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Original Research Article

Concordance between cytological and histopathological grading in invasive breast carcinoma – A cross sectional study

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ABSTRACT

Introduction: Invasive Breast carcinoma means that the cancer has spread beyond the ducts/lobules into the surrounding tissue.
Materials and Methods: The present 2 year study was carried out at a tertiary care hospital to find the concordance between cytological and histopathological grading in invasive breast carcinoma. It included all the 100 cases of invasive breast carcinoma diagnosed on histopathology during this period with available cytology reports. Concordance of Robinson's cytological grading system was calculated in each grade with respect to histological grading.
Results: All cases evaluated for presence of metastasis to axillary lymph nodes. We found Concordance rate between cytological and histological grade as 76%. The coefficient of correlation between cytological grade and histological grade was 0.83 and P value was <0.001 which indicated a strong correlation and significant association between the cytological and histological grade.
Conclusions: High degree of concordance is seen between cytological and histopathological grading system. Preoperative grading using FNAC helps in determining neo adjuvant chemotherapy as well as prognosis. This grading should be included in cytology reports on a regular basis because it correlates well with histological grade.

1. Introduction

Breast cancer is the most common cancer in women worldwide, accounting for nearly a quarter (25%) of all cancer cases in 2012, with an estimated 1.67 million new cases diagnosed. Women in less developed regions have slightly more incidence than women in more developed regions.[1] Every year over 100,000 new cases of breast cancer are diagnosed in India.[2] According to global and Indian studies, the incidence of cancer, as well as cancer related morbidity and mortality has increased significantly in the Indian subcontinent.[3–6] Fine needle aspiration cytology (FNAC) is becoming a popular test because it is both less expensive and effective in detecting breast lesions early. It also gives patients a prognostic value so that they can receive neo adjuvant therapy.[7,8] The FNA grading of breast cancer provides understanding into the nature of the disease and its potential outcomes, which aids in the selection of appropriate treatments and subsequent management.

In 1994, Robinson et al developed a grading system for Papanicolaou stained cytology smears that considered a broader range of features including structural configuration, cellular details, and nuclear features.[9] This method, like Elston's MRB method for histological grading had three cytological grades.[10] One of the system's strengths was that all cytological characteristics included in the score were important in regression analysis that also correlates with

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the recognized histological grades. Presence of nucleoli and their character were crucial in grading both individually and together with other cytological features. The mitotic count was not taken into account, which was the only flaw.[11,12]

The aim of our study was to analyze the concordance between cytological and histopathological grading in Invasive breast carcinoma and to find out the proportion of regional lymph node metastasis among cytological grades of breast carcinoma.

2. Materials and Methods

The present cross-sectional study was conducted in the Department of Pathology, tertiary health care hospital in India from Nov 2019-Oct 2021 among 100 diagnosed cases of carcinoma breast on histopathology whose cytology reports are available.

2.1. Sample size and inclusion criteria

As per an article by Phukan JP et al[13] (2015), the concordance rate between cytological and histological grading was 72%. Sample size was calculated by formula given by Phukan JP et al which came out to be 81 minimum sample size. Hence we included 100 cases in this study. Written consent were obtained from all 100 patients included in study. Male patients presenting with breast lumps, cases that lack either cytological or histopathological diagnosis and patients having inconclusive reports were excluded from the study.

2.2. Axillary lymph nodes

All the nodes found at grossing were submitted for histopathology. If the size of node < 5 mm, was submitted entirely. If the node is >5mm, bisected and submitted half the node. In case of metastatic mass we gave only one section or mention the number of sections taken separately or else a false increase on number of positive nodes would have been recorded.

All Sections were stained by hematoxylin and eosin (H&E) stain.

2.3. Statistical analysis

The means and standard deviations of the measurements per group were used for statistical analysis (SPSS 22.00 for windows; SPSS inc, Chicago, USA). Difference between two groups was determined using chi square test and the level of significance was set at $p < 0.05$.

3. Results

Grade 1, 2 and 3 breast cancer was found in 31%, 48% and 21% of the cases respectively as per Robbinson cytological grading. Grade 1, 2 and 3 breast cancer was found in 29%, 44% and 27% of the cases respectively as per modified Bloom Richardson histological grading (Table 1).

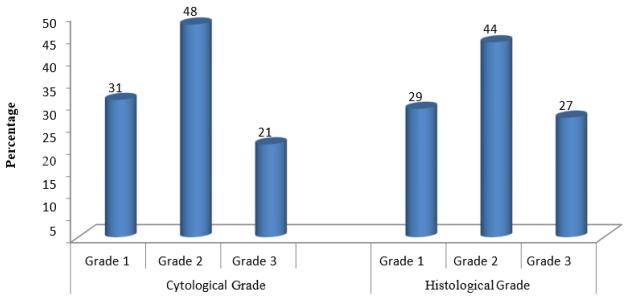

Figure 1: Cytological Grade according to Robbinson's Grading and Histological Grade according to Nottingham's modification of the Bloom – Richardson system

Cytological grade 1, 2 and 3 was seen in 21, 25 and 2 cases respectively in age group of 41 – 50 years. Only grade 2 and 3 tumors were seen in age group of more than 60 years. Cytological grade 1,2 and 3 was seen in 4, 38 and 4 cases respectively with tumor size of 3.1 to 6 cm. We found 23 cases with tumor size >6 cm of which 6 cases had cytologically grade 2 tumor 17 cases had grade 3 tumor.

