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PRE-OPERATIVE DIAGNOSTIC EVALUATION OF CARCINOMA BREAST-A COMPARATIVE ANALYSIS OF CONVENTIONAL FNAC AND LIQUID BASED CYTOLOGY

Pathology

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ABSTRACT

Fine needle aspiration cytology (FNAC) and Liquid based cytology (LBC) are minimally traumatic techniques used in the pre-operative diagnosis of lesions of breast. They can be used to determine ER, PR and Her-2/neu during the pre-operative period.

Aim Of Study - To compare the cytomorphological features of conventional FNAC and liquid based cytology and to evaluate the role of these techniques in the diagnosis of carcinoma breast.

Materials And Methods-30 cases of fnac proven malignant lesions of breast were chosen and the cytomorphological features of conventional fnac were compared with that of liquid based cytology smears prepared using U-prep and nanocyt technology

Results-The LBC was found to be better in terms of cellularity, clear background and monolayer while the cell architecture and the cytoplasmic and nuclear details were better preserved in conventional fnac

Conclusion-Conventional FNAC and LBC, though they have their own merits and demerits, they have comparable diagnostic accuracy and a combination of these methods have superior diagnostic value

KEYWORDS

Fine needle aspiration cytology, Liquid based cytology, Neoadjuvant chemotherapy

I. INTRODUCTION

Breast carcinoma is an important cancer affecting women in the industrialized world. It is estimated that 7% of global burden of breast cancer is borne by India. Breast cancer constitutes one fifths of cancer among women in India[1]. FNAC has been accepted by WHO as an important technique in the evaluation of breast cancer [2].It is a safe, cost-effective, minimally traumatic technique for rapid and accurate diagnosis of breast lesions. The effort to develop specific and scientific methods has led to liquid-based cytology preparation technique. The factors which help LBC to excel routine FNAC are enhanced fixation, paucity of background blood debris, and complete cell transfer. Another added advantage of LBC is that the residual material in the fixative can be used for pre-operative determination of ER, PR and Her-2/neu in breast cancer[3].There have been only few studies to compare and analyze the cytomorphological features of breast aspirates in conventional smears and liquid based preparations.

II. AIMS AND OBJECTIVES

1. To study the cytomorphology of breast cancer in conventional FNAC and LBC.
2. To evaluate the diagnostic value of conventional smears Vs Liquid based cytology.

III. MATERIALS AND METHODS

The present study is a prospective study to assess and compare the role of Conventional FNAC and Liquid based cytology in the pre-operative diagnosis of carcinoma of breast. Approval of the Institute Ethical Committee was obtained to conduct this research study. The study was conducted at the Department of Pathology, Tirunelveli medical college, Tirunelveli. The study was conducted over a period from November 2014 to September 2015.

INCLUSION CRITERIA

FNAC smears diagnosed as carcinoma of breast.

EXCLUSION CRITERIA

1. FNAC smears diagnosed as inflammatory lesions.
2. FNAC smears diagnosed as benign neoplasms.
3. FNAC smears diagnosed as atypical ductal hyperplasia.
4. FNAC smears of breast carcinoma patients on chemotherapy.

SAMPLE SIZE

A total of 30 cases of carcinoma breast diagnosed on FNAC were studied

METHODOLOGY

The details of the patient on the request are verified. This is followed by the examination of the patient with special emphasis on features like location of the lesion, the presence or absence of skin or chest wall involvement, involvement of nipple, tumor size, consistency of tumor and circumscription of the tumor

PREPARATION OF SMEARS

CONVENTIONAL FNAC

A 22 to 27-gauge, 1 or 1.5-inch needle attached to a disposable 20-ml syringe is used to obtain breast aspirates. The material obtained through first pass is used to make smears. They are stained with hematoxylin and eosin stain.

LIQUID BASED CYTOLOGY

The material obtained through second pass is rinsed in to U-prep cytopreservative solution. It is kept for a minimum of 30 minutes for fixation and then centrifuged. The supernatant is discarded and smears are made from the sediment by centrifuging samples using NANOCYT .Let the slides dry before staining. The smears are stained with hematoxylin and eosin.

IV. OBSERVATION AND RESULTS

The study analysed the conventional fine needle aspiration cytology samples of 30 cases of malignant lesions of breast along with the corresponding liquid based cytology samples to compare the cytomorphology.

