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Original Research Article

Prognostic role of robinson cytological grading system in breast cancer in correlation with the histological grading of modified bloom richardson in Iraq

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ABSTRACT

Background: The breast cancer is increasing in developing countries and the management options are widened, therefore providing the surgeon with accurate prognostic information on which the mode of therapy will be chosen became so important. Robinson grading system was found to be useful in grading breast carcinoma in fine needle aspirates. The objectives of the study were to estimate the benefits of using Robinson grading system in fine needle aspiration for breast cancer and to estimate the correlation of Robinson grading system in fine needle aspiration with histological grading.
Methods: There were Seventy cases of invasive ductal carcinoma was graded on FNA aspirates by Robinson grading system using six cytological parameters (cell dissociation, cell size, cell uniformity, nucleolus, nuclear margin, and nuclear chromatin).
Results: The concordance rate between grade I tumors on cytology and histology was 100%, while for grade II tumors it was 62.5% and for grade III tumors it was 100%. The absolute concordance rate was 87.5%, the Spearman rank correlation coefficient (r) was 0.762, p value was (0.00), the sensitivity of Robinson's cytological grading system in cytological grade I tumors was 73.33% and specificity was 100%. In cytological grade II tumors the sensitivity was 100% and specificity was 76% and in cytological grade III tumors the sensitivity is 100% and specificity was 100%.
Conclusions: Robinson's cytological grading of breast carcinoma correlates well with Bloom-Richardson's histological grading system and could be a helpful parameter in selecting a neoadjuvant treatment for the breast cancer patients on fine needle aspiration cytology alone.

Keywords: Breast carcinoma, Bloom richardson, Ductal carcinoma, Elston, FNA of breast, Robinson grading

INTRODUCTION

Breast carcinoma, the leading cause of cancer deaths in women, is considered to be the most common malignant tumor with more than 1,000,000 cases per year occurring worldwide.[1] In developed countries the incidence rate of breast cancer is still high in comparison with developing countries. However, breast cancer starts to appear as a serious issue for women health in Asia, Africa and South America.[2] Also, the incidence rate of breast cancer is increasing among developing countries of the Middle east including Egypt, Lebanon, Syria, and Jordan.[3-5]

As the choices of managing patients with breast cancer are widened, it becomes very important that the clinician is provided with accurate prognostic data on which management decisions depend. The Histological grading system of breast carcinoma described by Elston and Ellis (which is called Modified Bloom-Richardson system) is a commonly accepted system for tumor grading and has

been found to have a beneficial prognostic association.[6] Neoadjuvant therapy is now a known first line option in treatment of breast cancer. There is much emphasis on grading a tumor by using fine-needle aspiration cytology (FNAC). This grading would enable the pathologist to assess the tumor in situ, and thus helping in selecting the best appropriate therapy for the patients and reducing the morbidity accompanying the overtreatment of low-grade tumors. Of the many cytological grading methods analogous to Elston and Ellis's histological grading, Robinson et al, described a method that was found to be beneficial in grading the fine needle aspirates of breast cancer patients.[7]

This study aims to estimate the benefits of using Robinson grading system in fine needle aspiration for breast cancer and to estimate the correlation of Robinson grading system in fine needle aspiration and histological grading system of modified Bloom Richardson in breast cancer.

METHODS

Seventy cases of invasive ductal carcinoma (IDC) breast, diagnosed on cytology, and undergoing surgery were included in the study.

Heamatoxyline and eosin (H and E) stained smears were assessed and the tumor was graded according to the grading system described by Robinson et al.[7]

In the Robinson's grading system, six different cytological parameters, which are: cell size, cell dissociation cell uniformity, nucleolus, nuclear margin, and nuclear chromatin were used to grade these tumors. A score of 1-3 was given to each of these parameters, and the tumor was graded by score addition. Grade I tumors was given to tumors scored in the range (6-11), graded II tumors was given to tumors scored in the range of (12-14), and grade III was given for a score ranging from 15 to 18. The surgical specimens were evaluated and histologically graded according to the Elston's modification of Bloom-Richardson system.[8]

Three parameters were considered: Degree of tubule formation, nuclear pleomorphism, and mitotic figures. Each parameter was given a score of either 1, 2 or 3. The overall score for each case ranged from 3 to 9. Mitotic figures were scored using a Nikon Opitphot-2 microscope with a field diameter of 0.44mm. Sections were stained by hematoxylin and eosin (HandE) stain. Statistical analysis was done using Spearman rank correlation coefficient (r) to examine the degree of correlation between the cytological and histological grade. Sensitivity and specificity of Robinson's cytological grading method were calculated for each cytological grade. Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) statistical software package version 18 (SPSS- Inc., Chicago, IL). P value <0.05 was considered statistically significant.

