Journal of Cardiovascular Disease Research

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 08, 2022

ORIGINAL RESEARCH

Correlation between cytological and histopathological grading of invasive ductal carcinoma breast and nodal metastasis

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Received: 22 September, 2022 Accepted: 24 October, 2022

Abstract

Background: fine needle aspiration cytology FNAC plays a vital role in the initial evaluation and early diagnosis of the breast tumours, by providing the useful information on aggressiveness of the tumour as well as its prognosis.

Aim: This study has been carried out to evaluate the correlation between the cytological & histopathological grading of invasive ductal carcinoma with specific reference to nodal metastasis & its role in prognostication.

Material and methods: This was a cross sectional study in which Fifty six patients aged between 28-75 years who were cytologically proven duct cell carcinoma of breast with their corresponding histopathology. They were graded cytologically by Robinson's and correlated histologically with SBR grading method. Statical analysis was done using SPSS and Epi info online. Kohens kappa was calculated to assess the extent of agreement between two measurements. Diagnostic accuracy was calculated through sensitivity, specificity, positive predictive values and negative predictive values.

Result: Using aspirate samples, cases were cytologically graded according to Robinsons categories according to Robinson categories, with the following results: Grade 1:11cases, Grade II: 37 Grade III: 8. Using histologic samples 14 cases were considered grade I , Cases were Grade II 31 & 11 Were Grade III. In this study, majority of tumours were grade II on cytology (66.1%). The next frequency was grade I (19.6%) followed by grade III (14.3%).

Conclusion: Cytological grading of breast carcinoma can be done by Robinsons grading with quite relevance with histological grading and provide relevant information about invasive ductal carcinoma of breast which could be useful when selecting mode of therapy and to predict tumours behaviour.

Keywords: Comparative cyto-histopathological grading, Axillary metastasis, infiltrating ductal carcinoma

Introduction

Breast cancer is a malignant disease with varying prognosis evaluation of possible prognostic parameters is of developing interest. These include tumour histologic grading [(3)], cell proliferation index[(4)], estrogen receptor status,[(2)] lymph node status[(1)]. Since all these parameters have been well studied on surgical specimens, the evaluation of cytologic features of infiltrating ductal breast carcinoma in fine-needle aspiration cytology (FNAC) material is valuable and a number of authors have shown that this method can provide additional information regarding various features of the tumour as well as its prognosis. The information

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 08, 2022

provided by FNAC can be extremely useful when deciding about the neo adjuvant therapy for patients for whom surgical removal of the tumour is not the available option.[5,6] Cytologic grading based on Papanicolaou staining can be done easily everywhere and such grading would allow assessment of the tumour in situ, so that not only the most suitable treatment could be selected before primary surgery, but also the morbidity associated with over treatment of low grade tumours could be avoided by early diagnosis.

Material and Methods

The study was conducted in post graduate department of pathology government medical college Srinagar over a period of 18 months from January 2020 to June 2021 A total of 56 cases were taken into the study, whose age ranged between 28-75 years. The FNAC material was fixed with 95% alcohol and stained using the routine papanicolaou method. The smear was evaluated based on Robinsons grading system which takes into account six parameters. A score between 1-3 is given to each parameter analysed. Scores of each of six cytologic features were added together to give a total score for each case. Surgical specimens were obtained according to the routine procedures which were later given the diagnosis of invasive ductal carcinoma. These samples were evaluated based on histologic grade using bloom Richardson system. The parameters taken in consideration as under: tubule formation, nuclear pleomorphism and number of mitosis. Each parameter was scored between 1 & 3. All 56 patients were also evaluated for presence of metastasis to the regional lymph node.

Result

Using aspirate samples, cases were cytologically graded according to Robinsons categories according to Robinson categories, with the following results: Grade 1:11cases, Grade II:37 Grade III: 8.Using histologic samples 14 cases were considered grade I , Cases were Grade II 31&11Were Grade III. In this study, majority of tumours were grade II on cytology (66.1%). The next frequency was grade I (19.6%) followed by grade III (14.3%).

