

## ORIGINAL ARTICLE

# Association Between Cytological and Histological Grading of Breast Cancer and its Usefulness in Patient Treatment

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## ABSTRACT

**Introduction:** Breast cancer is the most common cancer in women throughout the globe, and the modern therapeutic available options have been widely researched currently. For a developing nation with limited resources, such as Pakistan, a quick, affordable, and least invasive technique like FNAC may give useful information.

**Aim:** The aim of this study was;

- 1 Perform and evaluate cytomorphological classification of all breast cancer patients using the Robinson's three-tier grading system.
- 2 Histopathological evaluation and classification of all samples of MRM by using a modified BR classification system.
- 3 Correlation of histo-morphological and cytomorphological classification systems.

**Place and Duration:** In the Pathology department of Khyber Teaching Hospital Peshawar for six months duration from February 2018 to July 2018.

**Material and methods:** A prospective study was conducted in which two independent observers classified all breast cancer patients on the basis of cytology and histology of the tissue and cyto-histological correlation.

**Results:** This study provided good individual correlation and inter-observer agreement in the cytopathological classification of breast cancer aspirates.

**Conclusion:** Cytopathological classification may be useful for these patients and should therefore be included in routine reports.

**Keywords:** Breast carcinoma; Cytopathology; Robinson classification system

## INTRODUCTION

Breast cancer is the most common cancer in women throughout the globe, and the modern therapeutic available options have been widely researched currently<sup>1</sup>. It also became the leading cause of cancer-related suffering in Pakistani women, defeating cervical cancer a few years ago. A triple assessment of breast lumps was recognized as the best guideline for the management of these patients, and FNAC is one of the main pillars<sup>2-3</sup>. Furthermore, for a developing nation with limited resources, such as Pakistan, a quick, affordable, and least invasive technique like FNAC may give useful information<sup>4</sup>. However, it is general practice to only use it to classify tumors as benign and malignant, which limits the usefulness of this procedure. In our country, there has not been a lot of interest in central biopsy, which costs a lot<sup>5-6</sup>. Therefore, FNAC should be used to obtain as much information as possible about the tumor prior to any radical surgery as it can help prevent or minimize surgical difficulties and related morbidity<sup>7-8</sup>. In the FNAC, there has been debate on tumour classification for some time, and no consensus has been achieved on the subject yet. Inclusion of routine immunocytochemistry in aspirate swabs for ER, PR and Her 2 can act as "icing on the cake" in such cases<sup>9-10</sup>. Several authors have reported that the system of Robinson Pap test is simple, objective, efficient, repeatable and practical, As a result, we selected Bloom Richardson's modified histological grading system to

be connected with it<sup>11-12</sup>. This prospective study was conducted in at least 40 cytologically reported breast cancer cases for one year and evaluated its usefulness in making decisions about neoadjuvant treatment before surgery. The objectives of our study were;

- 1 Perform and evaluate cytomorphological classification of all breast cancer patients using the Robinson's three-tier grading system.
- 2 Histopathological evaluation and classification of all samples of MRM by using a modified BR classification system.
- 3 Correlation of histo-morphological and cytomorphological classification systems.

## MATERIAL AND METHODS

A prospective study was conducted at the Pathology department Khyber Teaching Hospital Peshawar for six months duration from February 2018 to July 2018 in which all breast cancer patients were assessed in terms of tumor cytomorphology and histomorphology by two independent observers. Correlation was made between the cytomorphological and histo-morphological grading. Data were analyzed using a significance test to determine if cytological classification is appropriate in making decisions about neoadjuvant therapy. The criteria for inclusion in our study includes all operable patients with carcinoma of breast whereas the criteria for exclusion was all patients

with prior history of pre-operative chemotherapy / radiotherapy.

All aseptic measures were maintained while doing FNAC with a 5 mL syringe. The resulting material was dyed with giemsa, papanicolaou and Hematoxylin and eosin. Two independent observers evaluated the slides and scored them using Robinson's three-tier grading method. Using a modified BR system, samples of MRM were obtained and tumor segments were evaluated and reviewed by two independent observers. The data collected in this way was correlated analyzed and.

**RESULTS**

Totally, 40 patients were enrolled in our study. They were all women between the ages of 37 and 63. The mean lifetime of the lump was 3 months and 15 days, ranging from 20 days to 11 months.

Table 1: Distribution of cases based on Robinson's cytological grading and BR histopathological grading by observer 1

BR Grading Robinson's Grading	Grad e1	Grad e2	Grade 3	Total	Concordan ce
Grade 1	2	3	0	5	40.0%
Grade 2	0	23	1	24	95.8%
Grade 3	0	5	6	11	54.5%
Total	2	31	7	40	

For cancer of grade II and III, observer 1 established a strong cyto-histo correlation on his own, while observer 2 obtained good correlation for all grades of tumors.

