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COMPARATIVE EVALUATION OF THREE CYTOLOGICAL GRADING SYSTEMS ON FINE-NEEDLE ASPIRATES OF BREAST CARCINOMA

Pathology

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ABSTRACT

BACKGROUND: Assigning grades to breast carcinoma on Fine-needle aspirates provides prognostic information and guides optimal therapy.
AIM: The present study was undertaken to evaluate three cytological grading systems to determine which corresponds best to histological Modified Bloom Richardson grade.
MATERIALS AND METHODS: 44 patients of Infiltrating duct carcinoma of breast who underwent FNAC and mastectomy for breast carcinoma were graded cytologically by Robinson grading, Fisher's modification of Black's grading system and Howell's modification of SBR grading; followed by histological grading. Correlation between cytological grades and histological grades was determined using kappa-coefficient and absolute concordance values.
RESULTS: All three systems correlated strongly with histological grading with absolute concordance of 88.6%, 84.1% and 81.8% for Robinson, Fisher's and Howell's systems respectively. The Kappa-coefficients were 0.88 for Grade I, 0.86 for Grade II and 0.65 for Grade III tumors by Robinson's grading. Fisher's grading showed Kappa-coefficients of 0.68 for Grade I, 0.96 for Grade II, and 0.50 for Grade III tumors. Kappa-coefficients were 0.38 for Grade I, 0.78 for Grade II and 0.84 for Grade III tumors in Howell's system.
CONCLUSION: Robinson's grading system is simple, more objective and demonstrates best concordance with histological grading. So, Robinson's system should be used routinely for breast carcinoma aspirates.

KEYWORDS

Breast Carcinoma; Cytological Grading; Fnac; Prognosis.

INTRODUCTION

Carcinoma of the breast is the most commonly diagnosed cancer in women and is the leading cause of cancer death in women.[1] The histological grading proposed by Elston and Ellis using Nottingham modification of Scarff-Bloom-Richardson (SBR) method for breast carcinoma is accepted worldwide. It is a useful guide for selecting neoadjuvant therapy and has good prognostic correlation.[2] However, cytological grade of breast carcinoma is hardly reported. Selection of neoadjuvant therapy and assessment of tumors before surgery can be achieved by inclusion of a cytological grading system in fine needle aspiration cytology (FNAC) smears of breast carcinoma and thereby morbidity due to surgical intervention, especially in low-grade tumors can be avoided.[3],[4]

The role of FNAC earlier has been doubted by results obtained with core needle biopsy (CNB) that seem more reliable than FNAC. In general, CNB is now preferred in the first line of diagnosis.[5] However, CNB carries complications such as pain (1.7-3.7%), vasovagal reactions (1%), severe bleeding (0.72%), infections (0.15%), and hematoma (0.09%).[6] FNAC has advantages than CNB such as minimal invasiveness and minimal discomfort and could be better for aged or frail patients with comorbidities.[7] Compared to CNB, aspiration is easier in lesions located just beneath the skin or those close to the chest wall. Moreover, FNAC maintains tactile sensitivity, allows multidirectional passes allowing a broader sampling of lesion and immediate reporting where necessary.[8]

The National Cancer Institute, Bethesda, sponsored conference had also recommended that the tumour grading on FNA material should be incorporated in FNA reports for prognostication.[9] The concept of nuclear grading was introduced by Black *et al*[10] in 1955. It was modified and applied to cytological smears by Fisher *et al*.[11,12] There have been many studies assessing nuclear grade in breast carcinoma in the past few decades. Numerous grading systems were proposed. Unfortunately, however there is absence of agreement among pathologists regarding acceptance of a single cytological grading system. The purpose of this present study was to evaluate three such three-tier cytological grading systems to determine which corresponds best to the histological grading done by Nottingham modification of Scarff Bloom Richardson (SBR)'s method.

MATERIALS AND METHODS

The present study was a hospital-based prospective study done over a period of 12 months (01.10.2018 to 30.09.2019). 44 cases of infiltrating duct carcinoma(IDC)breast, diagnosed on FNAC and confirmed by histopathology were included. Exclusion criteria were patients having a history of preoperative chemotherapy or radiotherapy for breast carcinoma, male patients and pregnant patients.

