

Original Research Article

Robinson's cytological grading of breast carcinoma: its prognostic implications and correlation with bloom Richardson's histological grading of breast cancer

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ABSTRACT

Background: Cytological grading on aspirates of breast carcinoma is a useful tool for surgical maneuver and prognosis. The aim of the study is to find out the utility of grading in malignant breast tumors using Robinson's cytological grading on FNAC and correlating it with modified bloom-Richardson's histopathological grading of breast carcinoma along with lymph node status assessment post-operatively by histopathological examination.

Methods: This prospective study was carried out in 40 cases of invasive duct carcinoma of breast for a period of one and half year duration from December-2019 to July-2021. This study was done in department of pathology, Surat municipal institute of medical education and research (SMIMER), Surat. In all these cases the cytological diagnosis was confirmed by histological examination. All cases were graded by using Robinson's grading system. All these cases were also correlate with bloom Richardson's grading system on histopathology in mastectomy specimen.

Result: Robinson's cytological grading correlated well with bloom Richardson's histopathological grading. In this study of forty cases, thirty-three cases (82.5%) show concordance between cytologic and histologic grading system. Rest of the seven cases (17.5%) show discrepancy.

Conclusions: Thus, In the most of the cases, cytological grading of breast carcinomas correlate with histopathological grading and may be useful as a prognostic marker. It was concluded that the cytological grading should be included in all FNAC reports. So that appropriate decision regarding the preoperative neoadjuvant chemotherapy can be made and overtreatment of low-grade cancers has been avoided.

Keywords: Breast carcinoma, Bloom Richardson's grading, Robinson's grading, Fine-needle aspiration cytology, Lymph node status assessment

INTRODUCTION

Breast cancer is the second most common cancer in females worldwide. Breast cancer is the second leading cause of cancer related deaths in females all over the world.¹ Breast cancer have doubled in India in the last two decades. The number of women estimated to be dying of breast cancer every year has also been steadily raising. As per the statistics, the incidence of breast cancer is rapidly increasing in India and has overtaken carcinoma cervix. Indian council of medical research data

shows that breast cancer is the commonest cancer in Mumbai, New Delhi and Chennai. It showed that one in 22 per 100 women in India is likely to suffer from breast diagnosed in Indian women in metropolitan cities. Fine needle aspiration cytology is being increasingly used to determine the benign and malignant nature of lesion. This also provides additional information about intrinsic nature of lesion and the prognosis.² Attempts have been made to determine various prognostic parameters on FNA material to determine the best therapy in a given case.^{3,4} Due to its tremendous increase in incidence rates,

it is desirable to grade tumor while is still in vivo for the selection of appropriate therapy and to avoid overtreatment for low grade carcinoma. Significance of histological grading was accepted. It was also found to be useful supplementary prognostic parameter. So, when significant association was established between cytologic and histologic grading systems, cytologic grading may be helpful to decide level of treatment.

METHODS

This prospective study was carried out in 40 cases of invasive duct carcinoma of breast for a period of one and half year from December-2019 to July-2021. This study was done in department of pathology, SMIMER, Surat. In all these cases, the cytological diagnosis was confirmed by histological examination.

Inclusion criteria

Female patients with palpable breast mass, patients who were proved to have ductal carcinoma of breast by FNAC and patients whose cytological diagnosis of invasive duct carcinoma was confirmed in histological specimens were included in study.

Exclusion criteria

Known cases of invasive duct carcinoma of breast who have received chemotherapy or radiotherapy, patients those who do not have histological confirmation, male patients with ductal carcinoma of breast, patients who underwent lumpectomy alone, the patients were classified into three categories based on age, pre-menopausal (52 years), menopausal (47-52 years), post-menopausal (>52 years) were excluded from the study.

The consent was obtained from the patient.

FNAC procedure was done by the faculties and postgraduates of department of pathology using 23gauge needle with or without 10 ml disposable syringe by non-aspiration technique. The aspirated material was expressed on slide, smeared and fixed with 95% alcohol for 20 minutes. These wet fixed slides were stained with papanicolaou method and haematoxylin and eosin.