Table 2: Distribution of cases based on Robinson's cytological grading and BR histopathological grading by Observer 2

BR Grading Robinson's Grading	Grade			Total	Concordance
	1	2	3		
Grade 1	4	0	0	4	100.0%
Grade 2	2	24	4	30	80.0%
Grade 3	0	3	3	6	50.0%
Total	6	27	7	40	

Table 3: Interobserver arrangement for histopathological grades

Grades	Observer		κ- value	Agreement (%)	Agreement
	1	2			
1	2	6	0.378	90.70%	Fair
2	31	27	0.724	90.70%	Substantial
3	7	7	0.97	97.10%	Almost Perfect

Table 4: Inter-observer agreement for cytopathological grades

Grades	Observer		κ- value	Agreement (%)	Agreement
	1	2			
1	5	4	0.793	97.20%	Fair
2	24	30	0.751	90.70%	Substantial
3	11	6	0.774	93.90%	Almost Perfect

The first observer upgraded two of the three cases to grade 2 in histology that were grade 1 in cytopathology. Two of the four specimens identified as Grade 3 malignancies by Observer 2 were histo-pathologically reduced to Grade 2. Three cases that were cytopathologically evaluated as grade 2 were histopathologically rated as grade 3. Both observers

agreed on cyto-pathological and histological grades, and there was no significant difference in individual agreement for tumours of grade 2 and 3, however, inter-observer agreement was important for Grade 1 tumors.

Table 5: Assessment of concordance of histo-cyto association of both the observers

Grades	Observer		κ- value	p value
	1	2		
1	40.0%	100.0%	0.793	<0.00001
2	95.8%	80.0%	0.751	0.153
3	54.5%	50.0%	0.774	1.0

**DISCUSSION**

In the treatment of patients with breast cancer, initially neoadjuvant therapy was used to terminate the tumor, and instead of radical surgery, conserving surgery was allowed<sup>10-11</sup>. With progress, the role of neoadjuvant therapy has shifted towards improving the survival and prognosis of these patients. Neoadjuvant treatment has evolved throughout time to focus on improving these patients' survival and prognosis. Several genetically tailored hormonal and chemotherapeutic medications are employed for this goal<sup>12-13</sup>. The tumor grade reflects the changes that occur at the molecular level as different tumor grades show different genetic changes<sup>14</sup>.

The presentation of a cytopathological assessment of FNAC aspirates may be helpful in patient selection for neoadjuvant therapy. Robinsons is one of the most well researched cyto-pathological classification systems, and it corresponds strongly with histopathological grade<sup>15</sup>.

A good correlation (over 80%) between the Robinson cytopathological classification and the BR histopathological classification is shown in numerous studies. Robinson himself found 57% of the correlation, while Lingegowda, Chabra, and Das found 64%, 65%, and 71.2%, respectively. In addition, in this study, both observers obtained an excellent cyto-histo correlation for tumors of Grade 2 and Grade 3. This deviation may result in a smaller overall sample size and a very small number of tumors belonging to this class. Despite this variability, the inter-observer agreement for all grades of tumor was excellent<sup>16-17</sup>. The system of Robinson takes cell coherence, size and homogeneity into account, as well as nuclear properties such as nucleolus properties, nuclear margin, and chromatin to assign scores to aspirates. All of the cytological variables used in the regression analysis were equally essential, however the incorporation of nucleolus features gave an extra advantage. But, this method has a disadvantage in that it does not allow for mitosis. A well-known hallmark of detecting any epithelial carcinoma is the loss of cell integrity<sup>18</sup>. Moreover, in breast cancer, cell caries is extremely important in classifying and predicting lymph node metastases by influencing the staging assessment. Cell size is affected by the cytoplasmic fragility of malignant cells, so replacing it with the size of the nucleus and taking into account the cytoplasmic nuclear association will improve the report score. Including variations in cell / size, shape and staining properties of nucleus and pleomorphism, while subjective, has proved to be a simple and easy classification criterion for various. Nuclear characteristics have been identified as

an essential factor in breast cancer prediction<sup>19-20</sup>. Despite the fact that the nuclear border and chromatin pattern are only analysed in part in pleomorphism, they both play a significant role in tumour categorization. In cytological smears, both DCIS and invasive carcinomas might aspire to necrotic material, therefore the use of necrosis as a staging criterion may be difficult. The mitotic number represents the aggressiveness of any tumor and is significantly correlated with tumor advancement in cytopathological aspirates. It has been shown that in invasive ductal carcinomas the apparent lymphocyte response is related with negative ER and PR, and as such, it may be useful in determining treatment choices in the neoadjuvant situation. But, in many investigations, this criteria did not offer adequate cyto-histocorrelation<sup>21</sup>. Sampling inaccuracy has an impact on the assessment of the different criteria for categorising aspirate swabs. In addition, all cytopathological grading systems are based on IDC-NOS. However, IDC-NOS contains the commonest variant of tumor and therefore these patients must be benefited from cytopathological staging<sup>22-23</sup>. The classification of cytopathological aspirates was endorsed by the National Cancer Institute Bethesda in their meeting on a Uniform Approach to Fine Needle Breast Aspiration Biopsy<sup>24</sup>. The inter-observer agreement was good in many other studies, as was our study.

## CONCLUSION

Cytopathological classification may be useful for these patients and should therefore be included in routine reports. Accordingly, it is imperative to establish consensus criteria to increase the objectivity and uniformity of the reported grade of aspirate smears. These might includes the number of passes for a given size of tumor, smear suitability, staining preferences, and cytomorphological criteria.

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