Fine-needle aspiration was done under aseptic precautions and air-dried May-Grunewald-Giemsa (MGG) stained smears were evaluated and the tumor was graded based on the grading system described by Robinson *et al*.,[13] Fisher's modification of Black's grading system[11] and Howell's modification of SBR grading.[14]

In Robinson's *et al*. grading system,[13] six different cytological parameters ,cell dissociation, cell size, uniformity, nucleoli, nuclear margin, and chromatin were given a score of 1-3 and smears that scored in the range of 6-11 were graded I, smears with a score of 12-14 were graded II, and smears with a score of 15-18 were graded III [Table 1]

In Fisher's modification of Black's nuclear grading, [11] five nuclear parameters such as nuclear size, chromatin, nucleoli, anisonucleosis, and nuclear membrane were scored and tumours were graded I-III. [Table2]

Howell *et al*. grading system [14]is very similar to the histological SBR method with modification to the mitotic count as score 1 for 0-1/10 high power fields (HPFs), 2 for 2-4/10 HPF, and 3 for ≥5/10 HPF. The Grades were given as I, II, and III for scores in the range of 3-5, 6-7, and 8-9, respectively.[Table 3]

The cases were followed up. Representative tissue sections from the mastectomy specimens were formalin fixed ,processed and hemat oxylin & eosin stained sections were evaluated. Histopa thological features were studied and the breast carcinomas were graded as per modified Bloom- Richardson's grading system.[Table 4]

The histological grades were compared with each of the the three cytological grading systems and absolute concordance was calculated between all three corresponding grades. Kappa coefficient was used to compare the agreement for each grade.

Table 1: Robinson's criteria (1994) for cytological grading of breast carcinoma

	SCORE 1	SCORE 2	SCORE 3
Dissociation	Cells mostly in clusters	Mixture of single and cell clusters	Cells mostly Single
Cell size	1-2×RBC size	3-4×RBC size	≥5×RBC size

Cell Uniformity	Monomorphic	Mildly pleomorphic	Pleomorphic
Nucleoli	Indistinct	Noticeable	Pleomorphic or prominent
Nuclear Margins	Smooth	Folds	Buds or Clefts
Chromatin	Vesicular	Granular	Clumped and Cleared

Grade I=score 6-11; GradeII= score 12-14; GradeIII= score 15-18

Table 2: Fisher's simplification of Black's nuclear grading scheme (1980)

Nuclear Character	Nuclear Grade		
	1	2	3
Size	Variation with minimal respect to normal duct epithelium	Twice the size of that in nuclear grade 1	Larger than grade 2 often shows a three-fold variation in nuclear diameter
Nuclear Membrame Contour	Round, smooth	Smooth	Irregular
Anisonucleosis	Absent	Moderate	Marked
Chromatin	Fine	Uniform	Marked hyperchromatism, coarse, clearing may be present
Nucleoli	Absent	May or may not show small nucleoli	Macro-nucleoli

Table 3: Howell's modification of SBR's breast cancer grading system(1994)

Feature	Score
• Tubule formation (%) Majority of tumor (>75) Moderate degree (10-75) Little or none (<10)	 1 2 3
• Nuclear pleomorphism Small, uniform cells Moderate increase in size/variation Marked variation	 1 2 3
• Mitotic counts (per 10-40×fields) 0-5 (histo) or 0-1 (cyto) 6-10 (histo) or 2-4 (cyto) >11 (histo) or ≥5 (cyto)	 1 2 3
Grade 1 (well-differentiated) (sum) Grade 2 (moderately differentiated) (sum) Grade 3 (poorly differentiated) (sum)	3-5 6-7 8-9

Table-4. Nottingham modification of Bloom- Richardson Grading system

Score	1	2	3
Tubule formation	Tubule formation in > 75 % of the tumor	Tubule formation in 10 to 75 % of the tumor	Tubule formation in < 10 % of the tumor
Nuclear Pleomorphism	Nuclei with minimal variation in size and shape	Nuclei with moderate variation in size and shape	Nuclei with marked variation in size and shape
Mitotic count/ per 10 HPF (for field diameter 0.44 mm)	0-5	6-11	≥12

