Comparative Study of Fine Needle Aspiration Cytology and Histopathology in Grading Breast Carcinoma

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ABSTRACT

Introduction: Carcinoma of the breast is the most common non-skin malignancy in women and it follows lung cancer among deaths related to cancer. Fine needle aspiration cytology is a reliable method for the initial evaluation and diagnosis of palpable masses of the breast. Study aimed to correlate Robinson's Cytological grading of breast carcinomas with Elston-Ellis' modification of Bloom Richardson's Histological Grading.

Material and Methods: The materials for the study were collected from patients being referred for fine needle aspiration with clinical diagnosis of breast carcinoma for a period of 12 months. Cytological features were graded using Robinson's cytological system. Histological grading was done according to Elston's modified Bloom and Richardson method. Cytological and histological grades were correlated to find the concordance between the two grading systems.

Results: A total of 60 breast cancer cases in females were studied. In the study, concordance rate between grade I tumors in cytology and histology was 92%, for grade II tumors, it was 93.10%, and for grade III tumors it was 100%. The absolute concordance rate of all the three grades was found to be 93.33%.

Conclusions: Aspiration cytology is an important examination for the evaluation of any breast lesions preoperatively. As with the histological grading, the cytological grading would aid in the prognosis besides diagnosis and help the patients without additional burden. Cytology grading has an additional assistance for neo adjuvant chemotherapy too.

Key-words: Breast, Carcinoma, Fine Needle Aspiration Cytology, Grading, Histopathology

INTRODUCTION

Carcinoma of the breast is the most common non-skin malignancy in women and it follows lung cancer among deaths related to cancer. A woman who lives to age 90 has a one in eight chance of developing breast cancer.[1] So, any breast lesions becomes a matter of concern for the patient and the doctor.[2]

Most cancer patients are diagnosed lately, due to lack of education towards female health in most parts of India, and insufficiency of breast cancer screening programs including diagnostic facilities.[3]

The occurrence of breast cancer is increasing worldwide; with peak incidence occuring above the age of 50 years in developed countries whereas in India it is above the age of 40.[4]

Breast cancer is the commonest malignant tumor diagnosed among women (22%). The developed countries with a small proportion of the world population account for almost 50% of breast cancers diagnosed worldwide.[5] The lowest breast cancer incidence is reported from Far Eastern and South-East Asian countries.[6,7] In the developing countries of Asia, the health care burden on account of breast cancer has been steadily mounting so that these countries would account for majority of new breast cancer patients diagnosed globally in future.

In India, every year, over 100,000 new breast cancer patients are diagnosed.[7,8] The incidence of this disease has been consistently increasing, and it is estimated it has risen by 50% between 1965 and 1985.[9]According to data published by Indian Council of Medical Research (ICMR) in the Three-year Report of Population Based Cancer Registries: 2012-2014 of the National cancer Registry Programme, breast cancer is the commonest cancer among women in urban registries of Delhi, Mumbai, Ahmedabad, Kolkata, Bangalore, Wardha district, Bhopal, Chennai, Kollam, Nagpur, Pune, Aurangabad, Patiala district and Trivandrum where it constitutes > 29% of all cancers in females, with the highest incidence of AAR per 100,000 population reported in Chennai (37.9).[10] In the rural PBCR of Barshi, breast cancer is the second commonest cancer in women after cancer of the uterine cervix.[4] The age standardized incidence rates (AARs) range from 6.2 to 39.5 per 100,000 Indian women. The AARs vary from region, ethnicity, religion, with the highest incidencereported at 48.3 per 100,000 women in the Parsi community of Mumbai.[4]

In the North East region of India, it was reported that breast cancer is the highest incidence cancer in the three districts-Dibrugarh, Kamrup Urban, and Cachar of Assam and also in Manipur with AARs 19.0, 27.1, 12.8 and 9.7 respectively[10] according to the Three-Year Report of the Population Based Cancer Registries; 2012-2014.