Analysis of the data from table 2 showed that concordance rate between grade I tumours in cytology & histology was 78.57% , while for grade III was 72.73%. The overall sensitivity was 89.28%and specificity was 100%. The estimated Cohens kappa (underweighted) was 0.8108 indicating almost perfect agreement When further comparison was made of two grading systems by Z test showed that difference between the cytologic and histologic grading was significant in all three grades (P >0.001). Therefore, it can be stated that cytological grading is comparable to histological grading of tumour behaviour and prognosis.

Analysis of data from table 3 shows highly significant correlation between cytologically score and histopathological grade with a significant P value of <0.001

Table 4: As evident from the P-value of <0.001, there was a highly significant correlation between total histological score and histological grade.

Table 5 shows highly significant correlation with the tumour grade, as evident statically (P-value<0.001)

Table 6 shows that the tumour grade increased the total number of lymph nodes also increased. The number of lymph nodes shows highly significant correlation with the histopathological grade of tumour (P-value <0.001).

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Table1: cytologic grading with the method of Robinson et al

Criteron	Score 1	2	3
Nuclear size	1-2 times the size of an RBC	3-4 times size of RBCs	>5 times size of RBCs
Cell uniformity	Monomorphic	Mildly pleomorphic	Pleomorphic
Nucleoli.	Indistinct/small	Noticeable.	Abnormal
Nuclear margin.	Smooth	Slightly irregular/folds	Buds, clefts
Chromatin pattern.	Vesicular	Granular.	Clumping/clearing

Table 2: Cytologic and histologic correlation (concordance rate=approximate sensitivity)

Cytological grade	Histological grade			Total	Sensitivity
	3-5(Gr.I)	6-7(Gr.II)	8-9(Gr.III)		
6-11(Gr.I)	11	0	0	11	78.57%
12-14(Gr.II)	3	31	3	37	
15-18(Gr.III)	0	0	8	8	72.73%
Total	14	31	11	56	

Table 3: Correlation of total cytological score with histopathological grade

Total score cytology	Histological grade			Total
	3-5(Gr.I)	6-7(Gr.II)	8-9(Gr.III)	
10(Gr.I)	3	0	0	3
11(Gr.I)	8	0	0	8
12(Gr.II)	3	6	1	10
13(Gr.II)	0	23	2	25
14(Gr.II)	0	2	0	2
15(Gr.III)	0	0	5	5
16(Gr.III)	0	0	3	3
Total	14	31	11	56

Table 4: correlation of histopathological score with histopathological grade

Total score	Histological grade			Total
	3-5(Gr.I)	6-7(Gr.II)	8-9(Gr.III)	
5(Gr.1)	14	0	0	14
6(Gr.II)	0	4	0	4
7(Gr.II)	0	27	0	27
8(Gr.III)	0	0	11	11
Total	14	31	11	56

P-value(Fisher exact test) <0.001

Table5: correlation of Tumor size with histopathological grade

Tumor size	Histological grade			Total
	3-5(Gr.I)	6-7(Gr.II)	8-9(Gr.III)	
<2cm	8	2	0	10
2-5 cm	6	26	2	34
>5 cm	0	3	9	12

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Total	14	31	11	56

P-value(fisher exact test) <0.001

Table 6: Correlation of number of lymph nodes with the histopathological grade

Number of nodes	Frequency	Percent
0	11	19.6%
1	1	1.8%
2	8	14.3%
3	11	19.6%
4	15	26.6%
5	1	1.8%
6	5	8.9%
7	3	5.4%
8	1	1.8%
Total	56	100.00