1. Grading of carcinoma breast in FNAC: In Fine needle aspiration cytology, carcinoma breast can be divided in to Grades 1, 2 and 3 based on cell size, arrangement, pleomorphism, nuclear membrane, nuclear chromatin and nucleoli. In the present study, there were 10 cases of Grade 1 tumors, 13 cases of grade 2 tumors and 7 cases of grade 3

tumors. According to a study by Ahmed Wani.et.al on 110 cases of breast malignancy which was graded on FNAC by Robinson's method,25.45% cases were grade I tumors,41.81 % cases were grade II and 32.72% were grade III .In the present study,33.3 % cases were grade I,43.3% cases were grade II and 23.3% cases were grade III.

Table.1 Distribution of Grading of breast cancer in conventional smears

Carcinoma breast	Total No. of cases(n=30)
Grade-1	10
Grade-2	13
Grade -3	7

COMPARISON OF CYTOMORPHOLOGY ON FNAC AND LBC:

The cytomorphology of FNAC samples and LBC samples are compared based on the following parameters-cellularity, background blood-debris, monolayers, cell architecture, nuclear details and cytoplasmic details.

1. CELLULARITY

Table.2.Comparison of cellularity in conventional FNAC

CELLULARITY (CONV.FNAC)	GRADE-1	GRADE-2	GRADE-3	TOTAL
POOR	3	2	2	7
ADEQUATE	4	11	6	21
GOOD	1	1	-	2

Table.3. Comparison of cellularity in LBC

CELLULARITY (LBC)	GRADE-1	GRADE-2	GRADE-3	TOTAL
POOR	1	1	2	4
ADEQUATE	6	8	6	20
GOOD	1	5	-	6

Table.4 Percentage of cases with poor cellularity in FNAC and LBC

POOR CELLULARITY	No. of cases	%
FNAC	7	23.3 %
LBC	4	13.3%
COMBINED	1	3.3%

The percentage of cases with poor cellularity in conventional FNAC is 23.3%,while that in LBC is 13.3%.When the two methods were combined the number of cases with poor cellularity dropped down to 3.3%.

2. BACKGROUND BLOOD-DEBRIS

Table.5.Amount of background blood-debris in smears

BACKGROUND BLOOD-DEBRIS	zero	occasional	abundant
Conventional	4	10	16
LBC	12	15	3

The number of cases with abundant background blood-debris in conventional smears is about 16 while only 3 cases in LBC had abundant background blood-debris. The number of cases with no background blood-debris in LBC is around 12 while 4 cases in conventional smears had no background blood-debris.

Chart.1 Amount of background blood debris in conventional FNAC and LBC

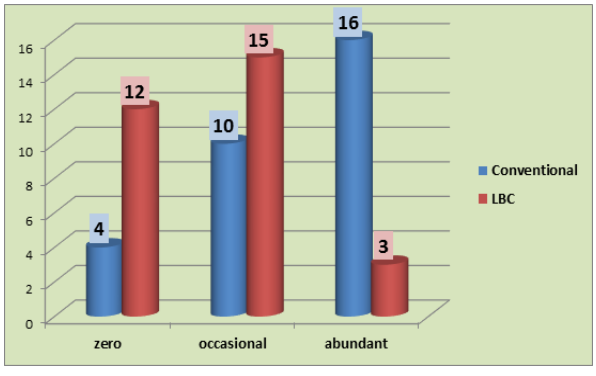

Table.6 Percentage of cases with abundant background blood debris in LBC and FNAC

Abundant background blood debris	No. of cases	%
CONV.FNAC	16	53.3%
LBC	3	10%

The number of cases with abundant background blood-debris in conventional smears is about 16 which constitutes around 53.3%while that in LBC is around 3 which constitutes only 10%.

3. MONOLAYERS

Table.7 Monolayering in conventional FNAC and LBC

Monolayer	Absent	Occasional	Good amount
Conventional	8	12	10(33.3%)
LBC	4	11	15(50%)

This study shows that 33.3% of cases had good amount of monolayering in conventional smears while 50% of cases had the same in LBC.

