ABSTRACT

BACKGROUND
Breast carcinoma is one of the most common cancer of women. Fine-Needle Aspiration Cytology (FNAC) is widely used, most convenient, quick and common preoperative diagnostic modality in breast lesions. Cytological grading on aspirates of breast carcinoma is a very useful tool for surgical manoeuvre and prognosis.

The aim of the study is to study the correlation of cytomorphological Robinson’s grading with modified Bloom-Richardson’s histopathological grading of breast carcinoma.

MATERIALS AND METHODS
In the present study, 140 cytologically malignant breast tumour cases were included in the study and out of which, 90 cases correlated with histology after mastectomy. FNA was performed with 22-24 gauze needle and smears were stained with Haematoxylin and Eosin, Papanicolaou and May-Grunwald-Giemsa and evaluated for cytological grading according to Robinson’s grading system. H and E stained histosections were graded according to Bloom-Richardson’s grading system and comparison were done between the two.

RESULTS
Robinson’s cytological grading correlated well with Bloom-Richardson’s histopathological grading. The concordance rate between cytology and histology of Grade I, Grade II and Grade III tumours were 84.61%, 79.16% and 87.5%, respectively. Overall, concordance was found to be 83.6%. The Kappa value showed 95% confidence level. Thus, the strength of agreement between two grading systems considered to be fair. The P value on chi-square analysis showed <0.0001, which was considered statistically significant. Hence, the cytological grading is comparable with histological grading.

CONCLUSION
Robinson’s cytological grading of breast carcinoma correlates well with Bloom-Richardson’s histomorphological grading system. Hence, cytological grading in FNAC smears can be used as a prognostic factor for choosing the newer treatment modalities.

KEYWORDS
Fine-Needle Aspiration Cytology, Breast Carcinoma, Robinson’s Grading, Bloom Richardson’s Grading.

HOW TO CITE THIS ARTICLE: Pradhan SP, Dash A, Choudhury S, et al. Robinson’s cytological grading on aspirates of breast carcinoma and correlation with Bloom-Richardson’s histological grading. J. Evid. Based Med. Healthc. 2017; 4(2), 86-91. DOI: 10.18410/jebmh/2017/17

BACKGROUND
Breast cancer is a heterogeneous disease with a wide array of histologic appearance.¹ The incidence of breast cancer is rising in India and is now the second most common cancer diagnosed in women after cervical cancer. It is estimated that by 2030, the number of new cases of breast cancer in India will reach just under 2,00,000 per year.² This rising trend of breast cancer in developed and developing countries is a real threat challenging all efforts to screening, prevention and treatment aspects to reduce this cancer. Early diagnosis and prompt therapy are essential to decease morbidity and mortality. Surgical biopsy specimens serve as the “gold standard” for diagnosis and the value of histological grading has been widely accepted.³ Histologic grade has been an important prognostic indicator that can predict overall and metastasis free survival for local and regionalised breast cancer.⁴ Nottingham histological grading of breast carcinoma by Elston and Ellis is a widely accepted tumour grading system and has been found to have good prognostic correlation.⁵

The utility of Fine-Needle Aspiration (FNA) cytology is increased due to the introduction of new adjuvant therapy for rapid diagnosis and to determine various prognostic parameters.⁶ The National Cancer Institute (NCI), Bethesda,
sponsored conference had also recommended that the tumour grading on FNA smears should be incorporated in cytological reports for prognostication.\(^7\) It also emphasised that cytological grading system on FNA smears should correspond to the grading system used in histopathology.\(^8\)

In literature, various studies compared cytological grading system with Bloom-Richardson’s grading. Among all, Robinson’s cytological grading\(^9\) correlates well with Elston’s modified Bloom-Richardson’s grading system.\(^10\)

Hence, it is desirable to grade tumours before surgery, so that most appropriate medical regimen can be selected. Assessment of the in situ tumours can be done and over treatment of low-grade tumours can be prevented. The aim of the study is to grade the FNAC smears of breast carcinoma according to Robinson’s et al and to correlate with its histologic grading proposed by Nottingham’s modification of Bloom-Richardson’s system.

MATERIALS AND METHODS

The present study is a prospective study carried out in the Department of Pathology of M.K.C.G. Medical College, Berhampur, Odisha, over a period of October 2012 to September 2014 with the approval of Institutional Ethics Committee. All female patients referred for FNAC of palpable breast lump to cytology section from surgical outpatient department. After taking consent, relevant clinical history as well as thorough clinical examination were done and recorded. Patients with palpable breast lump diagnosed on cytology along with histology were included into the study group. Unwilling patients, scanty aspirate and cytology without histopathological examination, all cases of breast carcinoma other than infiltrating ductal carcinoma and male breast lump were excluded from the study.