The stained smears were evaluated and diagnosed as ductal carcinoma of breast when there is definite features of malignancy like cellular dissociation, nuclear pleomorphism, nuclear abnormalities, absence of bare nuclei. Any special variants of ductal carcinoma were also included. These slides were graded based on grading system proposed by Robinson which is as follow.

The value between 1 to 3 is given for every factor analyzed. The sum of these values gives the total score. Total score ranges between 6 and 18. According to which grading was done. Grade 1: score 6-11, grade 2: score 12-14 and grade 3: score 15-18.

On follow up of already cytologically diagnosed cases of breast carcinoma, modified radical mastectomy specimens including axillary clearance fixed in 10% formalin were obtained. The tumor size and the tumor location were assessed in the gross specimens. Paraffin embedded sections obtained by routine procedures were cut at thickness of 3 microns using microtome.

These slides were routinely stained with haematoxylin and eosin stain. The slides were evaluated and the diagnosis of invasive duct carcinoma was confirmed. Special types of ductal carcinoma other than classical invasive duct carcinoma NOS were also included in this study histological grading was done using Nottingham modification of Scarff bloom Richardson method. This system considers three parameters. They include tubule formation, nuclear pleomorphism and mitotic rate.

Table 1: Robinson cytological grading system.

Variables	Score 1	Score 2	Score 3
Cell dissociation	Mostly in clusters	Single cells, with cell clusters	Mostly in single
Nuclear size	1-2 times the size	3-4 times the size of RBCs	>5 times the of RBCs
Cell uniformity	Monomorphic	Mildly pleomorphic	Highly pleomorphic
Nucleoli	Indistinct/small	Noticeable	Prominent/abnormal
Nuclear margin	Smooth	Slightly irregular/ folds/ groove	Buds and clefts
Chromatin pattern	Vesicular	Granular	Clumping and clearing

Table 2: Modified bloom Richardson histologic grading.

Variables	Score 1	Score 2	Score 3
Tubule formation	>75% of tumor shows tubule	10-75% of tumor shows tubule	<10% of tumor shows tubule
Nuclear pleomorphism	Small regular nuclei; similar to normal ductal nuclei	Intermediate size; 1.5-2 times size of normal ductal nuclei	High grade nuclei variation; > twice size of normal ductal nuclei.
Mitotic count	0-7 mitosis/10 HPF	8-14 mitosis/10HPF	>15 mitosis/10 HPF

Grade 1: score 3-5, grade 2: score 6-7 and grade 3: score 8-9.

The axillary lymph nodes received were also processed in a similar manner and assessed for metastasis. Statistical analysis was done to examine the degree of association between the cytologic and histologic grading system.

Finally, we correlate Robinson’s cytological grading on FNAC and modified bloom-Richardson’s histopathological grading of breast carcinoma along with lymph node status assessment post-operatively by histopathological examination.

RESULTS

Total of 40 cases were studied and the following observations were obtained.

Age distribution

The patients age ranges from 28-80 years with a mean age of 48 years. The minimum age and the maximum age reported in the present study was 28 and 80 years respectively.

The patients age group were divided into three age groups.

Table 3: Distribution of cases according to different age groups.

Age group	N (%)
Premenopausal (<47)	16 (40)
Menopausal (47-52)	05 (12.5)
Postmenopausal (>52)	19 (47.5)

Cytological grade

According to Robinson grading system, the cytological samples were graded into three groups.

Table 4: Distribution of cases with regard to cytological grade.

Cytological grade	N (%)
Grade-1	10 (25)
Grade-2	17 (42.5)
Grade-3	13 (32.5)

Of the forty cases, majority of the cases belong to grade 2 (42.5%) with 17 cases, next was grade 3 (32.5%) with 13 cases followed by grade 1 (25%) with 10 cases.

One special types were also reported. This includes mucinous pattern mixed with IDC.

Histological grade

According to Nottingham modification of Scarff bloom Richardson grading, forty cases were categorized under three categories.

Table 5: Distribution of cases with regard to histological grade.

Histological grade	N (%)
Grade-1	08 (20)
Grade-2	18 (45)
Grade-3	14 (35)

In this study of forty cases, majority of tumors were grade 2 tumors with eighteen cases (45%), eight cases were under grade 1 (20%) and other fourteen cases were classified as grade 3 (35%). Among these forty cases, there was one special types of invasive duct carcinoma and the rest of the 39 cases were invasive duct carcinoma, NOS. The special type was mucinous pattern mixed with IDC.

