

ROBINSON'S CYTOLOGICAL GRADING ON ASPIRATES OF BREAST CARCINOMA AND CORRELATION WITH BLOOM-RICHARDSON'S HISTOLOGICAL GRADING

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ABSTRACT

BACKGROUND

Breast carcinoma is one of the most common cancer of women. Fine-Needle Aspiration Cytology (FNAC) is widely used, most convenient, quick and common preoperative diagnostic modality in breast lesions. Cytological grading on aspirates of breast carcinoma is a very useful tool for surgical manoeuvre and prognosis.

The aim of the study is to study the correlation of cytomorphological Robinson's grading with modified Bloom-Richardson's histopathological grading of breast carcinoma.

MATERIALS AND METHODS

In the present study, 140 cytologically malignant breast tumour cases were included in the study and out of which, 90 cases correlated with histology after mastectomy. FNA was performed with 22-24 gauze needle and smears were stained with Haematoxylin and Eosin, Papanicolaou and May-Grunwald-Giemsa and evaluated for cytological grading according to Robinson's grading system. H and E stained histosections were graded according to Bloom-Richardson's grading system and comparison were done between the two.

RESULTS

Robinson's cytological grading correlated well with Bloom-Richardson's histopathological grading. The concordance rate between cytology and histology of Grade I, Grade II and Grade III tumours were 84.61%, 79.16% and 87.5%, respectively. Overall, concordance was found to be 83.6%. The Kappa value showed 95% confidence level. Thus, the strength of agreement between two grading systems considered to be fair. The P value on chi-square analysis showed <0.0001, which was considered statistically significant. Hence, the cytological grading is comparable with histological grading.

CONCLUSION

Robinson's cytological grading of breast carcinoma correlates well with Bloom-Richardson's histomorphological grading system. Hence, cytological grading in FNAC smears can be used as a prognostic factor for choosing the newer treatment modalities.

KEYWORDS

Fine-Needle Aspiration Cytology, Breast Carcinoma, Robinson's Grading, Bloom Richardson's Grading.

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BACKGROUND

Breast cancer is a heterogeneous disease with a wide array of histologic appearance.¹ The incidence of breast cancer is rising in India and is now the second most common cancer diagnosed in women after cervical cancer. It is estimated that by 2030, the number of new cases of breast cancer in India will reach just under 2,00,000 per year.²

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This rising trend of breast cancer in developed and developing countries is a real threat challenging all efforts to screening, prevention and treatment aspects to reduce this cancer. Early diagnosis and prompt therapy are essential to decrease morbidity and mortality. Surgical biopsy specimens serve as the "gold standard" for diagnosis and the value of histological grading has been widely accepted.³ Histologic grade has been an important prognostic indicator that can predict overall and metastasis free survival for local and regionalised breast cancer.⁴ Nottingham histological grading of breast carcinoma by Elston and Ellis is a widely accepted tumour grading system and has been found to have good prognostic correlation.⁵

The utility of Fine-Needle Aspiration (FNA) cytology is increased due to the introduction of new adjuvant therapy for rapid diagnosis and to determine various prognostic parameters.⁶ The National Cancer Institute (NCI), Bethesda,

sponsored conference had also recommended that the tumour grading on FNA smears should be incorporated in cytological reports for prognostication.⁷ It also emphasised that cytological grading system on FNA smears should correspond to the grading system used in histopathology.⁸ In literature, various studies compared cytological grading system with Bloom-Richardson's grading. Among all, Robinson's cytological grading⁹ correlates well with Elston's modified Bloom-Richardson's grading system.¹⁰

Hence, it is desirable to grade tumours before surgery, so that most appropriate medical regimen can be selected. Assessment of the in situ tumours can be done and over treatment of low-grade tumours can be prevented. The aim of the study is to grade the FNAC smears of breast carcinoma according to Robinson's et al and to correlate with its histologic grading proposed by Nottingham's modification of Bloom-Richardson's system.

MATERIALS AND METHODS

The present study is a prospective study carried out in the Department of Pathology of M.K.C.G. Medical College, Berhampur, Odisha, over a period of October 2012 to September 2014 with the approval of Institutional Ethics Committee. All female patients referred for FNAC of palpable

Cytological Grading with Methods of Robinson's et al.