RESULTS

In the present study, we compared the cytological and histological grades of the 44 cases diagnosed as Infiltrating duct carcinoma. By Robinson grading method, we found 29.5% cases to be grade I, 54.5% grade II cases and 15.9% grade III cases. Using Fisher's grading, 38.6% cases were categorized as grade I, 50% as grade II and 11.4% cases as grade III. By Howell's modification of SBR grading, 6.8% cases were identified as grade I, 59.1% cases as grade II and 34.1% as grade III. (Table 5)

Robinson's cytology grading system showed kappa coefficient of 0.88 for Grade I tumors, 0.86 for Grade II and 0.65 for Grade III tumors. The absolute concordance rate was 88.6%. [Table 6]

Fisher's grading system showed kappa coefficient of 0.68 for Grade I tumors, 0.96 for Grade II tumors, and 0.50 for Grade III tumors. The absolute concordance rate was 84.1%. [Table 6]

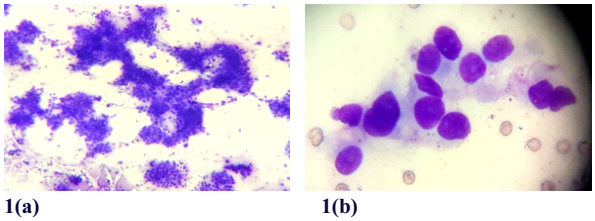
Howell's modification of SBR's grading showed kappa coefficient of 0.38 for Grade I tumors, 0.78 for Grade II and 0.84 for Grade III tumors. The absolute concordance rate was 81.8%.[Table 6]

Table 5: Distribution of study population(N=44) according to histological and cytological grades [HP: Histopathological grade(Modified Bloom-Richardson)]

Grade	Hp	Robinson's	Fisher's	Howell's
I	11 (25%)	13(29.5%)	17(38.6%)	3(6.8%)
II	21(47.7%)	24(54.5%)	22(50%)	26(59.1%)
III	12(27.3%)	7(15.9%)	5(11.4%)	15(34.1%)
Total(N)	44	44	44	44

Table 6: concordance analyses between cytological and the histological grading systems

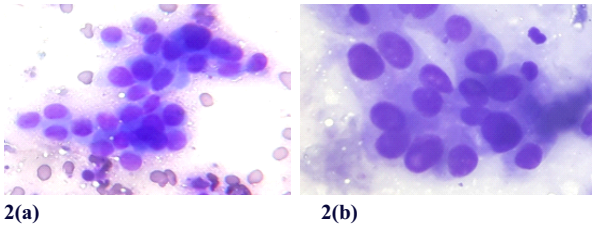
GRADES		ROBINSON'S	FISHER'S	HOWELL'S
k-coefficient	I	0.88	0.68	0.38
	II	0.86	0.96	0.78
	III	0.65	0.50	0.84
Absolute concordance	88.6%	84.1 %	81.8%	



1(a) 1(b)

Fig 1(a) Neoplastic cells arranged in clusters in a Robinson grade I carcinoma (MGG, x100).

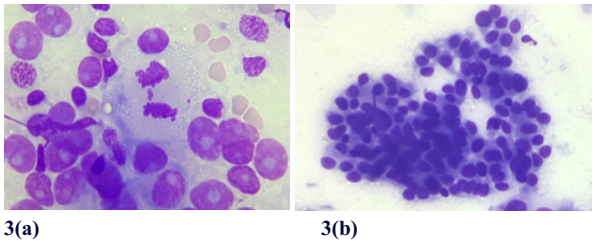
1(b) Robinson grade III tumour with large pleomorphic cells ≥5 xRBC size; hyperchromatic nuclei with irregular margins showing buds and clefts (MGG, 400)



2(a) 2(b)

Fig 2(a) Fisher grade1 tumour with mostly round smooth nuclear contours, fine chromatin and minimal variation of size compared to normal ductal epithelial cell. (MGG,x400).