Fine needle aspiration cytology (FNAC) is coming up as an important investigation as it is not costly as well it helps in

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early diagnosis of breast lesions. It also provides prognostic value for patients so that they can undergo neoadjuvant therapy.[11]

The National Cancer Institute (NCI) has recommended FNAC for breast cancer patients who undergo preoperative chemotherapy or radiotherapy, for its prognostic value.[12]

The grading of breast cancer given on fine-needle aspiration (FNA) gives an idea on the nature of the disease, its possible outcome, and thus helps in selecting suitable treatments and further management.[13]

Elston's modified Bloom and Richardson (SBR) method is a widely accepted tumor grading system and has been found to have good prognostic correlations.[12] Histological grade along with tumor size and lymph node stage forms the Nottingham prognostic index, that is used to stratify individual patients for appropriate therapy.[13]

Many studies have shown correlation between the cytological grading with SBR method. But among them, Robinson's cytological grading (RCG) correlate more with SBR method, because of better concordance rate and it has more definitive criterias. [14-16]

Study aimed to correlate Robinson's Cytological grading of breast carcinomas with Elston-Ellis' modification of Bloom Richardson's Histological Grading.

MATERIAL AND METHODS

The study was conducted on 60 female breast carcinoma patients for a period of 12 months at the Department of Pathology Assam Medical College and Hospital.

The material for the study were collected from patients being referred for FNAC with clinical diagnosis of breast carcinoma, whose mastectomy specimens were subsequently procured for histopathological examination at the Department of Pathology.

After taking informed consent, FNAC were performed on the breast lumps of the patients using 22- 23 G needle and 10 ml disposable syringe under aseptic precautions. The aspirated materials were expelled on glass slides and multiple smears prepared. Smears were air dried and stained with May-Grunwald Giemsa (MGG) stain.

Cytological features were carefully evaluated and breast carcinomas were graded using Robinson's grading system. Six parameters viz. Cell dissociation, Cell size, Cell uniformity, Nucleoli, Nuclear margin and Chromatin pattern were carefully evaluated [Table 1]. After observing cytomorphology of these six criteria, each criterion was given one to three score. Sum of each score of these criteria were added and based on total score, breast cancers were graded viz. Grade I with score of 6 to 11, Grade II with score of 12-14 and Grade III with score of 15-18.

Surgical specimens were received for histopathological examination, and tissue processing and Hematoxylin and Eosin (H & E) staining were done

Histological typing of tumors were done according to world health organization (WHO) 2012.[17] Histological grading wasdone according to Elston's and Ellis's modification of Bloom-Richardson method.[13] Criteria such as tubule formation, nuclear formation, and mitotic count were evaluated [Table 2]. After observing carefully, each criterion was given one to three score. Sum of each score of these criteria were added and based on total score, breast cancers were graded viz. Grade I with score of 3 to 5, Grade II with score of 6-7 and Grade III with score of 8-9.

Cytological and histological grades were correlated to find the concordance between the two grading systems.

STATISTICAL ANALYSIS

In this study, concordance rate of each grading both in cytology and histopathology has been calculated. At the end absolute concordance rate of all the gradings has been calculated. The kappa statistics was also done in this study to measure the strength of agreement between the gradings.

RESULTS

A total of 60 breast cancer female cases were studied over a period of one year. The commonest age group in the study was 40 to 49 years comprising 40% of cases, followed by 30 to 39 years and 50 to 59 years constituting 23.33% each. The mean age of presentation was 45.37 years (Mean ± SD = 45.37 ± 9.16).

| Score	1	2	3
Cell dissociation	Cells mostly in clusters	Mixture of single cells and clusters	Mostly single cells
Cell size	1-2 times size of RBC	3-4 time size of RBC	>= 5 times size of RBC
Cell uniformity	Monomorphic	Mildly pleomorphic	Pleomorphic
Nucleoli	Indistinct	Noticeable	Prominent or Pleomorphic
Nuclear margins	Smooth	Slightly irregular/folds and grooves	Buds and clefts
Chromatin	Vesicular	Granular	Clumped and cleared
Table-1: Cytological Grading According to Robinson's Grading System			

| Score	1	2	3
Tubule formation	Tubular formation in > 75% of the tumor	Tubular formation in 10 to 75% of the tumor	Tubular 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 high power fields	0-9/hpf	10-19/hpf	>20/hpf
Table-2: Modified Bloom- Richardson Histological Grading system (Elston-Ellis)			

Cytological grading	Histological grading			Total (n)	CR (%)
	I	II	III		
I	23	1	1	25	92.00
II	2	27	0	29	93.10
III	0	0	6	6	100.00
Total	25	28	7	60	
Absolute Concordance Rate: 93.33; k value: grade I- 0.86, grade II- 0.90, grade III- 0.91					

