Nottingham modification of Bloom Richardson score. Then, the cytological grade was compared with the histological grade and statistical analysis was done.

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Results: Based on Robinson grading method, cases were classified into grade I (15%), grade II (55%) and grade III (30%). Based on the Nottingham modification of Bloom Richardson (SBR) grading method, the cases were classified as grade I (5%) and grade II and III (47.5%) each. A total concordance rate between both the grading systems was seen in 65% of cases. A positive correlation was found and there was a significant association between Robinson cytological grading and SBR histological grading.

Conclusion: Grading breast carcinoma on cytology allows its prognostic evaluation along with diagnostic value without any additional morbidity or expense to the patient. Thus, it is recommended to grade breast carcinomas on FNAC. It helps in deciding the proper line of treatment, so that patients can have a better prognosis.

Keywords: fine needle aspiration cytology, Robinson grading on cytology, Bloom Richardson score.

INTRODUCTION

In India, amongst females, breast cancer accounts for the second most common position among all cancers. Prognosis of breast carcinoma depends on various parameters, including tumor type, status of hormone receptors, DNA ploidy, markers of cell proliferation and different oncogenes expression (1). Apart from these, its early diagnosis and grading also plays an important role. Nowadays, fine needle aspiration cytology (FNAC) along with core biopsy of the breast is routinely used for diagnosing breast cancer prior to surgery. Fine needle aspiration cytology and core biopsy are safe, reliable and time saving procedures for patients with breast cancer. Also, they cause little discomfort to the patient. Grading of the tumor on cytology provides information about aggressiveness and biological behaviour of the tumor. It also offers important information on prognosis and guides towards selecting optimal therapy for the patient (2). Nottingham modification of Elston and Ellis Bloom Richardson score is a widely accepted grading system on histopathology because it has a good prognostic correlation. Grading the breast carcinoma on FNA material is a not only simple and feasible method, but also a reproducible approach, especially for patients who may need chemotherapy and/or radiotherapy or neoadjuvant therapy prior to the resection of the tumor. For breast cancer, nuclear grading on cytology is easy to perform, correlates well with nuclear grade on tissue and hence, it should be incorporated in the FNAC reports whenever possible, as it is one of the important cytological parameters (3, 4), which is also recommended by the National Cancer Institute

Bethesda (5). The aim of the present study was to compare breast carcinoma grading on cytology by Robinson grading system with grading on histopathology by Bloom Richardson scoring method. □

MATERIALS AND METHODS

The present prospective study was conducted from December 2018 to June 2020 in the Pathology Department of Dhiraj Hospital, Sumandeep Vidyapeeth University Medical College, Pipariya, Waghodia, India, after approval of the ethics committee. All patients with breast carcinoma during the study period who underwent both cytology and histopathology examination were included in the study. Inadequacy of specimen for cytological or histopathological analysis was the exclusion criteria for our research. Detailed clinical history and physical examination was done in all participants to our study. Informed consent for FNAC was obtained from all patients. Fine needle aspiration cytology was performed using 22G disposable needle and plastic syringe of 10 mL (6-19). For the fixation of smears, 95% alcohol was used; staining was done by PAP, Giemsa and hematoxylin and eosin (H and E) staining system; and Robinson cytological grading system was used for tumor grading. In the Robinson's scoring system for breast tumors on cytology, six different cytological features were taken into consideration for grading the tumor viz. dissociation of cells, size of cell, cell uniformity, nucleolus whether prominent or not, nuclear membrane regular or irregular and nuclear chromatin. The biopsy of the same breast carcinoma cases was examined in histopathology and BR grading was given. Collected

data was analysed statistically by calculating concordance rates between two grading systems. Sensitivity and specificity were calculated for each cytological grade for the method of cytological grading described by Robinson. Spearman's correlation coefficient and Fisher exact test were used to find out the correlation and strength of association between the grading systems on cytology and histopathology. $\square$

