



Comparative Study of Fine Needle Aspiration Cytology and Histopathology in Grading Breast Carcinoma

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Abstract

Background & Objectives: Carcinoma of the breast is the commonest cancer in urban Indian women and the second commonest cancer in the rural women next to cervical carcinoma. Neo-adjuvant therapy including pre-operative chemotherapy and tamoxifen is becoming increasingly common for early breast cancer. Hence, it is desirable to grade tumors before surgery, so that, the most appropriate medical regimen can be selected. Hence, much attention is focussed on grading tumors on FNAC. This cytologic grade also corresponds well with the histologic grade. This study was done to correlate Robinson's cytological grading with modified Scarff Bloom Richardson's histological grading in cases of infiltrating ductal carcinoma breast.

Material and Methods: Total 50 breast carcinoma cases were studied. FNAC smears were graded according to Robinson's cytological grading system while the corresponding paraffin embedded histology sections were graded as per Modified Scarff Bloom Richardson's grading.

Results: Out of the total 50 cases, majority belonged to 40-50 years age group with the mean age as 50.22 years. On cytological grading 19(38%), 27(54%) and 4(8%) cases were of grade I, II and III respectively while on histological grading 17(34%), 28(56%) and 5(10%) cases were of grade I, II and III respectively. The concordance rates between cytological and histological grading for grade I,II and III were 73.7%, 81.5% and 50% respectively. There was a significant association (76%) between the cytological and histological grading ($p=0$).

Conclusion: Besides 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 comparable with histology grading and is useful in assessing the tumor behaviour and prognosis and guiding neo adjuvant chemotherapy. Hence, the cytological typing and grading should be incorporated in the FNAC report and this can be of great value in guiding the choice of the treatment protocols.

Keywords: Breast carcinoma, Robinson's cytological grading, modified Scarff Bloom Richardson's histological grading, FNAC.

Introduction

Carcinoma of the breast is the most common non-skin malignancy in women^[1]. Owing to the lack of awareness of this disease and in absence of a breast cancer screening program, the majority of breast cancers are diagnosed at a relatively advanced stage^[2]. Hence, any breast lump, whether it is benign or malignant, is a source of anxiety for the patient as well as for the treating doctor^[3].

Since last decade, cytodiagnosis has gained importance due to rapid results at low cost and may help in early diagnosis in country like India. FNAB is a reliable method for the initial evaluation and diagnosis of palpable masses of the breast. In addition, it also has the ability of providing necessary prognostic/predictive information, particularly for patients that may undergo neoadjuvant therapy^[4].

Fine needle aspiration of breast is one of the most common procedures performed on patients with a palpable mass.^[5] FNA is safe, reliable and time saving outdoor 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.^[6]

Histologic grade has been an important prognostic indicator that can predict overall and metastasis free survival for local and regionalized breast cancer.^[7]

A new era of systemic adjuvant therapy has been heralded by studies in which treatment was given before surgery either in conventional regimens or by cutaneous infusion of newer drugs. These studies have shown a high response rate with the tumors rapidly decreasing in size. Faster growing tumors respond more to chemotherapy than low grade slow growing tumors, which may be better suited to pre-treatment with tamoxifen. Assessment of the biological aggressiveness of the cancer without removing it would therefore be valuable.

FNAC grading allows such assessment and serial estimates to see how pre-treatment modulates the tumor grade. This cytologic grade also corresponds well with the histologic grade.^[8]

In present study, Robinson's cytological grading was done on cytology and compared with modified Scarff Bloom-Richardson's system on paraffin embedded sections.

Material 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 Cytological Grading system (Table 1). Histological grading of H&E stained tissue sections was done by Modified Scarff Bloom Richardson method (Table 2).

Table 1: Documentation of Cytological Features as per Robinson’s Grading^{[9],[10]}

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

Table 2: Documentation of Histological Features as per MBR Grading^[11]

Feature	Score
Tubule formation	
Majority of tumour >75%	1
Moderate degree 10-75%	2
Little or more <10%	3
Nuclear pleomorphism	
Small, uniform	1
Moderate increase in size/variation	2
Marked variation	3
Mitosis per 10 hpf in Nikon Labophaf microscope	
0-5 (histo)	1
6-10 (histo)	2
>11 (histo)	3

Scores: Grade I (well differentiated) 3-5; Grade II (moderately differentiated) 6-7; Grade III (poorly differentiated) 8-9

Concordance was calculated between cytological and histological grading systems for all the grades. Kappa statistical analysis was done to see the strength of agreement between the two grading systems. For this SPSS software was used.