**Table-3:** Comparison of cytological grading with histological grading
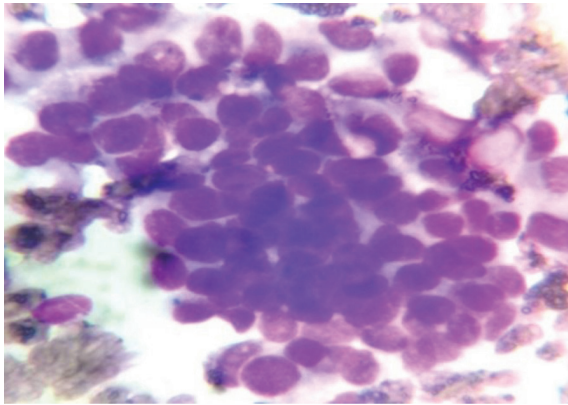
Figure-1: Smear showing cluster of mild pleomorphic ductal cells with smooth nuclear membrane and indistinct nucleoli—cytologic grade I. (MGG ×100)
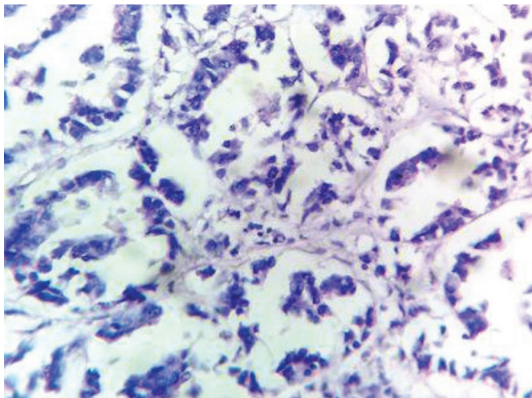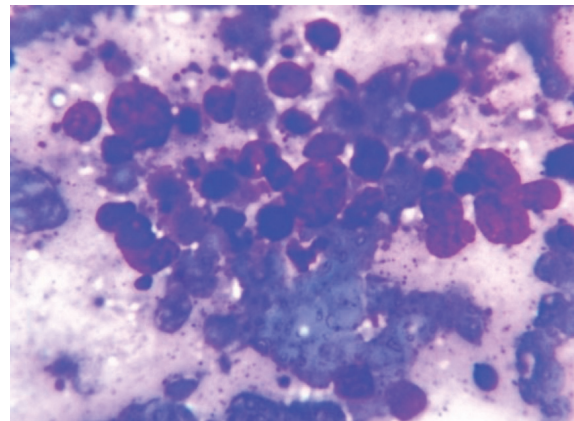

Figure-2: Grade I, Section of carcinoma breast showing cords and tubules of uniform tumour cells (H&E, x40)
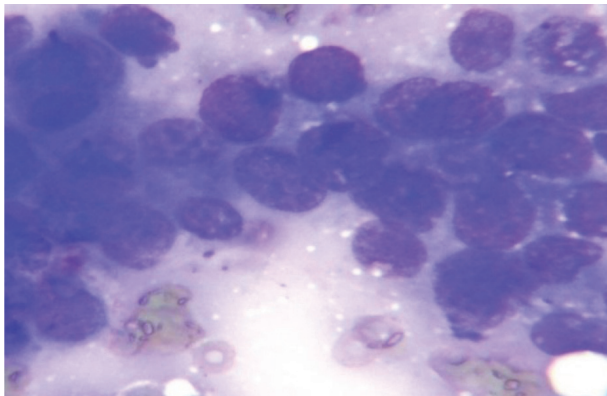

Figure-3: Smear showing cluster of pleomorphic ductal cells. Nuclei are three to four times the size of erythrocytes, with granular nuclear chromatin and smooth nuclear contour- cytologic grade II. (MGG ×100)
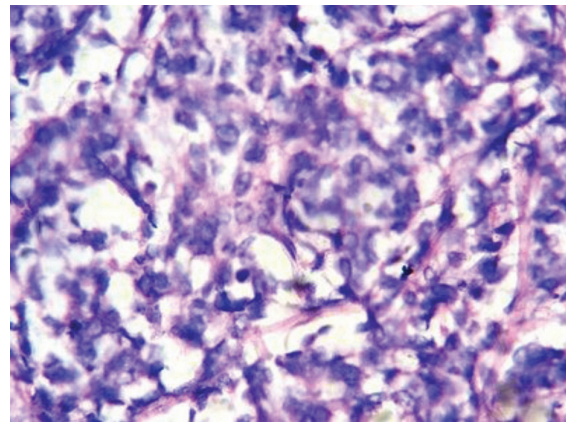
Figure-4: Grade II, Section of breast carcinoma showing ill-defined tubules and cords of moderately pleomorphic cells (H&E, x40)