Criterion	Score		
	1	2	3
Cell dissociation	Mostly clusters	Single cells, clusters	Mostly single cells
Nuclear size	1-2 times size of RBCs	3-4 times size of RBCs	More than 5 times size of RBCs
Cell uniformity	Monomorphic	Mildly pleomorphic	Pleomorphic
Nucleoli	Indistinct/small	Noticeable	Prominent/pleomorphic
Nuclear margin	Smooth	Slightly irregular/folds	Buds, clefts
Chromatin pattern	Vesicular	Granular	Clumping/clearing

Score- 6-11 Grade I; 12-14 Grade II; 15-18 Grade III.

The scores for each of 6 cytological features were added together to give a total score for each case. In each case, the final scores ranges from 6 to 18.

Histological grading was performed using Elston's modification of Bloom-Richardson's system⁵ with a microscopic field diameter of 0.45 mm. Three parameters taken into consideration- Degree of tubule formation, nuclear pleomorphism and number of mitosis. Each parameter was scored between one and three. Overall score for all cases ranged between 3 to 9.

BLOOM-RICHARDSON'S HISTOLOGICAL GRADING

Tubule formation (extent within tumour)

- >75% 1
- 10%-75% 2
- <10% 3

Nuclear Pleomorphism

- Small, regular, uniform 1
- Moderate variation in shape and size 2

breast lump to cytology section from surgical outpatient department. After taking consent, relevant clinical history as well as thorough clinical examination were done and recorded. Patients with palpable breast lump diagnosed on cytology along with histology were included into the study group. Unwilling patients, scanty aspirate and cytology without histopathological examination, all cases of breast carcinoma other than infiltrating ductal carcinoma and male breast lump were excluded from the study.

FNAC was done within all aseptic measures by using Cameco syringe holder with 22-24 gauze needle. All the smears were stained with May-Grunwald-Giemsa (MGG), Haematoxylin and Eosin (H and E) and Papanicolaou (PAP) stains. Subsequently, the stained smears were examined under microscope and graded according to Robinson's et al.¹¹

Reporting of the Smears

The smear was evaluated based on the grading systems described by Robinson's et al taking into account of six parameters cell dissociation, uniformity, cell size, nucleoli, nuclear margin and chromatin pattern. A value between one and three was given to every factor analysed.

Marked variation in shape and size 3

Mitotic Count per 10 hpf (Dependent on Microscopic Field Area)

Field diameter 0.44-mm diameter/0.152-mm² area

- 0-5 1
- 6-10 2
- >11 3

Total Score- 3-5 Grade I, well-differentiated; 6-7 Grade II, moderately-differentiated; 8-9 Grade III, poorly-differentiated.

STATISTICAL ANALYSIS

Association between different grading systems was measured by chi-square test. Correlation between cytological and histological grading system was examined by Spearman's correlation coefficient. A P value of 0.05 or less was considered to be statistically significant.

OBSERVATION

In the present study, a total number of 140 cases of breast lump underwent FNAC during the two years study period. Cytological diagnosis of infiltrating duct carcinoma were suggested in 106 cases, among which 94 mastectomy specimen were available for histopathological analysis. Out

of these 94 cases, 90 cases were diagnosed as infiltrating duct carcinoma NOS type, which constituted the study group. Maximum number of cases 52.22% of cases (n=42) were in the age group of 41-50 years. Only, 3.33% (n=3) found in age group of 22-30 years.

Grade	Cytology		Histology	
	Number of Cases	Percentage	Number of Cases	Percentage
Grade I	26	29	25	27.77
Grade II	24	27	28	31.11
Grade III	40	44	37	41.11
Total	90	100	90	100

Table 1. Distribution of Cases According to Cytological Grading (RCG) and Histological Grading (MBR)

On cytological grading, maximum number of cases 44% (n=40) were in Grade III followed by 29% (n=26) and 27% (n=24) belonged to Grade I and Grade II, respectively. Histologically, 27.77%, 31.11% and 41.11% cases were Grade I, Grade II and Grade III, respectively (Table 1).

Cytological Grade	Total Cases	Histological Grade			Concordance Rate
		Grade I	Grade II	Grade III	
I	26	22	04	00	84.61
II	24	03	19	02	79.16
III	40	00	05	35	87.50
Total	90	25	28	37	83.60

Table 2. Comparison between Cytological and Histological Grade (RCG and MBR)

The cytological and histological grading was compared and concordance rate found to be 84.61% in Grade I, 79.16% in Grade II and 87.5% for Grade III. The overall concordance rate was found to be 83.60% (Table 2).