Fig1: Grade 1 (dissociation) low power 10x

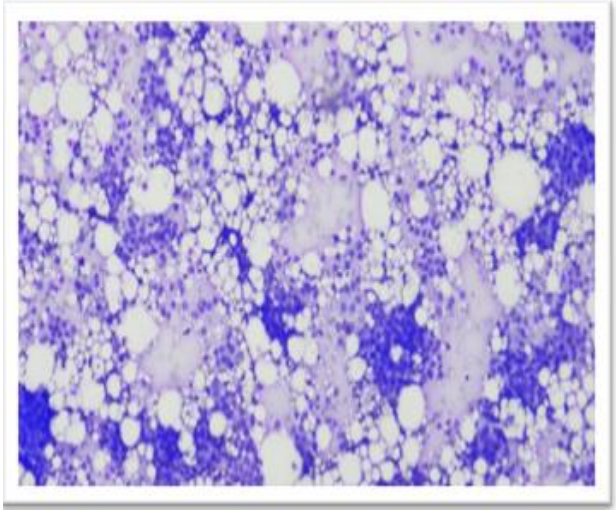

Fig 2: Grade 1(Tubule formation) 40x

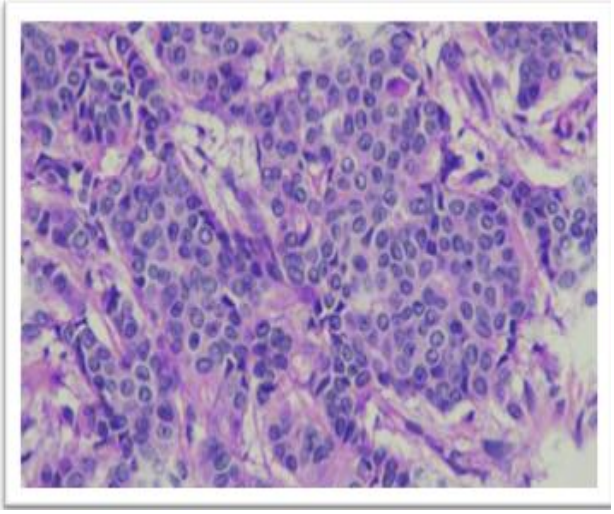

Fig 3: grade 1 nuclear size 40x

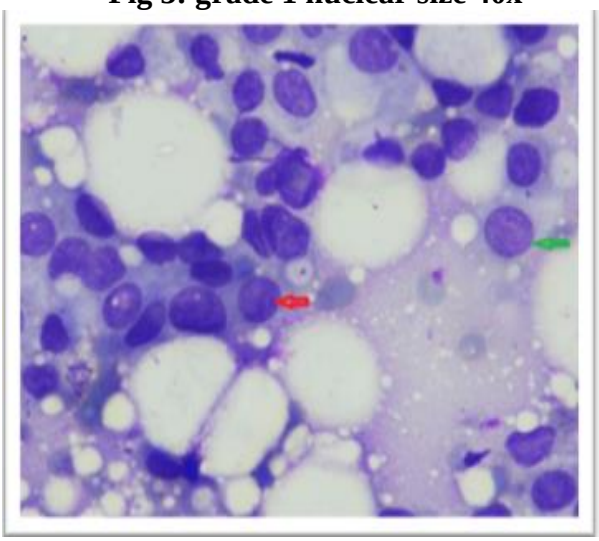

Fig4: Grade 1 high power 40x

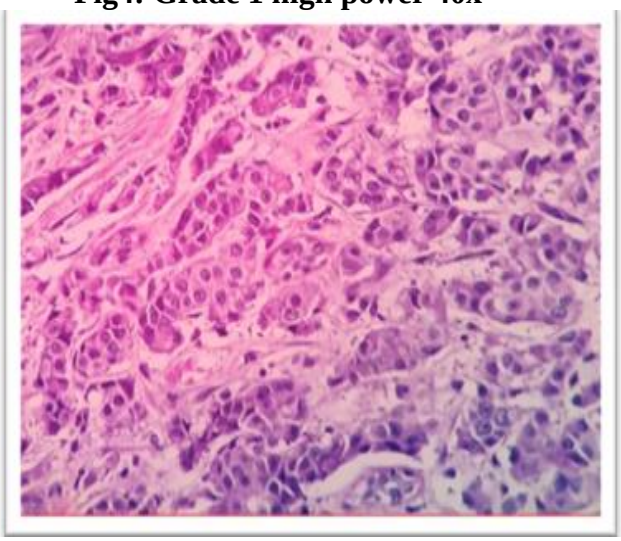

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Fig 5: Grade 2 (dissociation) low power 5x