FNAC was done within all aseptic measures by using Cameco syringe holder with 22-24 gauze needle. All the smears were stained with May-Grunwald-Giemsa (MGG), Haematoxylin and Eosin (H and E) and Papanicolaou (PAP) stains. Subsequently, the stained smears were examined under microscope and graded according to Robinson’s et al.\(^11\)

Reporting of the Smears

The smear was evaluated based on the grading systems described by Robinson’s et al taking into account of six parameters cell dissociation, uniformity, cell size, nucleoli, nuclear margin and chromatin pattern. A value between one and three was given to every factor analysed.

Cytological Grading with Methods of Robinson’s et al.

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Cell dissociation</td>
<td>Mostly clusters</td>
</tr>
<tr>
<td>Nuclear size</td>
<td>1-2 times size of RBCs</td>
</tr>
<tr>
<td>Cell uniformity</td>
<td>Monomorphic</td>
</tr>
<tr>
<td>Nucleoli</td>
<td>Indistinct/small</td>
</tr>
<tr>
<td>Nuclear margin</td>
<td>Smooth</td>
</tr>
<tr>
<td>Chromatin pattern</td>
<td>Vesicular</td>
</tr>
</tbody>
</table>

Score- 6-11 Grade I; 12-14 Grade II; 15-18 Grade III.

The scores for each of 6 cytological features were added together to give a total score for each case. In each case, the final scores ranges from 6 to 18.

Histological grading was performed using Elston’s modification of Bloom-Richardson’s system\(^5\) with a microscopic field diameter of 0.45 mm. Three parameters taken into consideration- Degree of tubule formation, nuclear pleomorphism and number of mitosis. Each parameter was scored between one and three. Overall score for all cases ranged between 3 to 9.

BLOOM-RICHARDSON’S HISTOLOGICAL GRADING

Tubule formation (extent within tumour)

- >75% 1
- 10%-75% 2
- <10% 3

Nuclear Pleomorphism

- Small, regular, uniform 1
- Moderate variation in shape and size 2

Marked variation in shape and size 3

Mitotic Count per 10 hpf (Dependent on Microscopic Field Area)

Field diameter 0.44-mm diameter/0.152-mm2 area

- 0-5 1
- 6-10 2
- >11 3

Total Score- 3-5 Grade I, well-differentiated; 6-7 Grade II, moderately-differentiated; 8-9 Grade III, poorly-differentiated.

STATISTICAL ANALYSIS

Association between different grading systems was measured by chi-square test. Correlation between cytological and histological grading system was examined by Spearman’s correlation coefficient. A P value of 0.05 or less was considered to be statistically significant.
In the present study, a total number of 140 cases of breast lump underwent FNAC during the two years study period. Cytological diagnosis of infiltrating duct carcinoma were suggested in 106 cases, among which 94 mastectomy specimen were available for histopathological analysis. Out of these 94 cases, 90 cases were diagnosed as infiltrating duct carcinoma NOS type, which constituted the study group. Maximum number of cases 52.22% of cases (n=42) were in the age group of 41-50 years. Only 3.33% (n=3) found in age group of 22-30 years.

<table>
<thead>
<tr>
<th>Grade</th>
<th>Number of Cases (Cytology)</th>
<th>Percentage</th>
<th>Number of Cases (Histology)</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade I</td>
<td>26</td>
<td>29</td>
<td>25</td>
<td>27.77</td>
</tr>
<tr>
<td>Grade II</td>
<td>24</td>
<td>27</td>
<td>28</td>
<td>31.11</td>
</tr>
<tr>
<td>Grade III</td>
<td>40</td>
<td>44</td>
<td>37</td>
<td>41.11</td>
</tr>
<tr>
<td>Total</td>
<td>90</td>
<td>100</td>
<td>90</td>
<td>100</td>
</tr>
</tbody>
</table>

*Table 1. Distribution of Cases According to Cytological Grading (RCG) and Histological Grading (MBR)*

On cytological grading, maximum number of cases 44% (n=40) were in Grade III followed by 29% (n=26) and 27% (n=24) belonged to Grade I and Grade II, respectively. Histologically, 27.77%, 31.11% and 41.11% cases were Grade I, Grade II and Grade III, respectively (Table 1).

<table>
<thead>
<tr>
<th>Cytological Grade</th>
<th>Total Cases</th>
<th>Histological Grade</th>
<th>Concordance Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>26</td>
<td>22</td>
<td>04</td>
</tr>
<tr>
<td>II</td>
<td>24</td>
<td>03</td>
<td>19</td>
</tr>
<tr>
<td>III</td>
<td>40</td>
<td>00</td>
<td>05</td>
</tr>
<tr>
<td>Total</td>
<td>90</td>
<td>25</td>
<td>28</td>
</tr>
</tbody>
</table>

*Table 2. Comparison between Cytological and Histological Grade (RCG and MBR)*

The cytological and histological grading was compared and concordance rate found to be 84.61% in Grade I, 79.16% in Grade II and 87.5% for Grade III. The overall concordance rate was found to be 83.60% (Table 2).

