CYTOLOGICAL GRADING OF BREAST CANCER ACCORDING TO ROBINSON'S GRADING SYSTEM

Rubina Younis, Iqbal Muhammad, Alia Zubair, Shahzad Azam, Aiza Saadia

Army Medical College/National University of Medical Sciences (NUMS) Rawalpindi, Pakistan

ABSTRACT

Objective: To see the correlation between cytological parameters and grading of breast cancer according to Robinson's grading system on Fine needle aspiration smears. Study design: It was a correlational descriptive study.

Study Design: It was a corelational descriptive study.

Place and Duration of Study: It was conducted in the Histopathology Department, Army Medical College, National University of Sciences and Technology (NUST), Rawalpindi, Pakistan from Nov 2012 to Nov 2013.

Material and Methods: All cases diagnosed as breast cancer (C 5) or suspicious of breast cancer (C 4), on Fine needle aspiration cytology, were included in the study and women already taking treatment were excluded. A total of 102 samples were included in the study through non probability convenience sampling.

Result: The cytological parameters of Robinson's grading system including cell dissociation, nuclear margins and nuclear chromatin showed weak correlation with tumor grade. While cell size, cell uniformity and nucleoli showed moderate correlation. All the parameters were statistically significant with *p*-value<0.05.

Conclusion: This study concludes that all the cytological parameters of Robinson's grading system have correlation with tumor grade.

Keywords: Anaplasia, Breast, Carcinoma, Chromatin, Ductal, Fine- Needle Aspiration, Pakistan.

INTRODUCTION

The incidence rate of carcinoma breast in Pakistani women is 50.1 per 100,000 per year, which is the highest rate among most of Asian countries[1]. Determination of histological grade is one of the best established prognostic factors that help the clinician in decision making to choose a suitable treatment option[2]. Modified Scarf Bloom Richardson Grading System is considered as a gold standard procedure for grading breast cancer on biopsy[3]. However, histological grading on breast biopsy is expensive and time consuming[4]. In resource limited situations, as in Pakistan there is a need to replace core or excision biopsy by Fine Needle Aspiration Cytology, which is a simple, quick procedure, does not require expensive equipment, and is affordable[5]. As grading system on biopsy, there is no recommended grading system on FNA that can be followed. Breast cancers have been graded cytologically on FNA in West [6,7] but not in our set up. The present study used Robinson's method to determine the tumor grade on fine needle aspiration smears[6]. Such an assessment of grade will be of immense value for preoperative treatment.

MATERIAL AND METHODS

This study was conducted in the Department of Pathology, Army Medical College, National University of Sciences and Technology, Rawalpindi, Pakistan. Permission from the college ethical committee was taken. A total of 102 female patients with a diagnosis of ductal carcinoma on FNAC of breast, seen consecutively over a period of oneyear, November 2012 to November 2013, were included in the study. Aspirate from breast lump was taken using 10 ml disposable syringe and 22/23 gauge needle without local anesthesia. Wet fixed smears were stained with Papanicolaou and Haematoxylin and Eosin stains (H&E). Cytological grade of the

Correspondence: Dr Rubina Younis, Dept of Pathology, AM College Rawalpindi Pakistan (*Email:rubina@hotmail.com*)

Received: 20 Feb 2014; revised received: 5 Oct 2015; accepted: 21 Jan 2016

tumor was assessed by Robinson's grading system (table-1)[6].

Grading was reported qualitatively in terms of percentages. Correlation between the cytological parameters and tumor grade was evaluated by Spearman rank correlation. The most influential parameters in determining the

weak correlation with tumor grade. While cell size, cell uniformity and nucleoli showed moderate correlation (table-2). Nucleoli, nuclear chromatin pattern and cell dissociation were considered most influential features (table-3). All the parameters were statistically significant with $p<0.05$.

Table-1: Robinson's cytological grading system.

Parameters	Score 1	Score 2	Score 3
Cell dissociation	Mostly in clusters	Mixture of single & cell clusters	Cells mostly single
Cell size	1-2 x RBC size	3-4 x RBC size	> 5 x RBC size
Cell uniformity	Monomorphic	Mildly pleomorphic	Pleomorphic
Nucleoli	Indistinct	Noticeable	Prominent
Nuclear margins	Smooth	Folds	Buds/ Clefts
Nuclear chromatin	Vesicular	Granular/ Clumped	Cleaved

Grade I- score 6-11, grade II- score 12-14, grade III- score 15-18

Table-2: Correlation between cytological parameters and tumor grade.