The concordance rate between the cytological grade (using Robinson's method) and histological grade obtained in our study was 76% (kappa value: 0.86). The lack of correlation between cytological and histological grading may be the presence of varying degrees of atypia within the same tumor and inter observer subjectivity when assigning a cytological nuclear grade (Table 3). Significant positive correlation was found between cytological (Robinson's grading) and histopathological (Nottingham's modification of the Bloom – Richardson system) as r=0.83.

In the present study, we found an increasing incidence of axillary lymph node metastasis with increasing cytological grade.

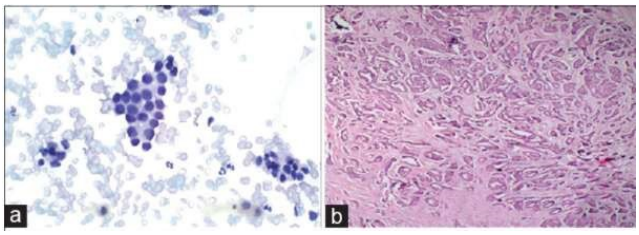

Figure 2: a: Cytological Grade 1 (Papanicolaou stain, x400); **b:** Histological Grade 1 (H and E, x100).

Photomicrograph (Figures 2, 3 and 4) showing Concordance between Cytological grades with Histological grades.

Table 1: Robinson's criteria for grading of breast cancer on cytology (FNAC) smears[9]

Parameter	Score 1	Score 2	Score 3
Cell dissociation	Mostly in clusters	Mixture of single cell and clusters	Mostly of single cells
Cell size	1-2 times of RBC	3-4 times of RBC	>5 times of RBC
Cell uniformity	Monomorphic	Mildly Pleomorphic	Pleomorphic
Nucleoli	Indistinct	Noticeable	Prominent
Nuclear margins	Smooth	Folds	Clefts
Chromatin	Vesicular	Granular	Clumped

Grade 1 : 6-11, Grade 2 : 12 -14 , Grade 3 : 15 -18
RBC – Red Blood cell

Table 2: Nottingham modification of the bloom-richardson histologic grading[14]

Parameter	Point 1	2 Point	3 Point	Summary of Points and Grade
Tubule formation	>75%	10 -75%	< 10%	Grade I = 3 – 5
Nuclear Pleomorphism	Minimal Variation	Moderate Variation	Marked variation	Grade II = 6-7
Mitotic count (Nikon Microscope)	0 – 5	10 – 19	>20%	Grade III= 8-9

Table 3: Concordance between cytological (Robinson's grading) and histopathological (Nottingham's modification of the Bloom – Richardson system)

		Nottingham's modification of the Bloom – Richardson system			Total
		Grade 1	Grade 2	Grade 3	
Robbinsons Grading	Grade 1	24	4	3	31
	Grade 2	4	36	8	48
	Grade 3	1	4	16	21
	Total	29	44	27	100
Chi Square			96.13		
Kappa value			0.86		
p value			<0.01*		

*: statistically significant

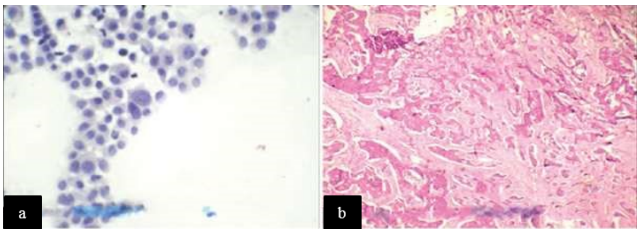

Figure 3: a: Cytological Grade 2 (Papanicolaou stain, x400); **b:** Histological Grade 2 (H and E, x100).

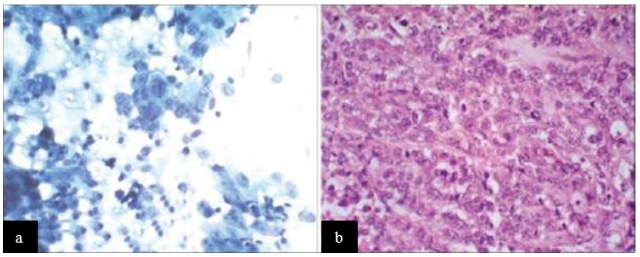

Figure 4: a: Cytological Grade 3 (Papanicolaou stain, x400); **b:** Histological Grade 3 (H and E, x100)