RESULTS

The current study included 40 patients with breast cancer aged between 30 and 82 years, out of which 39 subjects had NOS (not otherwise specified) invasive breast carcinoma and one patient had invasive lobular carcinoma. Out of the 40 cases with breast carcinoma, 37 subjects were of females and three males. The left sided breast was more commonly involved than the right sided one. The central quadrant of the breast was the most common site for tumor involvement. Tumor size ranged between 1.5 cm and 14 cm, with the majority of cases having a tumor size of 3–10 cm. The 51–60-year-old age group had the highest number of cases (n=11, 27.5%), followed by the 31–40- (n=9, 22.5%) and 41–50-year-old age groups (with n=9, 22.5% each), the 61–70-year-old age group (n=5, 12.5%), the 71–80-year-old age group (n=4, 10%), and the 21–30- and 81–90-year-old age groups (with n=1, 2.5% each) (Table 1).

Robinson cytological grading identified six (15%) cases with grade I, 22 (55%) with grade II and 12 (30%) with grade III (Figures 1, 2 and 3). The total numbers of cases with various cytologic nuclear grades are summarised in Table 2. Gra-

TABLE 2. Distribution of cases – Robinson cytological grade

Grade	Number of cases	Percentage (%)
I	06	15
II	22	55
III	12	30
Total	40	100

TABLE 3. Distribution of cases – SBR histological grade

Grade	Number of cases	Percentage (%)
I	02	5
II	19	47.5
III	19	47.5
Total	40	100

TABLE 4. Calculation of sensitivity and specificity of Robinson cytological grading system in each cytological grade considering histological grade as a base

Cytology grade	True positive cases	False positive cases	True negative cases	False negative cases	Sensitivity (%)	Specificity (%)
I	1	5	33	1	50	86.8
II	14	8	13	5	73.6	61.9
III	11	1	21	8	58	95.4

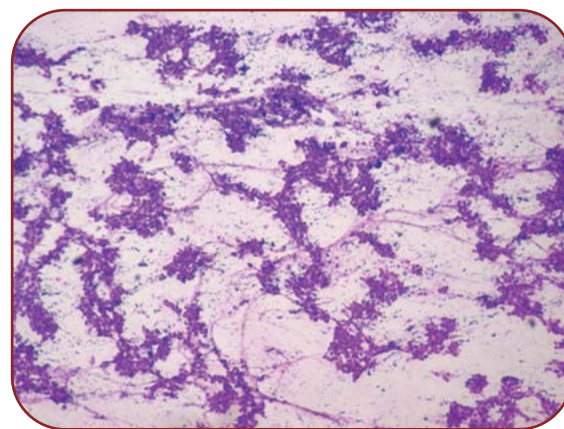


FIGURE 1. Pleomorphic cells with single and multiple prominent nucleoli in cluster as well as singly scattered on FNA smear (H & E stain, 4X)

TABLE 1. Complication rates in operated versus non-operated cases

Age range (years)	Total number of cases	Percentage (%)
21-30	1	2.5
31-40	9	22.5
41-50	9	22.5
51-60	11	27.5
61-70	5	12.5
71-80	4	10
81-90	1	2.5

ding on histopathology was done by Nottingham modification of SBR histological grade, which showed two cases with grade I (5% of total number of cases), 19 cases with grade II (47.5%) and 19 cases with grade III (47.5%). The total num-

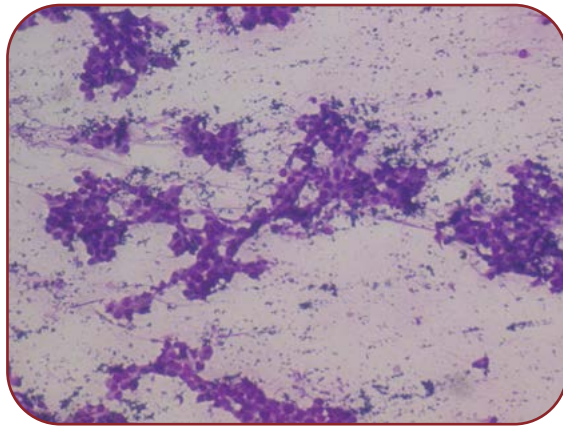


FIGURE 2. Grade III breast carcinoma on Robinson grading on FNA smears (H & E stain, 10X)