RESULTS

Seventy cases of invasive ductal carcinoma were collected. The cytological features are evaluated according to Robinson cytological grading system as shown in Table 1.

Table 1: Cytological parameters of robinson grading system.

	Parameters	Cytological grading	Features	On FNAC
		Grade I	**Grade II**	**Grade III**
Cell	Mostly clusters	18	0	0
Dissociation	Single cells and clusters	15	30	2
	Mostly single cells	0	2	3
Cell size	1-2x RBC	29	12	0
	3-4x RBC	2	20	5
	5x or more RBC	2	0	0
Cell	Monomorphic	6	0	0
Uniformity	Mildly pleomorphic	27	0	0
	Pleomorphic	0	32	5
Nucleoli	Indistinct/small	14	8	0
	Noticeable	19	24	0
	Abnormal	0	0	5
Nuclear	Smooth	2	0	0
Margin Slightly irregular/folds and 31 32 3 grooves				
	Buds and clefts	0	0	2
Chromatin	Vesicular	2	0	0
Pattern	Granular	31	24	2
	Clumping and clearing	0	8	3

The mean age of the patients was 55 years, minimum age was 36 while maximum age of the patient was 75 years.

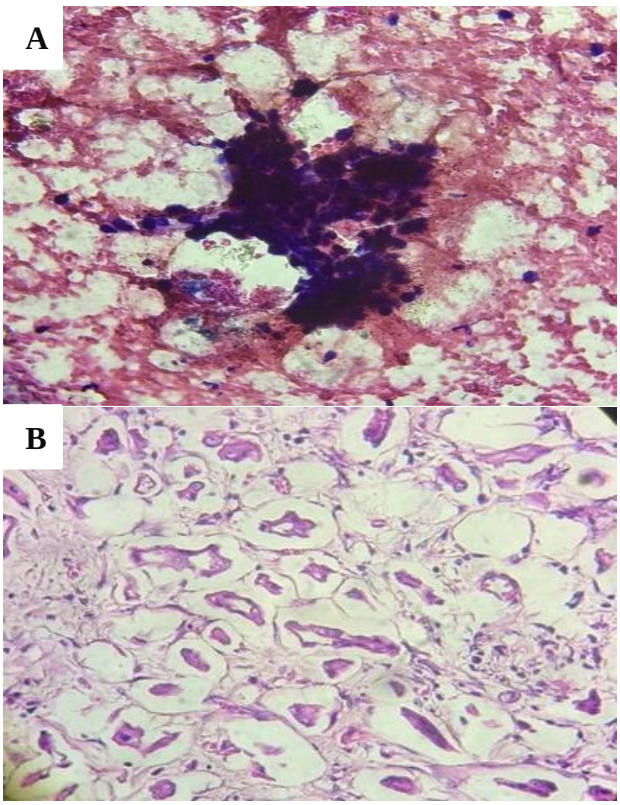

Figure 1: A.) Cytological grade I tumor showing cohesive clusters of cells with smooth nuclear membranes, vesicular chromatin, and inconspicuous nucleoli (HandE stain 40x); B.) Histological grade I tumor showing tubule formation more than 75% of the tumor with minimal nuclear pleomorphism (HandE stain 40x).

The seventy cases were cytologically graded on FNAC smears according to Robinson's grading system. The highest number of cases which was 33 (47.14%) were cytological grade I (Figure 1A), 32 (45.71%) cases were cytological grade II (Figure 2A), and 6 (8.5%) cases were cytological grade III (Figure 3A), as shown also in Table 2.

All cases were subsequently graded on histology using Elston's modification of Bloom-Richardson grading system. On histological grading 20 (28.57%) cases belonged to histological grade II (Figure 2B) and 45 (64.29%) cases belonged to histological grade I (Figure 1B) and 5 cases (7.14%) was histological grade III (Figure 3B), as shown also in Table 2.

The absolute concordance rate was 87.5%. For grade I tumors, the concordance rate between cytology and histology was 100%, while for grade II tumors it was 62.5% and for grade III tumors it was 100%.