Figure-5: Smear shows loosely cohesive, markedly pleomorphic ductal cells, irregular nuclear margin and prominent nucleoli with coarse chromatin— cytologic grade III. (MGG ×100)
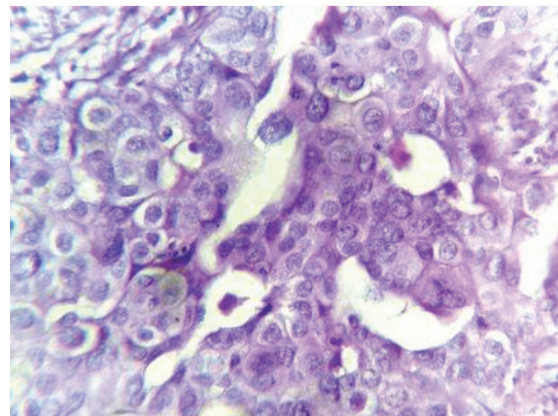
Figure-6: Grade III, Section of carcinoma breast showing highly pleomorphic malignant cells with hyperchromatic nuclei and prominent nucleoli (H&E, x40)

In the study, all the cases presented with lump in the breast (100%), followed by pain seen in 39 cases (65%). In this study, breast cancer lesions were most common in the upper outer quadrant seen in 31 cases (51.67%), followed by upper inner quadrant in 9 cases (15%).

The present study showed that infiltrating ductal carcinoma was the most common invasive breast carcinoma seen in 54 cases which is 90% of all cases, followed by invasive lobular carcinoma seen in 4 cases (6.67%). IDC with DCIS were

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seen in 8 cases, whereas IDC with medullary features were seen in 3 cases. Invasive papillary carcinoma was diagnosed in 2 cases constituting 3.33% of cases.

In the present study, the cytological diagnosis was accurate in 56 cases (93.33%). Out of these 56 cases, the cytological diagnosis was accurate in 54 cases (93.10%) of IDC and in 2 cases (100%) of IPC.

In our study, out of 25 cases in cytological grading of grade I, 2 cases turned out to be grade II and III each in histology grading. Among cytological grade II, 2 cases were grade I in histology grading.

Axillary lymph node positivity (1-3 in no.) were seen in 36 cases (60%), whereas over 4 lymph nodes were positive in 8 cases (13.33%) and overall nodal metastasis constituted 73.33% seen in 44 cases.

DISCUSSION

In the present study, concordance rate (CR) between grade I tumors in cytology [Figure 1] and histology [Figure 2] was 92%, for grade II tumors [Figure 3,4], it was 93.10%, and for grade III tumors [Figure 5,6] it was 100%. The absolute concordance rate of all the three grades was found to be 93.33%.

Kappa value for grade I tumors was 0.86, grade II tumors was 0.90, and grade III tumors was 0.91 [Table 3]. In studies by Gore CR et al.[18], Vasudev V et al.[19], Das et al.[20], Meena SP et al.[21] and Handa U et al.[22], the absolute concordance rate was 82.76%, 64.4%, 71.2%, 83.10% and 78% respectively.

In studies conducted by Rajan J et al.[23], Lingegowda J B et al.[24], and Robles-Frías A et al.[25] there were significant association (P < 0.000), (P < 0.001) and (P < 0.0005) respectively between the grades assigned to cytologic and histologic specimens.

From the present study, we have observed that absolute concordance rate was 93.33% with predominance of grade II tumors and concordance rate is highest in grade III tumors, which is in corroboration with other studies. There was almost perfect agreement between cytological and histological grading systems as calculated with kappa statistics.

From various studies cited above, it has been proved that the agreement between cytological and histological grading is good enough for cytological grading to substitute for histological grading.

CONCLUSION

Aspiration cytology is an important examination for the evaluation of any breast lesions preoperatively. But grading of breast cancer in FNA report is usually not given. This study shows that the gradings of cytology and histology correlated well. The cytological diagnosis was accurate in almost all cases of breast carcinoma in the study. Thus cytology of breast helps to confirm the clinical impression without open biopsy and hence, cytological grading should be reported which will help in further management.

Thus fine needle aspiration cytology besides being noninvasive is rapidly diagnostic, with high accuracy, insignificant complications and easy repeatability. The cytology grading is comparable with histological grading which makes it useful in assessing the tumor behavior and prognosis with additional assistance for neo adjuvant chemotherapy.

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