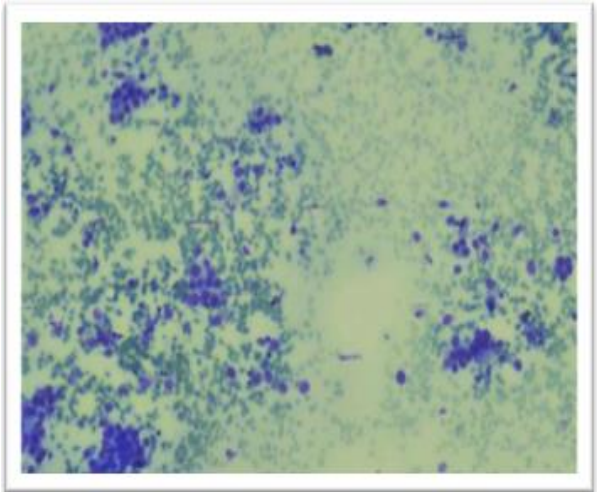

Fig 6: Grade 2 mild pleomorphism H&E 40x

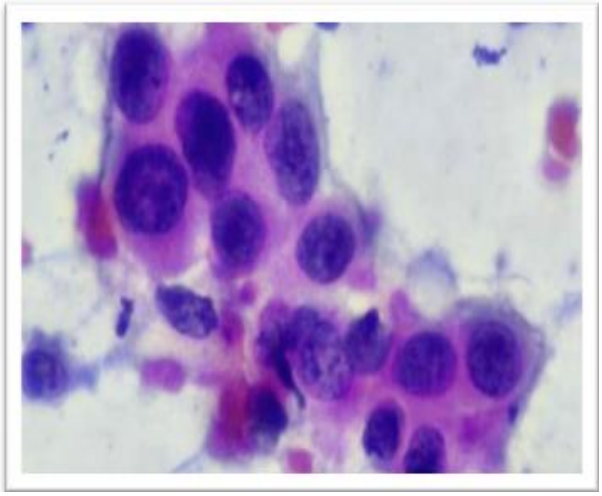

Fig 7: Grade 2 noticeable nucleoli H&E 40x

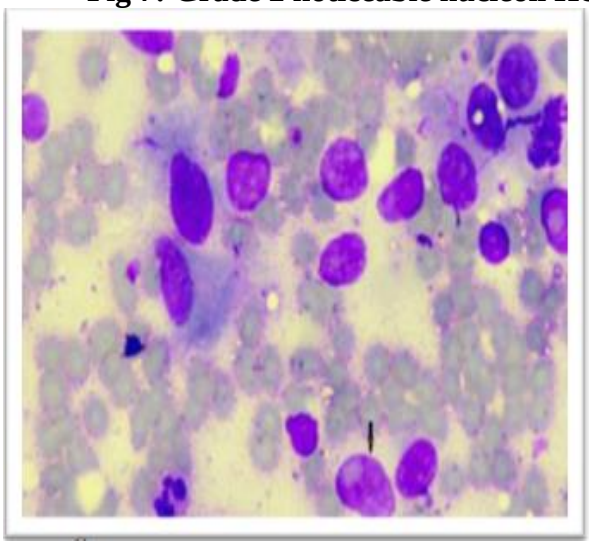

Fig 8: Grade 2 H&E 20x

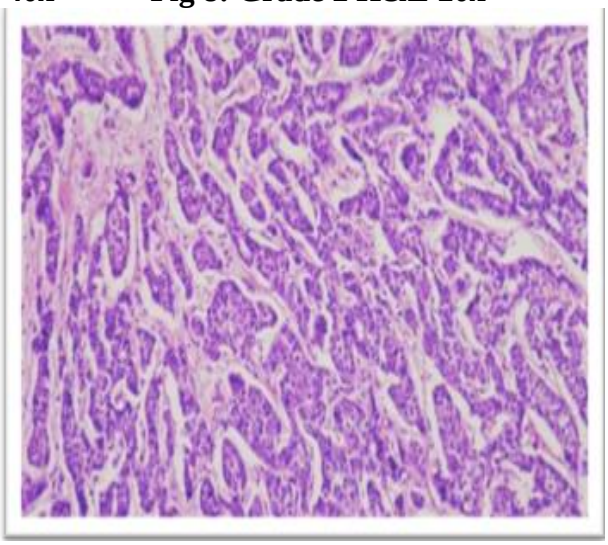