Parameters	Spearman's rank correlation coefficient r- value	*p*-value
Cell dissociation	0.416	< 0.001
Cell size	0.662	< 0.001
Cell uniformity	0.655	< 0.001
Nucleoli	0.739	< 0.001
Nuclear margin	0.355	< 0.001
Nuclear chromatin	0.488	< 0.001

Table-3: Regression analysis of cytological parameters and tumor grade.

Parameters	Regression Coefficient (β)	*p*-value
Constant	-1.702	< 0.001
Cell dissociation	0.335	< 0.001
Cell size	0.290	< 0.001
Cell uniformity	0.323	< 0.001
Nucleoli	0.357	< 0.001
Nuclear margin	0.246	0.006
Nuclear chromatin	0.343	< 0.001

Adjusted R^2 = 0.894

tumor grade were assessed by Multiple regression analysis. Results were considered significant with *p*-value less than 0.05 ($p<0.05$).

RESULTS

The mean age of the patient was 51 years with standard deviation of 11.072. The present study revealed 30 (29.4%) cases graded as cytological grade I, 51 (50%) cases graded as grade II, and 21 (20.6%) cases as grade III.

The parameters including cell dissociation, nuclear margins and nuclear chromatin showed

DISCUSSION

The present study was aimed to grade breast cancer on fine needle aspiration, which has many advantages over biopsy[5] and can be helpful in determination of treatment plan[2].

The mean age of patients was 51 years. This finding was similar to the age reported by other studies in Pakistan i.e. an average age of 48 years was observed at the time of diagnosis[8].

Many studies have been carried out in past on Robinson's grading system[9-17], after the initial

research by Robinson in 1994. All these studies, including the present study, revealed grade II tumors to be the predominant group.

However, the literature shows conflicting results regarding the frequency of grade I and grade III tumors. Das et al[9] reported maximum number of cases as grade II (46.2%) followed by grade I (28.8%) and grade III (25%). Pandya et al[13] also reported predominance of grade II tumors (44.07%) followed by grade I (40.68%) and grade III (15.25%). However, in our study, grade III tumors (29.4%) formed the second largest group and grade I tumors (20.6%) were least common. The most probable reason for the grade III tumors forming the second largest group could be the late presentation of the patients in our setup[18].

On cytology, the loss of cell cohesion is represented by the extent of cell dissociation and at molecular level, by reduced E- Cadherin/ Catenin expression[19,20]. A study conducted by Suciuet al[21], at Romania proved association of reduced E-Cadherin expression, and thus loss of cell cohesion, with high histological grade.

In the present study, we found a weak significant correlation between cell dissociation and tumor grade. This finding is similar to results by Robles et al[22].

Variation in cell sizes and shape i.e. loss of cell uniformity is characteristic of neoplastic cells. The nuclear cytoplasmic ratio is variably increased and may approach 1:1. The neoplastic cells may assume bizarre shape and large cell size. The chromatin is usually coarse and clumped, and nucleoli may be of astounding size. Loss of differentiation is considered a hallmark of aggressive tumors[23].

Cangiarella[24] observed that all the cytological parameters had a strong correlation with cytological grade. However, in the present study, moderate correlation was found between cell size, cell uniformity, presence of nucleoli and tumor aggressiveness. We also found significant weak correlation between cell dissociation, nuclear margins, nuclear chromatin and tumor grade.

In multiple regression analysis, nucleoli, nuclear chromatin and cell dissociation appeared to be the most influential features. While a study conducted by Sahaet al in 2013[25] concluded that all the cytological parameters except cell size and nucleoli had high significance in predicting the tumor grade.

CONCLUSION

All the cytological parameters of Robinson's grading system have correlation with tumor grade. In resource limited situations, Robinson's grading system can be considered for grading breast cancer on FNA smears.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