Correlation of cytologic grade with histologic grade

The cytological grade of the tumor was correlated to the histologic grade to assess the concordance between the two grading systems.

Table 6: Correlation of cytologic grade with histologic grade.

Variables	Histological grade, n (%)			Total
	1	2	3	
Cytological grade	07 (70)	03 (30)	00	10
	01 (5.9)	14 (82.4)	02 (11.8)	17
	00	1 (7.7)	12 (92.4)	13

In this study of forty cases, thirty-three cases (82.5%) show concordance between cytologic and histologic grading system. Rest of the seven cases (17.5%) show discrepancy. Among the ten grade 1 tumors, seven cases (70%) show concordance with the histological grade whereas 3 cases were discordant. All these three cases were upgraded. Among the seventeen grade 2 tumors, three cases did not correlate, two was upgraded to grade 3 and other was downgraded to grade 1. Rest of fourteen grade 2 tumors show good concordance (82.4%). Grade 3 tumors show good concordance with twelve cases (92.4%). Only one of the grade 3 tumor was downgraded to grade 2. This study shows high correlation between cytological grade and histological grade.

Lymph-node status

The lymph node status was classified into positive and negative nodes.

Table 7: Distribution of cases according to lymph node status.

Nodal status	Positive nodes, n (%)
Positive nodes	20 (50)
Negative nodes	20 (50)

Of the forty cases, twenty (50%) cases were lymph node negative. Among the 20 lymph node positive cases, ten cases had 1-3 nodes, six cases had 4-9 nodes, four cases had more than 10 nodes.

DISCUSSION

Breast carcinoma is a malignant disease with a variable prognosis. Assessment of prognostic parameters is of growing interest in recent days. The parameters consist of tumor size, lymph node status, estrogen receptor status, histological grading and cell proliferation index.⁵⁻⁸ All these features have been well studied on surgical specimens, however evaluation of prognostic factors and grading of cytologic samples have not been included in the routine practice. Cytologic grading is valuable, feasible and reproducible.^{9,10} This method also depicts the intrinsic characteristics of the tumor as well as its prognosis.¹¹

The need for prognostic grading in cytological samples of breast cancers is to identify rapidly growing tumors, which were more responsive to chemotherapy and better suited to pre-treatment with tamoxifen. Overtreatment of slow growing tumors was also reduced. Assessment of biological aggressiveness by cytological grading without removing the tumor would therefore be of immense value.¹²

In this present study predominant tumors were grade 2 (42.5%) followed by grade 3(32.5%) and grade 1 (25%) in cytological samples. A study by Wani et al¹⁸ showed a similar a result, the predominant tumors were grade 2, grade 3 forms the second largest group followed by grade 1. A study by Robles et al showed the predominant tumors were grade 2 (39%) followed by grade 1 (36%) and then grade 3 (25%). Studies done by Dash et al, Chhabra et al, Robinson et al also showed similar results.¹³⁻¹⁶ This shows the lack of awareness and late presentation of the patients in our setup.

This study showed a high degree of concordance (82.5%) between the cytological and histological grading systems. Khan et al and Nijahawan et al showed a concordance value of 84% and 82.5% respectively.^{11,17} A study by Milentijevic et al also show a concordance value of 81%.¹⁸ High concordance value was also 5 of 8 found by Taniguchi et al, Chhabra et al and Bhargava et al.^{15,19} Concordance between cytologic and histologic grading was observed more frequently in purely invasive carcinomas (85%).²⁰ This study was close to these studies. However, Dash et al, Moriquand et al and Gayathri et al showed concordance of 77.5%. Sinha et al showed a concordance rate of 69.5%.^{14,21}

Low concordance in these all above studies was probably due to the inclusion of patients receiving chemotherapy and inclusion of cases diagnosed as atypical ductal hyperplasia and in situ carcinomas in cytological samples. In the present study the patients receiving

neoadjuvant chemotherapy were excluded and only cases showing definitive features of ductal carcinoma in both cytology samples and histologic specimens were included. This explains the high concordance between the grading systems.