Results

In the present study, age of the subjects ranged from < 40-60+ years. Mean age was 50.22 years. Majority 26 cases (52%) belonged to 41-50 years age group followed by 9 cases (18%) in >60 years age group, 8 cases (16%) 51-60 years, 7 cases (14%) in <40 years. In the present study, all cases were females.

In the present study, 14 tumors (73.7%) were Grade I on cytology (figure 1) and histopathology (figure 2), 4 tumors (21.1%) were Grade I on cytology and Grade II on histopathology and 1 tumor (5.2%) was Grade I on cytology and Grade III on histopathology. Out of the 27 cases with cytological grade II (figure 3), 22 tumors (81.5%) were Grade II also on histopathology (figure 4), while 3 (11.1%) were Grade I and 2 (7.4%) were Grade III. Out of the 4 tumors with cytological Grade III (figure 5), 2 (50%) were Grade III also on histopathology (figure 6) while 2 (50%) were Grade II on histopathology. Total concordance between cytological grade and histological grade was seen in 38 cases out of 50 cases (table 3) accounting for 76% of total cases

Table 3: Correlation between cytological and histological grading

Cytological grades	Histological grades						Total	
	I		II		III			
	No.	%	No.	%	No.	%	No.	%
I	14	73.7	4	21.1	1	5.2	19	100
II	3	11.1	22	81.5	2	7.4	27	100
III	0	0	2	50	2	50	4	100
Total	17	34	28	56	5	10	50	100

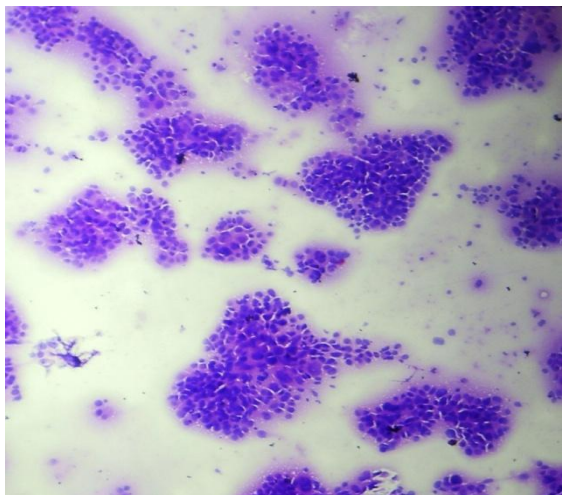


Figure 1 : Cytological grade 1 (x100 H&E)

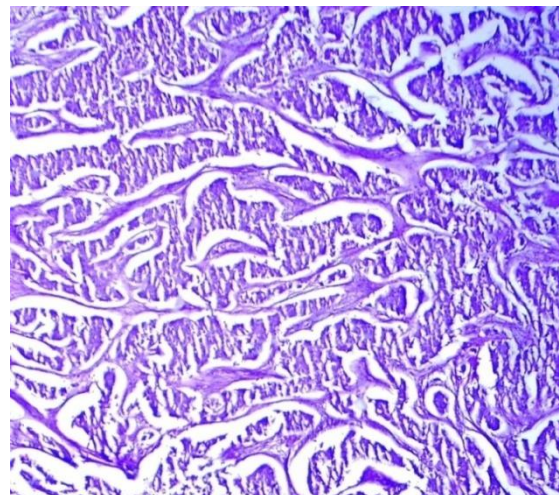


Figure 2 : Histological grade 1 (x100 H&E)