REFERENCES

1. Sohail S, Alam SN. Breast cancer in Pakistan-awareness and early detection J Coll Physicians Surg Pak 2007; 17(12): 711-2.
2. Khan N, Afroz N, Rana F, Khan MA. Role of cytologic grading in prognostication of invasive breast carcinoma. Journal of Cytology. 2009; 26(2): 65–68.
3. Tavassoli, F.A. Devilee, P.World Health Organization Classification of Tumors. Tumors of the Breast and Female Genital Organs. IARC press, International Agency for Research on Cancer: Lyon 2003; pp.18-19.
4. Koss, LG. Diagnostic cytology and its histopathologic basis, Walters kluver, fifithedition, LipincottWiliams and Wilkins, USA 2006; p 1592-1601.
5. He Q, Fan X, Yuan T, Eleven years of experience reveals that fine-needle aspiration cytology is still a useful method for preoperative diagnosis of breast cancer. Breast, 2007; 16: 303–306
6. Robinson IA, McKee G, Nicholson A, D'Arcy J, Jackson PA,Cook MG, et al. Prognostic value of cytological grading offine needle aspirates from breast carcinomas. Lancet 1994; 343: 947-9.
7. Mouriquand J, Pasquier D. Fine needle aspiration of breastcarcinoma: a preliminary cytoprognostic study. Acta Cytol 1980; 24: 153-9.
8. Mamoon N, Sharif M., Mushtaq S, Khadim MT, Jamal S. Breast carcinoma over three decades in northern Pakistan –are we getting anywhere? J Pak Med Assoc, 2009; 59(12): 835–8.
9. Das AK, Kapila K, Dinda AK, Verma K. Comparative evaluation ofgrading of breast carcinomas in fine needle aspirates by two methods.Indian J Med Res, 2003; 118: 247-50.
10. Chhabra S, Singh PK, Agarwal A, Bhagoliwal A, Singh SN. Cytologicalgrading of breast carcinoma: A multivariate regression analysis. J Cytol, 2005; 22: 62–5.
11. Sinha SK, Sinha N, Bandyopadhyay R, Mondal SK. Robinson's cytological grading on aspirates of breast carcinoma: Correlation with Bloom Richardson's histological grading. J Cytol, 2009; 26: 140-3.
12. Pandya AN, Shah NP. Comparative evaluation of Robinson's cytological grading for breast carcinoma. Natl J CommunityMed 2012; 3(3): 491-5.

13. Wani FA, Bhardwaj S, Kumar D, Katoch P. Cytological grading of breast cancers and comparative evaluationof two grading systems. J of Cytology, 2010; 27(2): 55-8.

14. Das S, Kalyani and Kumar H. Breast carcinoma aspirates: A study on cytological grading. Int J Basic and Applied Med science, 2012; 2(2): 189-195.

15. Gore CR, Shirish C, Aggarwal R, Vimal S, Deshpande AH. Robinson cytological grading of breast carcinoma on fine needle aspiration cytology, IJPBS. 2013; 3(2): 563-570.

16. Sood N, NS Jitendra, Y Poonam, "Comparative Study of Cytomorphological Robinson's Grading for Breast Carcinoma with Modified Bloom-Richardson Histopathological Grading," Pathology Research International, vol. 2013, Article ID 146542, 5 pages, 2013.

17. Khokher S, Qureshi MU, Riaz M, Akhtar N, Saleem A. Clinicopathologic profile of breast cancer patients in Pakistan: ten years data of a local cancer hospital. Asian Pac J Cancer Prev. 2012; 13(2): 693-8.

18. Yoshida R, Kimura N, Harada Y, Ohuchi N. The loss of E-Cadherin, alpha- and beta- catenin expression is associated with metastasis and poor prognosis in invasive breast cancer. Int J Oncol, 2001; 18: 513-20.

19. Robles-Frias A, Gonzalez-Campora R, Martinez-Parra D, Robles-Frias MJ, Vazquez-Cerezuela T, Otal-Salaverri C, et al. Robinson cytologic grading in invasive ductal carcinoma of the breast: Correlation with E-cadherin and α-β and γ-catenin expression and regional lymph node metastasis. ActaCytol, 2006; 50:151–7.

20. Suciu C, Cîmpean AM, Mureşan AM, Izvernariu D, Raica M. E-cadherin expression in invasive breast cancer. Rom J Morphol Embryol, 2008; 49(4): 517-23.

21. Robles Frias A, Gonzalez Campora R, Martinez Parra D, Robles Frias MJ, Vazquez Cerezuela T, Otal Salaverri C, et al. Robinson cytologic grading of invasive ductal breast carcinoma: Correlation with histologic grading and regional lymph node metastasis. Acta Cytol 2005; 49: 149 53.

22. Kumar,V, Abbas, A.K., Fausto, N, Aster J. Robbins and Cotran Pathologic basis of Disease 8thed Elseivier, 2010; China. P1080-1088.

23. Cangiarella, J. Simsir, A. Fine Needle Aspiration Cytology, S. R. Orell and G. F. Sterrett, Churchill Livingstone, Philadelphia, Pa, USA; Elsevier Limited, Beijing, China, 5th edition, 2012; pp. 156–61.

24. Saha K, Raychaudhuri G, Chattopadhyay BK, Das I. Comparative evaluation of six cytological grading systems in breastcarcinoma. J Cytol 2013; 30:87-93.

....