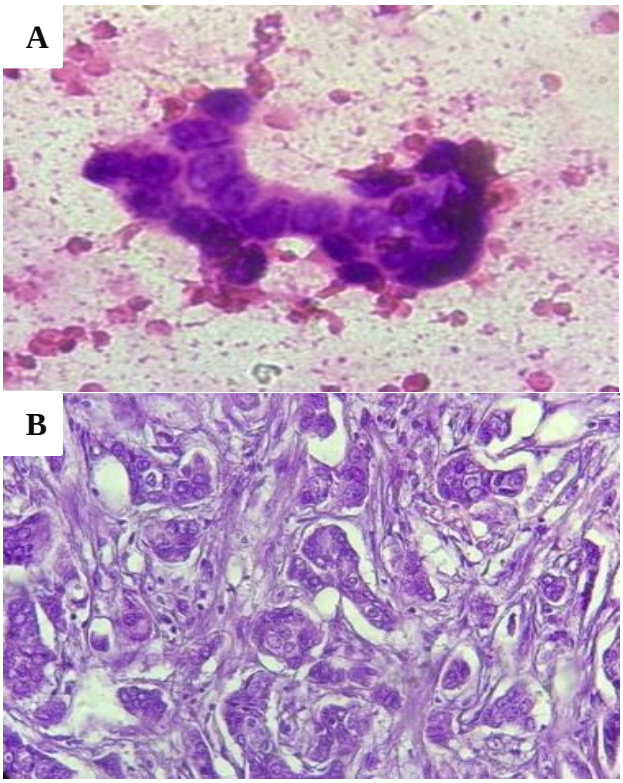

Figure 2: A.) Cytological grade II tumor showing mixture of single cells and clusters, mildly pleomorphic nuclei and nucleoli are noticeable (HandE stain 1000x); B.) Histological grade II tumor showing moderate degree of tubule formation (10%-75%) and moderate nuclear pleomorphism (HandE stain 40x).

The absolute concordance rate was 87.5%. For grade I tumors, the concordance rate between cytology and histology was 100%, while for grade II tumors it was 62.5% and for grade III tumors it was 100%.

Table 2: Comparison of concordance rates between the cytological and histological grades Grade.

Histological grading		Grade			Concordance rate	Correlation coefficient
		I	II	III		
Cytological grading	Grade I	33	0	0	100%	Correlation (r) = 0.762 P=000
	Grade II	12	20	0	62.5%	
	Grade III	0	0	5	100%	
Absolute concordance rate					87.5	

The Spearman rank correlation coefficient showed that there is a strong correlation between the cytological and histological grade (P <0.005), as shown in Table 2.

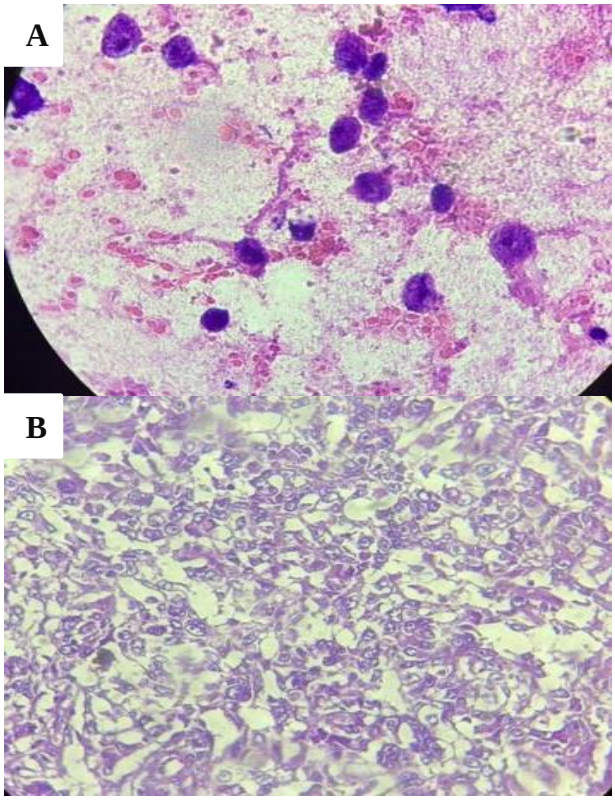

Figure 3: A.) Cytological grade III tumor showing mostly single cells, highly pleomorphic nuclei, and prominent nucleoli (HandE stain 1000x); B.) Histological grade III tumor showing less than 10% tubule formation with marked nuclear pleomorphism (HandE stain 40x).

