



# ORIGINAL RESEARCH PAPER

# Pathology

## RELATIONSHIP OF CYTOLOGICAL GRADING OF BREAST CARCINOMA WITH REGIONAL LYMPH NODE METASTASIS

**KEY WORDS:** Robinson's Cytological Grading, Breast Carcinoma, Lymph Node Metastasis

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### ABSTRACT

**Background and objectives:** Breast carcinoma is the second most common cancer among Indian females. FNAC is a reliable method for the diagnosis of palpable masses of the breast. In addition it provides prognostic information for the patients undergoing neoadjuvant therapy. Objective: This study was carried out to evaluate the relationship between cytological grading of breast carcinoma and regional lymph node metastasis.

**Materials and methods:** 50 breast carcinoma cases were studied. FNAC smears were graded according to Robinson's cytological grading system. Relationship between grading and lymph node metastasis was evaluated.

**Results:** By Robinson's method, grade I, II, and III tumors showed lymph node involvement in 16%, 37% and 75% respectively. A statistically significant relationship was seen between the cytological grades and lymph node involvement.

**Conclusion:** Cytological grading is a strong predictor of regional lymph node metastasis. Higher grades were associated with higher incidence of lymph node metastasis.

### INTRODUCTION

Carcinoma of the breast is the most common non-skin malignancy in women[1]. FNA is safe, reliable and time saving out door procedure with little discomfort to the patient. It is helpful not only in diagnosis and planning of treatment, but also helpful in prognostication of the tumor factors like nuclear grading, mitotic index, hormone receptor status and DNA contents.[2] Cytologic evaluation of prognostic markers is important and useful in patients with inoperable tumors and in cases with high risk for surgery. In patients with advanced stage breast cancer requiring neo-adjuvant radiotherapy or chemotherapy, cytologic evaluation of prognostic markers can be useful to provide baseline data as these parameters may be modified by treatment. [3]

Robinson et al developed a protocol in 1991 for cytological grading of invasive ductal carcinoma – not otherwise specified (NOS). In the Robinson's grading system, six different cytological parameters namely cell dissociation, cell size, cell uniformity, nucleolus, nuclear margin and nuclear chromatin are used for grading the tumors. A grade of 1-3 is given to each of these parameters and the tumor is graded by adding up the scores.[4,5] The degree of cell dissociation is an indicator of cell cohesion status and to an extent, of the degree of expression of the E-cadherin/catenin complex. Loss of cell cohesion appears to facilitate vascular infiltration by tumor cells which produces an increased incidence of regional lymph node metastasis.[6]

The presence or absence of metastasis to axillary lymph nodes is the single most influential predictor of recurrence [7]. Axillary lymph node status has been shown to be an important predictor of disease-free survival and overall survival in breast cancer. Only 20%-30% of node negative patients develop recurrence within 10 years, as compared to the other 70% of patients with axillary node involvement. The absolute number of involved nodes is also of prognostic importance. Patients with 4 or more involved nodes have a worse prognosis than those with fewer than 4 involved nodes [8].

Higher cytological grades were seen associated with higher incidence of regional lymph node metastasis. Thus, cytological grade plays an important part in predicting the disease prognosis.

### MATERIALS AND METHODS:

The material for the present study constituted 50 cases of breast carcinoma with preoperative cytologic diagnosis followed by mastectomy received at the Department of pathology over a period spanning 18 months (January 2013 – June 2014).

Patients having palpable breast lumps with clinical and cytological

diagnosis of breast carcinoma and subsequent histopathological follow-up were included in the study. Patients who had benign breast lesions and who refused biopsy examination were excluded from the study.

After the preliminary documentation, the FNA procedure was explained in detail to the patient and informed consent obtained. The breast lump was palpated and immobilized between the thumb and forefinger. After disinfecting the skin with alcohol, a 22 gauge needle was applied to a 5-10 ml syringe and introduced into the skin upto the anterior edge of the mass and a negative pressure was created. Several passes were made without removing the needle from the mass. The aspirated material was expressed onto a clean glass slide and spread with a similar slide applied by separating them with a horizontal motion. The preparation was fixed immediately in 95% ethanol or in Carnoy's fixative (whenever the aspirate was haemorrhagic). The slides were stained with H&E, Papanicolaou and/or Giemsa stain and examined under the microscope. The breast carcinomas were graded cytologically by Robinson's Grading system (Table 1).