<table>
<thead>
<tr>
<th>Grade</th>
<th>Number of Cases Diagnosed on Cytology</th>
<th>Number of Cases Diagnosed on Histology</th>
<th>Kappa Value</th>
<th>95% Confidence Interval for Concordance</th>
<th>Standard Error</th>
<th>Strength of Agreement</th>
<th>'P' value</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>26</td>
<td>22</td>
<td>0.335</td>
<td>0.150 to 0.520</td>
<td>0.094</td>
<td>Fair</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>II</td>
<td>24</td>
<td>19</td>
<td>0.310</td>
<td>0.105 to 0.515</td>
<td>0.104</td>
<td>Fair</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>III</td>
<td>40</td>
<td>35</td>
<td>0.348</td>
<td>0.203 to 0.492</td>
<td>0.074</td>
<td>Fair</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

*Table 3. Comparison between Cytological (RCG) and Histological Grading (MBR) with Statistical Analysis*
DISCUSSION

As neoadjuvant therapy including preoperative chemotherapy and tamoxifen is becoming increasingly common for early breast cancer, it is desirable to grade tumours before surgery so that the most appropriate medical regime can be selected. By administration of preoperative therapy, several studies have shown that, there is rapid decrease in the tumour size. So, assessment of biological aggressiveness of cancer in high-grade tumour without removing it would therefore be valuable. FNAC grading allows such assessment and serial estimates to see how pretreatment modulates tumour grade.

There are many cytological grading systems of breast carcinoma and they have good correlation with Elston-Ellis Grading system (modified Bloom-Richardson’s grading). Robinson’s method was considered better than the other methods because of its more sensitivity, simplicity, more objective setup criteria and easy reproducibility, which has been used in present study.

In this study, the age range of the patients were from 21-70 years with maximum number of cases in premenopausal years (40-50 years), which corroborate with the study of Farley et al (2011).

In Robinson’s cytological grading of our study, out of 90 cases maximum 44% (n=40) were in Grade III followed by Grade I 29% (n=26) and Grade II 27% (n=24). These findings were comparable with Bhargava et al and Sinha et al. But, in contrast, previous studies by Khan et al, Das et al, Wani et al and Robinson’s et al observed predominance of Grade II tumour. In the present study, maximum number of cases, i.e. 41.11% (n=37) belonged to histological Grade III, which is corroborative with the study of Bhargava et al and Sinha et al.

In the present study, the absolute concordance rate was 83.60%. By Robinson’s cytological grading with Bloom-Richardson’s histopathological grading (n=90) showed substantial strength of agreement for Grade III and Grade I tumours with nearly perfect concordance in Grade II tumours, which is comparable to other studies (Figure 2). So, cytologic grade could be used to predict histologic grade as a significant relationship exist between them.
Our study level is at higher end of spectrum and lack of correlation in 16.4% (n=15) could be attributed to tumour heterogeneity and observer subjectivity while assigning nuclear grade.

Kappa (κ) statistical analysis was done to find out the strength of agreement between cytological and histological grades and value interpreted according to Landis and Koch classification, which indicates substantial agreement for Grade I tumours between cytological and histological grading system. The present study showed K value for Grade I, Grade II and Grade III were 0.335, 0.310 and 0.348 respectively, signifying statistically fair agreement.

In present study, cytohistological correlation between grading system using chi-square analysis revealed P value less than 0.0001, which statistically extremely significant and correlates with studies conducted by Frias et al23 (<0.0005) and Lingegowda et al22 (<0.001).

Multiple regression studies were done by various authors. In a study done by Khan et al23 in multiple regression analysis of various cytological features found regression coefficient of cell dissociation, chromatin pattern and nucleoli 0.780, 0.584 and 0.461, respectively (P<0.001) were most specific for determining cytological grade. Similar results were also observed by a study done by Robinson et al22 and Cangiarella and Simsir et al.24

In the present study, on multiple regression analysis, cytological features showed regression coefficient of cell uniformity, nucleolus and chromatin pattern 0.75, 0.58, 0.57 respectively with P value <0.0001. These parameters were found to be most sensitive factors in determining the cytological grade and it corroborates well with previous studies. So, FNAC grading by Robinson’s method is comparable with histological grading and useful in assessing tumour behaviour and prognosis.

CONCLUSION
Cytological grading of breast carcinoma is simple, feasible and provides valuable prognostic information. So, we conclude that, FNAC of malignant breast lesion should be graded to assess tumour behaviour, prognosis and guiding neoadjuvant chemotherapy preoperatively.

REFERENCES