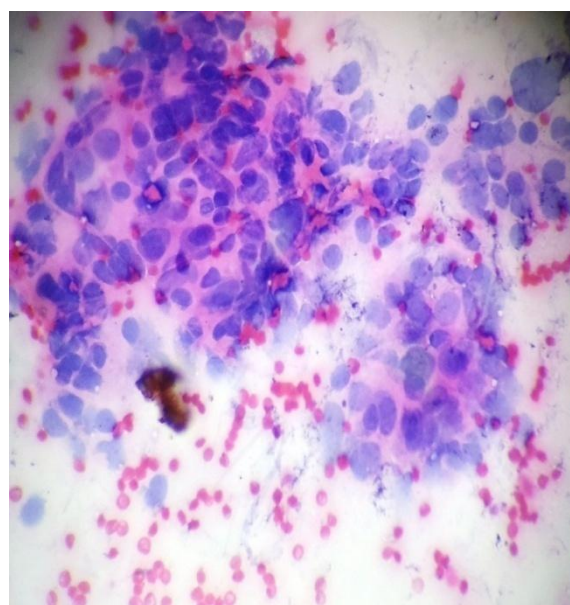


Figure 3 : Cytological grade 2 (x400 Pap)

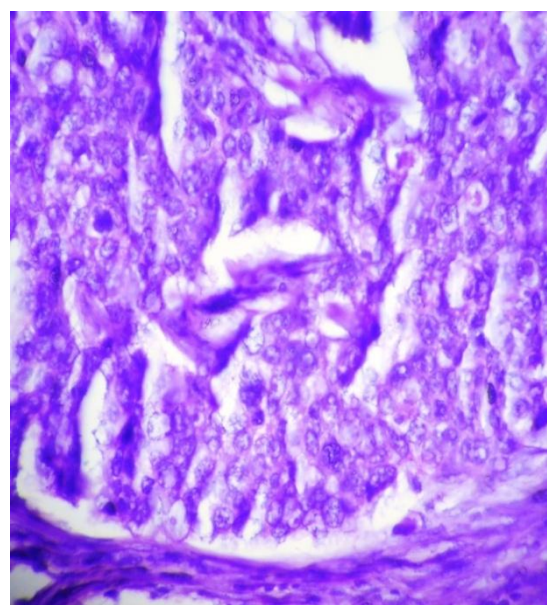


Figure 4 : Histological grade 2 (x400 H&E)

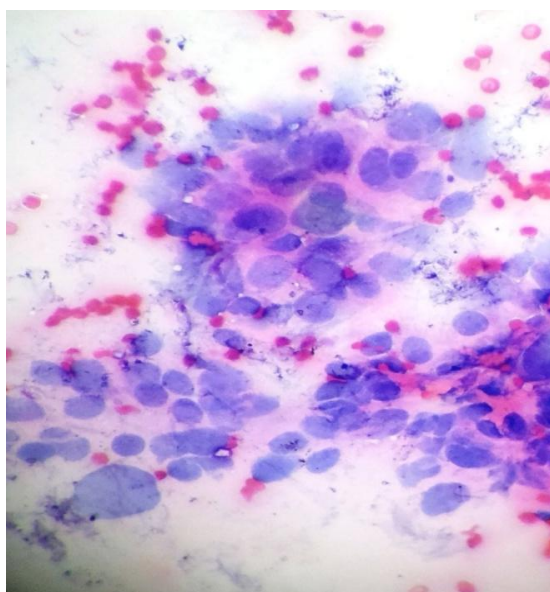


Figure 5: Cytological grade 3 (x400 Pap)

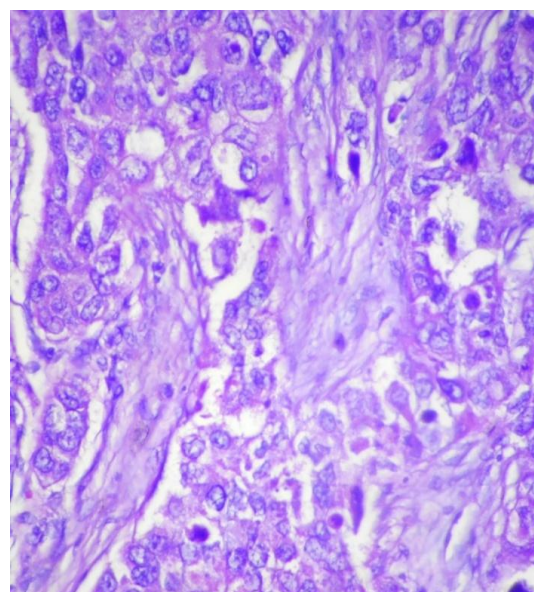


Figure 6: Histological grade 3 (x400 H&E)