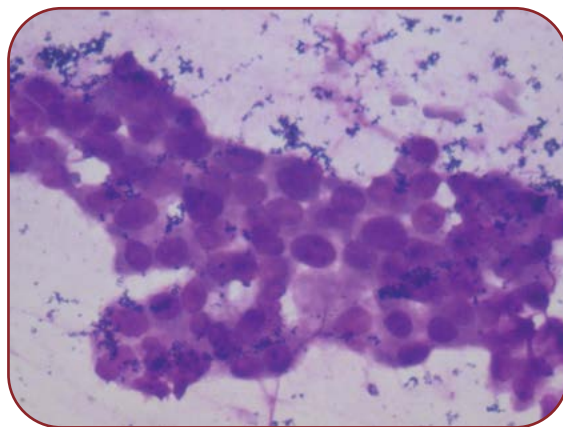


FIGURE 3. Highly pleomorphic cells with prominent nucleoli on FNA smear (H & E stain, 40X)

bers of cases with various histologic nuclear grades are summarised in Table 3. There were six cases with grade I on Robinson cytological grading, of which one case was grade I, four cases were upgraded as grade II and one case upgraded to grade III on SBR histological grading system. Similarly, there were 22 cases with grade II on Robinson cytological grade, of which 14 with grade II and seven upgraded as grade III; one case was downgraded as grade I on SBR histological grading system. Out of the 12 cases with grade III on Robinson cytological grading system, 11 cases were grouped as grade III and one case was downgraded as grade II on SBR histological grade. A total concordance rate between Robinson cytological grading system and SBR histological grade was seen in 26 (65%) of the 40 studied cases.

According to Table 4, for cytological grade I tumors, sensitivity was 50% and specificity 86.8%. For cytological grade II tumors, sensitivity

was 73.6% and specificity 61.9%, while for cytological grade III tumors, sensitivity was 58% and specificity 95.4%.

The Spearman correlation coefficient was determined. The r-value of 0.570 and p value of 0.000 indicated a positive correlation and a significant association between Robinson cytological grading and Nottingham modification of Bloom Richardson score on histopathology.

Also, Fisher Exact test was performed to check the association between the cytological and histological grades. The p-value of Fisher exact test was 0.01 (<0.05), which indicated a significant association between Robinson cytological grade and Nottingham modification of Elston and Ellis's Bloom Richardson score. □

DISCUSSION

Nowadays in India, the incidence rate of breast cancer is on rise, causing severe morbidity as well as mortality. To build up satisfactory treatment regimens for different types of breast cancer, more reliable methods are necessary for evaluating the factors predicting the tumor progression. Many scientific efforts have been undertaken to establish predictive markers in breast cancer. Among them, tumor grade is an important prognostic parameter besides the acknowledged impact of tumor size and lymphnode status (20). There are numerous published reports on nuclear grading of breast carcinoma in surgical pathology but only few are found in the recent cytology literature. Currently, FNAC is used for the preoperative diagnosis of breast cancer in developing countries due to its low cost, and it is usually followed by core biopsy. From FNAC samples, clinically relevant information like estrogen and progesterone receptors, proliferative fraction and oncogenes products can be obtained in addition. It also gives information on cytological nuclear grade that is obtained easily and reproducibly (21). Tumor grading on FNAC does not require any special procedure and hence, there is no additional cost. It is also considered to be one of the most significant prognostic factors in predicting outcome in breast cancer patients (22). Nottingham modification of Elston and Ellis Bloom Richardson score is a widely accepted grading system on histopathology due to its good prognostic correlation (23). Various grading systems based on cytological fea-

tures have been developed. Of different cytological grading methods, the one that corresponds to histological grading is the technique described by Robinson on fine needle aspirates (24). In the present study, we compared breast tumor grading on histopathology by Bloom Richardson scoring method and Robinson grading system in FNAC.