Grade	Number of Cases Diagnosed on Cytology	Number of Cases Diagnosed on Histology	Kappa Value	95% Confidence Interval for Concordance	Standard Error	Strength of Agreement	'P' value
I	26	22	0.335	0.150 to 0.520	0.094	Fair	<0.0001
II	24	19	0.310	0.105 to 0.515	0.104	Fair	<0.0001
III	40	35	0.348	0.203 to 0.492	0.074	Fair	<0.0001

Table 3. Comparison between Cytological (RCG) and Histological Grading (MBR) with Statistical Analysis

The Kappa statistics was done to measure the strength of agreement between cytological and histological grade. Kappa value for Grade I, Grade II and Grade III tumours were 0.335, 0.310 and 0.348, respectively, which indicates fair agreements.

The Kappa (k) value showed 95% confidence level and standard of error between the cytological and histological grading system. Thus, strength of agreement between the two grading systems considered to be fair.

The calculated P value less than 0.0001 was extremely significant, hence the cytological grading was comparable to histological grading (Table 3).

On multiple regression analysis of cytological features such as cell uniformity, nucleolus and chromatin pattern were most specific parameters (P<0.0001) in determining the grades of tumour followed by other parameters like cell dissociation cell size (P<0.005), nuclear margin (P<0.01) (Figure 1).

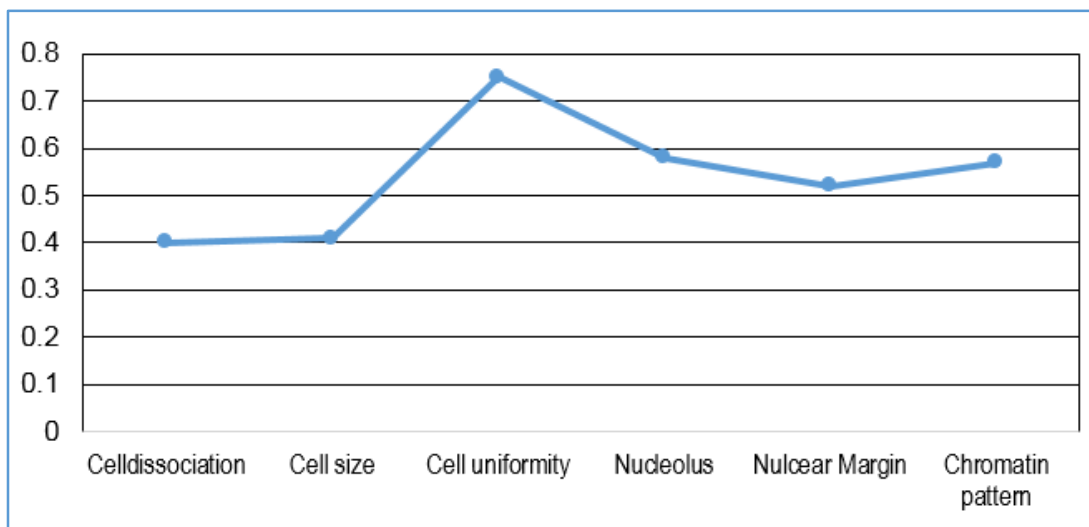


Figure 1. Cytological Parameters and Regression Coefficient Correlation

DISCUSSION

As neoadjuvant therapy including preoperative chemotherapy and tamoxifen is becoming increasingly common for early breast cancer, it is desirable to grade tumours before surgery so that the most appropriate medical regime can be selected.⁸

By administration of preoperative therapy, several studies have shown that, there is rapid decrease in the tumour size. So, assessment of biological aggressiveness of cancer in high-grade tumour without removing it would therefore be valuable. FNAC grading allows such assessment and serial estimates to see how pretreatment modulates tumour grade.^{5,12}

There are many cytological grading systems of breast carcinoma and they have good correlation with Elston-Ellis Grading system (modified Bloom-Richardson’s grading). Robinson’s method was considered better than the other methods because of its more sensitivity, simplicity, more objective setup criteria and easy reproducibility, which has been used in present study.^{13,14}

In this study, the age range of the patients were from 21-70 years with maximum number of cases in

premenopausal years (40-50 years), which corroborate with the study of Farley et al (2011).¹⁵

In Robinson’s cytological grading of our study, out of 90 cases maximum 44% (n=40) were in Grade III followed by Grade I 29% (n=26) and Grade II 27% (n=24). These findings were comparable with Bhargava et al¹⁶ and Sinha et al.¹⁷ But, in contrast, previous studies by Khan et al,¹⁸ Das et al,¹⁹ Wani et al²⁰ and Robinson’s et al⁹ observed predominance of Grade II tumour.