**TABLE1: Documentation of Cytological Features as per Robinson's Grading[3],[5]**

Criteria	Score		
	1	2	3
Cell dissociation	Mostly in clusters	Mixture of single cells and cells in clusters	Mostly single cells
Cell size (times of RBC)	1-2	3-4	≥5
Cell uniformity	Monomorphic	Mildly pleomorphic	Pleomorphic
Nucleoli	Indistinct	Noticeable	Prominent or Pleomorphic
Nuclear margin	Smooth	Folds	Buds/Clefts
Chromatin	Vesicular	Granular	Clumped and Clear

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

### STATISTICAL ANALYSIS

It was done using SPSS software. Chi square test was performed and p value was determined. A p value of less than 0.05 was considered statistically significant.

**RESULTS:**

In the present study, lymph node metastasis was seen in 3 out of 19 cases of grade I , 10 out of 27 cases of grade II and 3 cases out of total 4 cases of grade III breast carcinomas. Total about 16 cases among the 50 cases studied showed lymph node metastasis which accounted for 32% of cases. There was no lymph node involvement in the remaining 34 patients i.e. 68% of the total cases.

Lymph node metastasis was seen in 75% of grade III cases. Grade II cases showed lymph node metastasis in 37% of cases. Grade I cases showed metastasis in 16% of cases.(Table 2)

**TABLE 2: Relationship of cytological grade with lymph node metastasis**

Cytological Grade	Lymph node +ve	Lymph node -ve	Total
I	3(16%)	16(84%)	19
II	10(37%)	17(63%)	27
III	3(75%)	1(25%)	4
Total	16(32%)	34(68%)	50

Chi square test was performed using SPSS software  
 Chi square value-6.008  
 P value-0.04

P value is less than 0.05 which shows statistically significant relationship between cytological grades and lymph node metastasis. Higher cytological grades were seen associated with higher incidence of lymph node metastasis

**DISCUSSION:**

Breast cancer is the second most prevalent cancer among Indian women, the first being cervical cancer.[9] In India, the breast is reported as the most common site of cancer in Mumbai, and Thiruvananthapuram, whereas it is the second most common site of cancer in Chennai and Dibrugarh. In Bangalore, it is ranked third according to data reported from hospital based cancer registries (ICMR).[10]

Utility of cytologic grading is to detect fast growing grade III tumors which are more likely to respond to chemotherapy than low grade (slow growing) tumor. Slow growing tumor may be better suited to pretreatment with tamoxifen.[6] Preoperative neo adjuvant chemotherapy is becoming common for treatment of breast cancer. So, it is desirable to grade tumor before surgery. So, most appropriate regime can be selected.[11]

Lymph node status is an important prognostic factor in breast cancer. We have studied lymph nodes for regional metastasis and found that out of 19 cases of grade I, 3 cases (16%) showed metastasis. Out of 27 cases of grade II, metastasis was seen in 10 cases (37%) and out of 4 cases of grade III, metastasis was seen in 3 cases (75%) . Totally out of 50 cases, metastasis was seen in 16 cases accounting for 32 % of lymph node positivity.

As per study done by Sinha et al[12], lymph node metastasis was observed in three with cytological grade II, 28 of grade III and none of grade I. Overall out of 55 cases, 31 cases showed lymph node metastasis accounting for 56.3% of lymph node positivity.

A study was done by Frias et al[4] in 100 cases of breast carcinoma where metastasis was seen in 3 cases out of 36 grade I cases, 25 out of 39 grade II cases and 22 out of 25 grade III cases. Overall 50% cases showed lymph node positivity.(Table 3)

**CONCLUSION:**

Fine-needle aspiration cytology plays a major role in the primary diagnosis of breast carcinoma. Cytological grading of the smears can provide valuable prognostic information and aid in planning the management options. Robinson's grading system is simple, quick, has more objective set of criteria and easy reproducibility Thus besides from having minimal subjective discomfort, insignificant complications, negligible risk of tumor spread, rapidity of diagnosis, utility for multiple lesions, readily repeatability, high accuracy of FNAC; FNAC grading is useful in assessing the tumor behaviour and prognosis and guiding neo adjuvant chemotherapy. Now-a-days, attempts have been made to determine various prognostic parameters on FNA materials.The National Cancer Institute (NCI), Bethesda, sponsored conference had also recommended that tumor grading on FNA material should be incorporated in FNA reports for prognostication. Cytological grading is strongly related with lymph node metastasis and thus predicts the prognosis of patient.

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**TABLE 3 : Comparative table of Cytological grade and nodal metastasis**

Cytological grade	Present study		Frias et al.[4]		Sinha et al[12]	
	No.of cases	Metastasis	No.of cases	Metastasis	No.of cases	Metastasis
I	19	3	36	03	5	0
II	27	10	39	25	18	3
III	4	3	25	22	32	28
Total	50	16	100	50	55	31

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31