Fig 9: Grade 3 pleomorphism cells H& E 40x

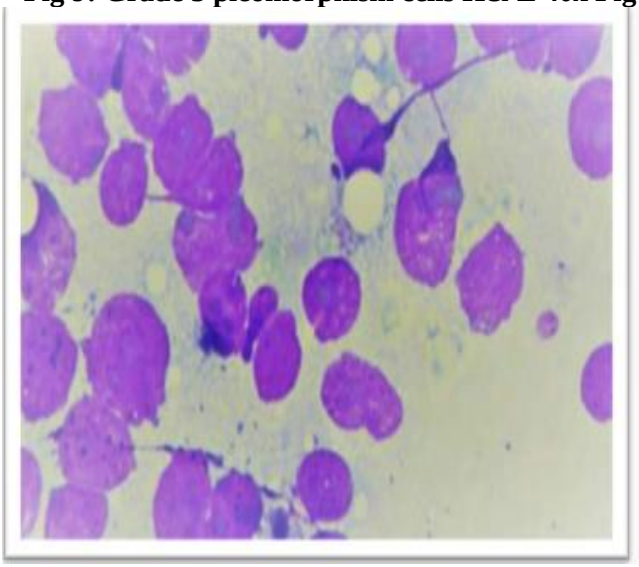

Fig 10: Grade 3 prominent nucleoli H& E 40 x

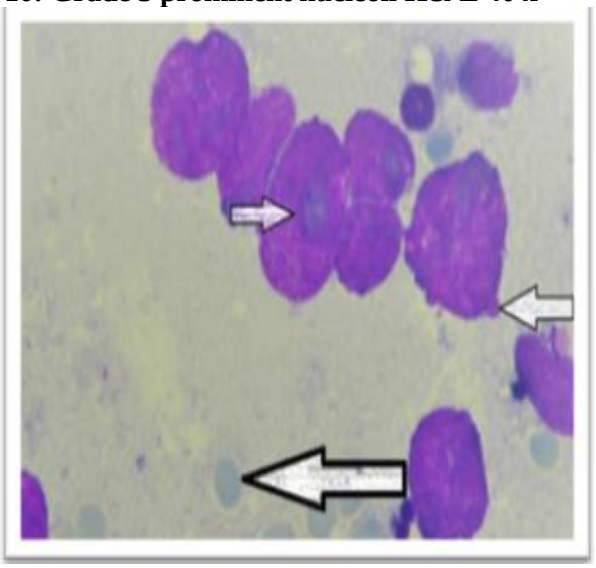

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Fig11: Grade 3 mitosis H&E 40x **Fig 12: Grade 3 comedo necrosis high power 40x**