In the present study, maximum number of cases, i.e. 41.11% (n=37) belonged to histological Grade III, which is corroborative with the study of Bhargava et al¹⁶ and Sinha et al.¹⁷

In the present study, the absolute concordance rate was 83.60%. By Robinson’s cytological grading with Bloom-Richardson’s histopathological grading (n=90) showed substantial strength of agreement for Grade III and Grade I tumours with nearly perfect concordance in Grade II tumours, which is comparable to other studies (Figure 2). So, cytologic grade could be used to predict histologic grade as a significant relationship exist between them.

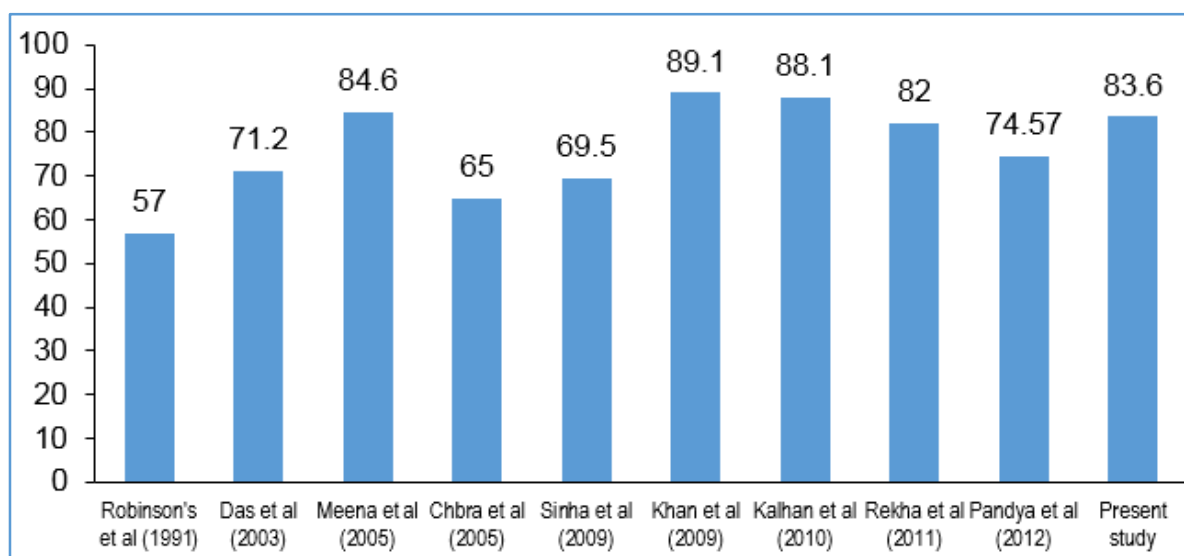


Figure 2. Comparison of Cytological Grading with Concordance Rate.

Our study level is at higher end of spectrum and lack of correlation in 16.4% (n=15) could be attributed to tumour heterogeneity and observer subjectivity while assigning nuclear grade.

Kappa (k) statistical analysis was done to find out the strength of agreement between cytological and histological grades and value interpreted according to Landis and Koch classification, which indicates substantial agreement for Grade I tumours between cytological and histological grading system. The present study showed K value for Grade I, Grade II and Grade III were 0.335, 0.310 and 0.348 respectively, signifying statistically fair agreement.

In present study, cytohistological correlation between grading system using chi-square analysis revealed P value less than 0.0001, which statistically extremely significant and correlates with studies conducted by Frias et al²¹ (<0.0005) and Lingegowda et al²² (<0.001).

Multiple regression studies were done by various authors. In a study done by Khan et al²³ in multiple regression analysis of various cytological features found regression coefficient of cell dissociation, chromatin pattern and nucleoli 0.780, 0.584 and 0.461, respectively (P<0.001) were most specific for determining cytological grade. Similar results were also observed by a study done by Robinson et al⁹ and Cangiavella and Simsir et al.¹⁴

In the present study, on multiple regression analysis, cytological features showed regression coefficient of cell uniformity, nucleolus and chromatin pattern 0.75, 0.58, 0.57 respectively with P value <0.0001. These parameters were found to be most sensitive factors in determining the cytological grade and it corroborates well with previous studies. So, FNAC grading by Robinson's method is comparable with histological grading and useful in assessing tumour behaviour and prognosis.

CONCLUSION

Cytological grading of breast carcinoma is simple, feasible and provides valuable prognostic information. So, we conclude that, FNAC of malignant breast lesion should be graded to assess tumour behaviour, prognosis and guiding neoadjuvant chemotherapy preoperatively.

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