Table 3 shows that in cytological grade I tumors, the sensitivity of Robinson's cytological grading system was 73.33% and specificity was 100%. In cytological grade II tumors the sensitivity was 100% and specificity was 76% and in cytological grade III tumors the sensitivity is 100% and specificity was 100%.

DISCUSSION

FNAC is generally considered as a rapid, reliable, and safe diagnostic tool. In both benign and malignant breast lesions and it is the initial method of pathological assessment as a component of the triple test in the diagnosis of palpable breast lesions in developing countries.[9]

The ability to predict the grade accurately on cytology smears would add to the diagnostic value of FNAC, without any additional morbidity or expense for the patients.[10]

In this study, the mean age of the patients was 55 years, ranging from 36 to 75 years, which was nearly similar (52 years) to that found in other study done in Iraq.[11]

This study showed that (47.14%) of the cases were cytological grade I, (45.71%) cases were cytological grade II, and (8.5%) cases were cytological grade III while other studies, found that maximum number of cases in grade II (46.6%), (44.75%), (62.2%) respectively.[12-14]

Table 3: Sensitivity and specificity of Robinson cytological grading system.

Cytological grade	Number of positive cases		Number of negative cases		Sensitivity (%)	Specificity (%)
	True	False	True	False		
I	33	0	25	12	73.33	100
II	20	12	38	0	100	76
III	5	0	65	0	100	100

A study done by Pradhan et al, found that maximum number of cases were in grade III (44%) followed by 29% in grade I and 27% in grade II.[15]

Authors found show a 100% concordance rate between grade I tumors on cytology and histology, while for grade II tumors it was 62.5% and for grade III Tumors it was 100%. The absolute concordance rate was 87.5% with a Spearman rank correlation coefficient (r) 0.762. These findings agree with many studies like Agarwal et al, who found 100% concordant rate between grade I tumors on cytology and histology grading, 85.71% and 100% concordance rate in grade II and grade III respectively and the absolute concordance rate was 93.33%.[12] Pradhan et al, study showed the concordance rate between cytological grading and histological grading as follows:[15] 84.61% in Grade I, 79.16% in grade II, 87.5% in grade III and an absolute concordance rate 83.60%. Pal and Gupta et al, findings was 78% absolute concordance rate and the spearman rank correlation coefficient (r) was 0.804.[10] However, in their study done on 116 breast carcinoma patients, Neelam Sood et al, had found a 75% concordance rate between grade I tumors in cytology and histology, 70.67% concordance rates for grade II tumors, 60% concordance rates for grade III tumors, and 68.97% absolute concordance rate among all three corresponding grades.[16]

The cause for discrepancy may be resulted from the fact that in cytological grading, the nuclear features were chiefly considered for the grading whereas the degree of

tubule formation and mitotic count were not assessed by this cytological grading system.

In this study, authors found a significant correlation between Robinson cytological grading system and modified Bloom histological grading system (p value was 0.000) which is similar to the result of Ravikumar et al, and Pal and Gupta et al.[10,14]

In the present study, the highest sensitivity (100%) was in cytological grade II and III tumors while the lowest sensitivity was in cytological grade I tumors (73.33%). The specificity in grade I and III tumors were (100%) and (76%) for grade II tumors. In comparison, Pal et al, study, conducted on 50 patients with invasive ductal carcinoma, found that the highest sensitivity in grade I tumors (100%) and a specificity of (92.30%), in grade II tumors the sensitivity was 82.14% and specificity was 72.72%, and in grade III tumors the sensitivity was 45.45% and specificity was 94.87%.[10] Observer variability and subjectivity may lead to the discordance in assigning the scores and thus affect the sensitivity and specificity. Also, the large tumor size or tumor heterogeneity is common in breast carcinomas cases which is a pitfall of FNAC where entire tumor cannot be assessed simultaneously.

CONCLUSION

Grading of breast carcinoma cytologically is simple, applicable, and provides important prognostic information. So, this study concludes that FNAC of neoplastic breast lesion should be graded to assess tumor behavior, prognosis and guiding the neoadjuvant chemotherapy preoperatively.

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