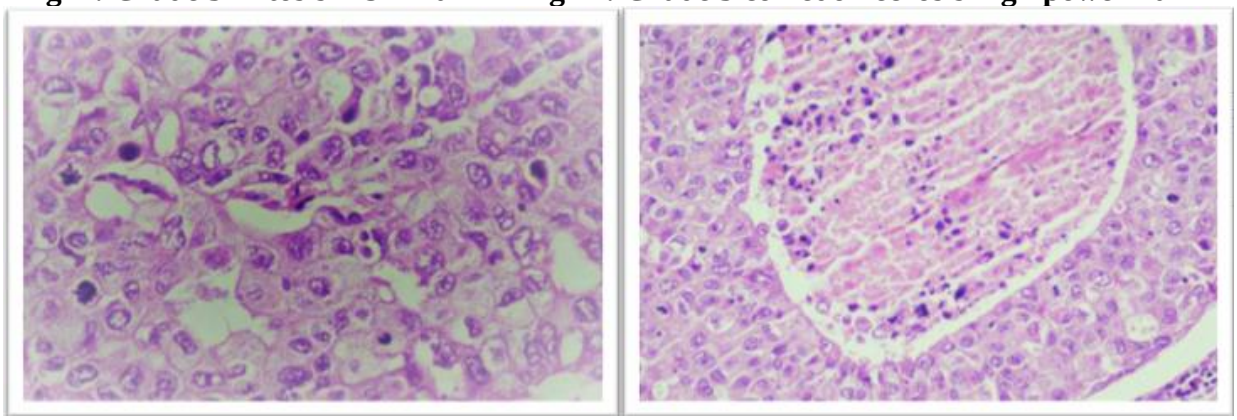


Fig 13: Grade 3 perineural invasion high power 40x Fig 14: Nodal invasion high power 40x

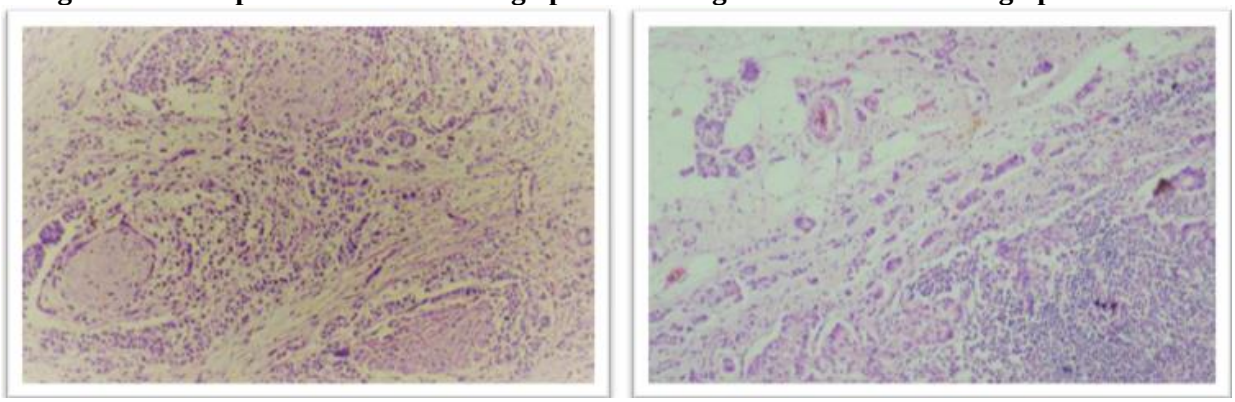
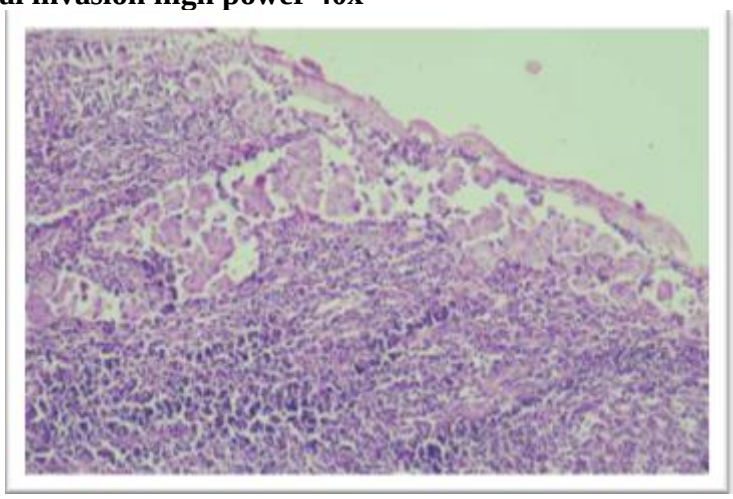