In this study, association between cytological grading and histological grading system was highest among grade 3 tumors (92.4%) followed by grade 2 (82.4%) and least with grade 1 (70%). Sinha et al states that grade 3 tumors showed a greater concordance.²² Jayaram et al states that concordance was found to be higher among grade 3 tumors (83.3%) and low among grade 1 tumors (75%).²³ Khan et al states that higher concordance was found among grade 1 tumors (92.3%).¹¹ Several studies states that concordance was high among high grade tumors. The present study also supports this view. Out of the seven discordant cases, three of grade 1 tumors were upgraded. Among three discordant grade 2 tumors, two was upgraded to grade 3 and other was downgraded to grade 1. The one discordant grade 3 tumor was downgraded. The reason for the upgrading of tumors may be due to sampling errors in large size tumors and heterogenous tumors. As orientation of the tumor cannot be made more accurate clinically, multiple passes in FNAC were aimed at the central portion of the tumor neglecting the active periphery. In histologic specimens the infiltrating edge of the tumor was correctly assessed, and multiple blocks were made from that site to assess the grade. Another reason of the upgrading of tumors may be due to inadequate samples. One of the reasons for downgrading of tumors may be due to the fact that only nuclear features were taken into consideration, while grading the cytologic samples. Tubule formation and mitotic count were not included. There may be subjective variability among the observers which explains the discrepancies.

Regarding the association between the cytological grade and lymph node status, node positivity was seen in 70%, 29.5% and 61.6% of grade 1, 2 and 3 tumors respectively. In this study nodal metastasis is highest in grade 3 (61%). In a study by Dash et al 74.2% of grade 3 tumors showed nodal metastasis.¹⁴ Our study correlates more with the study by Dash et al.¹⁴ The association between the cytological grading and lymph node status was not significant. When this association had been proved, level of resection can be assessed preoperatively by the cytological grade itself. But in this study cytologic grade did not correlate with axillary lymph nodes status. This is because in this study, criteria for the minimum number of nodes to be examined was not defined. When the minimum number of nodes to be examined was increased to 10 nodes, better association can be obtained.

Regarding the tumor size majority of tumors (80%) were T2 tumors (2-5cm, TNM staging). Since the size of the tumor was an independent time dependent prognostic factor, an attempt was made to correlate tumor size with the cytological grade. No clinical significance was

obtained. Similar results were observed in a study by Kim et al, Gann et al and Gayathri et al.^{5,21,24}

Numerous studies have shown survival decreases with increasing tumor size and coincidental increase in axillary node positivity.⁶ Roger et al reported significant distribution of frequency of axillary lymph node involvement in relation to tumor size. But in our study, there is no significant correlation between tumor size and lymph node status.

Regarding tumor location most of the tumors were located in outer quadrant accounting for 70%. However, most of the grade 1 tumors were located in the central quadrant with 18.2%. A study by Harzah et al shows that tumors in peri areolar location are associated with poor prognosis.¹² In the present study, tumors located in the central quadrant (18.2%) show more lymph node positivity than other quadrant tumors.

CONCLUSION

Due to the increasing incidence of breast cancer in recent years, the role of FNAC in the early identification of breast cancer has been tremendously increased. This present study evaluates prognostic factors in cytological samples of the various prognostic factors, cytological grading is the one which is more feasible and reproducible. The histological grade is one of the well-known morphological prognostic factors and had been included in all reports of breast malignancies. This study shows a significant correlation between the cytologic grade and histologic grade. This indicates that cytological grade predicts the tumor aggressiveness.

So, it was concluded that the cytological grading should be included in all FNAC reports. So, that appropriate 6 of 8 decision regarding the preoperative neoadjuvant chemotherapy can be made and overtreatment of low grade cancers has been avoided. In this study cytological grading did not correlate with the lymph node status. When this correlation has been proved, the level of lymph node resection can be planned preoperatively. In spite of adequate efforts made to reduce the distortion in estimates, there is some degree of measurement bias and interobserver variability in this grading system.

This present study suggests the use of ancillary techniques like nuclear morphometry, immunohistochemistry for hormone receptors and proliferative indices done on cytological samples for further evaluation the tumor biology and aggressiveness.

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