4. Discussion

Breast FNA cytology has gained widespread acceptance as a method of detecting breast cancer. Aspirated samples may be processed and reported more quickly and initial diagnosis can be given during outpatient visits only. Regional lymph node metastasis is more common in neoplasms with more cell dissociation. The cytological characteristics of malignant cells in FNA smears could also be analyzed using the appropriate scores like Robinson's grading system.[15]

In Our study Out of 100 subjects, 48% cases were from age group of 5^{th} decade followed by >60 years (26%). With increase in age; there are more chances of higher cytological grade, proving positive correlation between age and cytological grade. The age distribution of cases was in the range of 34–79 years as mentioned by Dinisha Einstien et al[16] in their study. Gayatri Ravikumar et al[17] in their study reported that patients age ranged from 28 to 98 years with a mean of 52.17 years.

In our study; tumor location at central, inner and outer part of breast was found in 34%, 18% and 48% of the

cases respectively. Higher cytological grade were revealed in outer part of breast followed by inner part. In the study by Gayatri Ravikumar et al,[17] tumors were located in the outer quadrant in 59% cases, the inner quadrant in 23 % and central quadrants in 14% cases.

In our study; grade 1, 2 and 3 breast cancer was found in 31%, 48% and 21% of the subjects respectively as per Robbinson grading. We found 76 percent agreement between the cytological grade (as determined by Robinson's method) and the histological grade (kappa value: 0.86). The presence of varying degrees of atypia within the same tumor, as well as inter observer subjectivity when assigning a cytological nuclear grade, may explain the lack of correlation between cytological and histological grading. Because of the nature of the lesion, certain benign and malignant conditions have cytological features that overlap (true grey zone).

Significant positive correlation was found between cytological (Robinson's grading) and histopathological (Nottingham's modification of the Bloom – Richardson system) as r=0.83.

In the studies by skrbinc et al[15] and Milentijevi'c et al[18] reported that the concordance between cytological and histological grade were 79.73% and 65% respectively. The observed differences were due to a lack of differentiation between histological grades I and II. Shweta Pal et al[19] in their study revealed that the majority of the cases, 58% were cytologically grade II, 28% were grade I, and 14% were grade III.

There was a 78% absolute concordance rate. The Spearman rank correlation coefficient was 0.804, indicating that the cytological and histological grades are highly correlated. The significant and marked association (P 0.001) between the grades assigned to FNAC smears and surgical pathology specimens was revealed by the high value of the coefficient of correlation. Our study has similar findings. SK Sinha et at[20–24] in their study showed the kappa values for grade I and II tumours were 0.63 and 0.656, respectively, indicating that the cytological and histopathological grading systems were in good agreement.

In present study; axillary lymph node metastasis was revealed in 64% of the subjects. We found an increasing incidence of axillary lymph node metastasis with increasing cytological grade. According to Frias et al[25] and Khan et al,[26] with increasing cytological grade, there was also an increased rate of axillary lymph node metastasis. These findings suggest that FNAC can be used to predict axillary lymph node metastasis, which is one of the most important breast cancer prognostic factor. Similarly in a study by Shweta Pal et al,[19] axillary lymph node metastasis was found in 62 percent (%) cases. Lymph Node metastasis was found in 21.43% cytological grade I tumors, 72.41% cytological grade II tumors, and 100% cytological grade III tumors. The link between increasing cytological grade and axillary lymph node metastasis was discovered to be statistically significant.

In node negative CA breast cancer, tumor size is one of the strongest predictors of dissemination and relapse. When measured microscopically, size has a greater prognostic significance than when measured grossly. Over half of the women with cancers > 2 cm in diameter present with lymph node metastasis. With tumor size, we can guide the clinicians about the prognosis and further management of breast cancer. With increase in tumor size there are more chances of higher cytological grade, proving positive correlation between age and cytological grade. In a study by Gayatri Ravikumar et al,[17] 69.4% of cases the tumor size was between 2 to 5 cm whereas 18.4% had a tumor size <2 cm and 12.2% had a tumor >5 cm..

The aggressiveness of the tumor is determined by cytological grading on FNAC smears, which is an important factor to consider when choosing neo adjuvant chemotherapy/hormonal therapy. In low-resource settings, where core biopsy is not routinely performed for diagnosis and treatment is often based on the cytology report alone, FNAC is especially useful.

5. Conclusion

In the present study, we found a high degree of concordance between cytological and histopathological grading system and also an increasing incidence of axillary lymph node metastasis with increasing cytological grade. Preoperative FNAC grading aids in the determination of neo-adjuvant chemotherapy and prognosis, hence this grading should be included in cytology reports on a regular basis. We would like to suggest that FNAC diagnosis and grading of such cases should only be performed by a pathologist with sufficient experience in breast cytology. Despite the existence of various cytological grading systems, Robinson's method is preferable for routine use because it is simple, objective, and repeatable.

6. Source of Funding

None.

7. Conflict of Interest

None.

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