2(b) Fisher grade 2 tumour showing moderate anisonucleosis, nuclei with smooth membranes and size twice that of grade1 nuclei(MGG,x400)



3(a) 3(b)

Fig 3(a) Mitosis and pleomorphism in a Howell grade III carcinoma. (MGG, x400) .

3(b) Mild nuclear pleomorphism and tubule formation in a Howell grade II tumour (MGG, x400)

DISCUSSION

Fine-needle aspiration cytology plays a significant role in the primary diagnosis of breast carcinoma. Various studies have highlighted the merits of Robinson's cytological grading system, but only few studies have evaluated other three-tier systems of cytological grading. In this study, we have compared three three-tier cytological grading systems with the histological grading.

In the present study majority of cases were clustered in grade II cytologically by Robinson's, Fisher's as well as Howell's grading systems; as well as histopathologically. A study by Saha *et.al*[15] had similar findings to our study. They identified high proportion of cases as grade II using Fisher's grading (54.4%), Robinson's grading (47.4%) and Howell's grading (54.4%) . Chandanwale *et.al*[16] also found that by Robinson's, Fisher's and Howell's grading systems majority of cases, 56%, 54% and 64% respectively, were gradeII. Similarly, Walke *et a*l. [17] found grade II tumors were maximum (47.3%) by SBR cytology grading method and by Robinson grading 46.7% were Grade I.

When we evaluated the strength of agreement between cytological and histological grades by kappa coefficient, for grade I cases it was highest in Robinson's system (k=0.88). For grade II cases, strength of agreement was highest in Fisher grading(k=0.96), followed by Robinson's system (k=0.86). Howell's modification of SBR grading system had highest k-value for grade III cases (k= 0.84) , followed by Robinson's system (k= 0.65). (Table 6)

The absolute concordance rates between cytological and histological grades was high in all three systems, maximum in Robinson's system (88.6%), followed by Fisher's and Howell's grading systems.(Table 6) Different studies comparing Robinson's cytological grading with histological grading by Modified Bloom-Richardson system observed different agreements. The agreement was 57% by Robinson *et al.*, [13] 71.2% by Das *et al.*,[18] 65% by Chhabra *et al.*,[19] 83% by Meena *et al.*, [20] 88.89% by Bhargava *et al.*,[4] 81% by Sinha *et al.*,[21] 88% by Khan *et al.*, [22] 64% by Lingegowda *et al.* [23] , 78% by Pal *et al.,*[24] and 88.6% in the present study.

Likewise, different studies observed different agreements when Fisher's modification of Black's nuclear grading was compared with histological grading by Modified Bloom-Richardson system. It was 95% by Dabbs *et al.*,[25] 70.4% by Zoppi *et al.*,[26] 77.8% by Bhargava *et al.*[4] and 84.1 % in the present study.

In this study, we observed 81.8% concordance rate for Howell's modification of SBR grading. It is comparable to other studies- 74.5% by Arul P *et al.,*[27] 68% by Walke *et al*., [17] 57.1% by Howell *et al*.,[14] 50% by Bhargava *et al*.,[4] 82% by Lingegowda *et al*.,[23] 63.2% by Saha *et al*.,[15] and 69.4% by Einstien *et al.* [28]

In our study, moderate (kappa value: 0.41-0.60) to very good agreement (kappa value: 0.81-1.00) was observed in histological grading and all cytological gradings, except in Howell's system where we got the kappa value for grade I cases in the fair agreement range (0.21-0.40). The variations of kappa value indicate the subjective nature of assessment of cytological parameters.

CONCLUSION

The present study revealed that it is possible to grade invasive breast carcinoma on aspirates by Robinson's, Fisher's and Howell's system as they corroborate well with histological grade by Modified Bloom-Richardson's method. Among the three cytological grading systems, however, absolute concordance was highest for Robinson's system. Hence, according to our study, being simpler, objective and multiparametric, Robinson's grading of breast carcinoma should preferably be included in routine cytological reports.

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