Fig 15: Extranodal invasion high power 40x



Discussion

Different studies have been done to compare the different cytological grading systems with the histopathological grade to assess the accuracy of the different methods.[72]

By using different cytological grading systems, a significant correlation was seen between cytological and histological grade.[112]

The Robinson's method of cytological grading was more specific when Bloom Richardson method of histological grading was considered as gold standard. The criteria for grading a tumor by the Robinson's method were simpler and easier to reproduce as compared to other methods.

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By applying Robinson's grading system to our aspirates, an absolute concordance rate between all three corresponding grades was significant 89.28%. Out of the 6 cases that showed discrepancy, 3 cases were upgraded 0n histology and 3 cases were downgraded. The cases which were downgraded on histology may be due to the fact that in cytological grading, the nuclear features are predominantly considered for grading. On the other hand the tumors that were upgraded on histology may be attributable to large tumor size or tumor heterogeneity. When the tumor size is large, multiple passes may be required to sample the most undifferentiated areas of the tumor, which may not be done on routine FNAs. Instead, the tumor is adequately sampled in histopathology by taking representative blocks allowing evaluation of the most undifferentiated areas. When assigning the grade observer subjectivity may also be a significant contributing factor for the discrepancies.

A significant correlation was observed by Khan et al between cytological grade and histological grade in 84% of the cases, in a study comprising of 50 Indian woman.98 the results of Khan et al were similar to Nijhawan et al (82.9%) study.113The study by Dr Jigna et al showed a concordance of 88.5% which was very similar to the present study (89.28%).The current study showed a substantial strength of agreement between cytology and histopathology grades similar to the study of SK Sinha et al 97. The overall diagnostic accuracy shown by the current study was 94.64% which was similar to the study conducted by T Sultana et al 96.3% 95.The sensitivity, specificity and diagnostic accuracy of the current study are almost the same as shown by Alpeshpuri P Goswami et al[89]

Correlation of cytological features with histopatholocal grade

Discriminant analysis showed that the features with the closest correlation with the histopathological grade were nuclear size, cell uniformity, nucleoli and nuclear margin with p-value of <0 .001 which is highly significant. Similar results were obtained by CM Hunt et al., 83 Anamika Sinha et al, 104 and BS Ducatman et al,.87

Correlation of cytological grade and axillary lymph node status

Lymph node metastasis is a factor of known prognostic significance in carcinoma breast. There are several factors which predict the lymph node metastasis like tumor size, younger age and higher grade.110, 114

Patients with definitive lymph node involvement have significantly poor prognosis than those without nodal metastasis.57

Various studies on cytological grading of ductal carcinoma breast have correlated the cytological grade with the lymph node involvement and found that higher grade tumors are more likely to metastasize than low grade ones.86, 107,115

Dash et al in his study on 93 cases showed nodal metastasis in 74.2% of grade III carcinomas in contrast to only 27% of grade 1 tumors.107

Similarly another study by Frias et al found nodal metastasis in 64% of grade II tumors in contrast to 88% of cytological grade III tumors.108

The current study showed a highly significant correlation between cytological grade and lymph node metastasis with only 9% of grade1 tumors showing nodal metastasis, while as 97% of the grade II and 100% of grade III tumors show nodal metastasis. Similar results were observed by SK Sinha et al 97 and Tanjguchi E et al 86, in their studies.

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