Kappa statistical analysis was done to show the strength of agreement between cytological and histological grades. Kappa values were interpreted according to Landis and Koch classification. As shown in table 4, Kappa value for grade I tumors is 0.65 which indicates substantial agreement between cytological and histological grading

systems. Kappa value for grade II and III tumors are 0.55 and 0.39 respectively which indicates moderate agreement between cytological and histological grading systems. Overall for all the grades kappa value came out to be 0.572 which shows moderate agreement between cytological and histological grading systems.

Table 4: Kappa statistical analysis to show the agreement between cytological and histological grades

Grade	Kappa value (95% CI) for concordance	Standard error	Strength of agreement
I	0.653	0.111	substantial
II	0.556	0.118	moderate
III	0.390	0.219	moderate
Total for all the grades	0.572	0.105	moderate

Thus, cytological grading is comparable to histological grading in assessing the tumor behaviour. Also it can be stated that grading system showed stronger correlation in lower grade (grade I) than higher grades (grade II and III).

Discussion

The breast lesions are easily accessible to FNAC, which is an easy, cost effective and less time-consuming procedure. Despite the polar variance in views as to the extent of information that can be derived from breast fine-needle aspirates, most of the cytopathologists agree that nuclear grading should be done on FNAs of primary and metastatic breast carcinomas. As definitive treatment regimens assume a vital role prior to or in lieu of surgery, it seems the wealth of information provided by the FNA alone is becoming increasingly important^[12].

There are many cytologic grading system for mammary carcinoma and they have good correlation with Elston and Ellis grading system. Robinson's method was considered better because of its more sensitivity, simplicity and more objective set of criteria and easy reproducibility.^[3] 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.^[9] 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.^[13]

In the present study, cytological grading was done by using Robinson grading. Majority 27(54%) were grade II tumors, followed by 19 (38%) grade I and 4 (8%) grade III. In concurrence with our study, Taniguchi et al.^[14], Robinson et al.^[10], Meena et al.^[6], Frias et al.^[15], Das et al.^[16], and Pandya et al.^[2] observed majority of tumors in grade II, followed by grade I and grade III. In contrast, Jayaram et al.^[17], and Sinha et al.^[18] observed majority of tumors in grade II followed by grade III and grade I.

In the present study, histological grading was done using Modified Scarff Bloom Richardson grading. It was found that, majority of the tumors 28(56%) were grade II, followed by 17 (34%) grade I, and 5(10%) grade III. The study by Frias et al.,^[15] Robinson et al.^[10] and Meena et al.^[6] showed similar observations. In contrast, Jayaram et al.^[17], Taniguchi et al.^[14], and Das et al.^[16] observed that majority of the tumors were grade II followed by grade III and grade I.

Different studies in the past have shown varying concordance between cytological and histological grading. Comparison studies between Robinson's grading and histological grading showed agreement of 57% by Robinson et al.^[10], 71.2% by Das et al.^[16], 83% by Meena et al.^[6], 44.4% by Taniguchi et al.^[14], 71% by Jayaram et al.^[17],

74.6% by Pandya et al.^[2], and 76 % in the present study.

Out of the total 50 cases, disconcordance was seen in 12 out of 50 cases which accounts for 24%. This disconcordance rate was comparable to study done by Pandya et al.^[2]-25.4%, Das et al.^[16]-28.8%, Jayaram et al.^[17]-29%. The lack of correlation (24 %) in the present study may be due to the presence of different degrees of atypia within the same tumor and subjective nature of grading process.

Conclusion

Robinson's cytological grading system is simple, quick, has more objective set of criteria and easy reproducibility. This cytological grading is comparable with MBR histological grading and is useful in assessing the tumor behaviour and prognosis and guiding neo adjuvant chemotherapy. Hence, the cytological grading should be incorporated in the FNAC report which can be of great help in guiding the treatment regimen.

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