Various similar studies aimed to find the concordance rate between cytological grading of breast carcinoma with histopathological grading. In the present study, grading on histopathology was done by Nottingham modification of Scarff Bloom-Richardson (SBR) histological grade, which identified two out of 40 cases (5%) with grade I, 19 cases with grade II (47.5%) and 19 cases with grade III (47.5%). These findings were comparable with those reported by Chalise *et al* (25), Charusheela *et al* (26) and Sweta Pal *et al* (27).

In the present study and other studies as well, the maximum number of cases belonged to grade II of histological grades. Amid the three grades, more than 50% of cases belonged to grade II, this unequal distribution being one of the limitations of SBR grading on histopathology. Furthermore, there is an obvious foretelling separation between grades I and III, even though grade II patients overlapped grade I and grade III (28). In our study, a total concordance rate between Robinson cytological grading system and SBR histological grade was seen in 26 out of 40 cases, accounting for 65% of the total number of cases. In the study by Chalise S *et al* (25), there were 11 cases with grade I on Robinson cytological grading, of which five cases belonged to grade I and five cases were upgraded as grade II, and one case was upgraded to grade III on SBR histological grading system. Similarly, there were 36 cases with grade II on Robinson cytological grade, of which 29 cases with grade II and four cases were upgraded as grade III and three cases were downgraded as grade I on SBR histological grading system. Out of 11 cases with grade III on Robinson cytological grading system, eight cases were grouped as grade III and three cases were downgraded as grade II on SBR histological grade. The total concordance rate between Robinson cytological grading system and SBR histological grade was 65.9%. Similar findings were also obtained by Charusheela *et al* (26) and Sweta Pal *et al* (27), who found a total concor-

dance rate between Robinson cytological grading system and SBR histological grade of 82.76% and 78%, respectively. The precision of the grading system found by other researchers varied from 65.9 to 83% (25-27). This unpredictability in the study of other authors may be due to several factors such as assessment in air dried material, different staining techniques, etc. The lack of correspondence (%) may be because of different degrees of atypia in the same studied tumor, and also in few cases the Robinson score was on the higher side of grade I, which could have easily overlapped grade II because of the subjective nature of Robinson grading system (21).

In this study, Spearman correlation coefficient (r value) was 0.57, as the p value was <0.05 , which indicated a positive correlation and a significant association between Robinson cytological grading system and Nottingham modification of Elston's and Ellis Blook Richardson score on histopathology. Chalise S *et al* (25) found an r value of 0.575 and hence, the correlation of Robinson cytological grading with SBR histological grading was statistically significant; for them too, cell dissociation and nuclear margins were determining features on cytology. Chhabra *et al* (29) investigated 60 cases with breast carcinoma where cytology smears were graded by Robinson method and histological grading was done by SBR grading. Agreement between both grades was seen in 65% of cases, with an r value of 0.774, and thus, cytological and histological grades correlated positively; also, they found that the amount of cell dissociation and nucleoli were the most significant feature. Similarly, 50 cases with breast carcinoma were studied by Sweta Pal *et al* (27), with smears on cytology being graded by Robinson grade and on histopathology by Nottingham modification of Bloom Richardson score; their study indicated a strong correlation between both the grading systems, with an r value of 0.804. Thus, improved breast cancer detection with grading and treatment have contributed to a drop in mortality over the last several decades (30). $\square$

CONCLUSIONS

Robinson cytological grading system is a simple, less time consuming and reproducible grading system for breast carcinoma on cytology, which correlates very well with SBR grading on

histopathological examination. Thus, it is suggested that FNAC along with core biopsy will definitely help breast carcinoma patients in deciding the proper line of treatment and use of neoadjuvant therapy. We can thus achieve a proper ma-

agement of breast carcinoma as well as less morbidity and mortality among these patients. □

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