4. CELLARCHITECTURE

Table.8.Cell architecture in conventional FNAC and LBC

CELL ARCHITECTURE	Non-recognized	Moderately recognized	Well-recognized
Conventional	4(13.3%)	13	13
LBC	7(23.3%)	15	8

The numbers of cases with non-recognized architecture in conventional FNAC are 4(13.3%) and the number of cases with moderately recognized and well recognized architecture is around 13 each. The numbers of cases with non-recognized architecture in LBC are 7(23.3%), while the number of cases with moderately recognized and well recognized architecture are around 15 and 8 respectively.

5. CYTOPLASMIC AND NUCLEAR DETAILS

Table.9. Cytoplasmic and nuclear details in FNAC and LBC

CYTOPLASMIC AND NUCLEAR DETAILS	POOR	GOOD	EXCELLENT
CONVENTIONAL FNAC	3	20	7
LBC	5	18	7

In the present study ,the number of cases which had poor cytoplasmic and nuclear details in conventional FNAC were 3,while the number of cases which had poor cytoplasmic and nuclear details in LBC were 5.

I. DISCUSSION

Breast cancer is now considered as a heterogeneous disease which can be divided into distinct molecular subtypes that has prognostic significance. FNAC is a rapid, cheap, atraumatic procedure that does not require admission of the patient in the hospital. In the 1930s [4, 5] Martin and Ellis and Stewart used Fine-needle aspiration biopsy of the breast for the first time at Memorial Hospital. This method is found to have good accuracy and sensitivity, and is also a relatively simple procedure to procure tumor cells for ancillary studies, such as prognostic and predictive biomarkers. This is a popular procedure because it is also cheap[6,7] and is a quick procedure. The risks regarding the procedure is low and it has high diagnostic accuracy[8,9]In the present study, the cytomorphology of breast malignancy in conventional FNAC and liquid based preparations stained by H&E Stain are compared and analyzed. The percentage of cases which had adequate/good cellularity in conventional FNAC was around 76.6 % while that in LBC was 86.6% .The number of cases which had poor cellularity in conventional FNAC is 7 while the number of cases with poor cellularity in LBC is around 4. In the present study, the p value found using Mcnemar test is around 0.508. Thus, the cellularity in LBC was found to be superior as compared to that in conventional smears. A study by Ryu.et.al showed that the number of cases with adequate to good cellularity in conventional FNAC was around 68.3%, while that in LBC was 76.7%.The present study shows better yield of cellularity in conventional as well as Liquid based cytology as compared to the study by Ryu.et.al. A study by Michael. C.W et.al [10]also showed that the cellularity in LBC was found to be slightly superior as compared to that in conventional smears. Another study by Daskalopoulou.et.al also showed that there is great increase in cellularity in LBC aspirates of breast. The percentage of cases with abundant background blood debris in conventional FNAC was 53.3% and that in LBC was 10%.The p value found by Mcnemar test is 1. Other studies by Michael.C.W et.al[10]and Leung.C.S et.al[11]also showed that background is clear in LBC.Thus, LBC is superior to conventional smears with respect to clean background. The present study shows that the

percentage of cases with good monolayering in conventional FNAC is 33.3% while that in LBC is 50%.The Mcnemar test shows that the p value is around 0.307.Thus the study shows that LBC smears has more monolayering than conventional smears. A study by Gerhard.et.al also showed that the LBC smears had less overlapping and more monolayering than conventional smears. Thus the study shows that LBC smears have more monolayering than conventional smears. The numbers of cases with non-recognised architecture in conventional FNAC are 4(13.3%), while the numbers of cases with non-recognised architecture in LBC are 7(23.3%). The p value by Mc nemar test was found to be 0.210. This is analogous to the study conducted by Michael CW.et.al and Feoli.F.et.al which also showed that cellular aggregates are fragmented, shortened and less distinct in LBC preparations, resulting in smaller clusters and cellular dissociation which leads to poor preservation of cell architecture in LBC as compared to that in conventional FNAC.

In the present study 10% of the smears in conventional FNAC showed poor cytoplasmic and nuclear details while 16.6% of smears in LBC showed poor cytoplasm and nuclear details. The p value by Mcnemar test was found to be 0.727.The cells in LBC are more rounded and smaller than the flattened cells of conventional smear because the fixative used in LBC is a liquid medium. A study by Biscotti.C.V.et.al also showed that there is better-preservation of cells with enhanced nuclear detail, including a well-defined, usually more pronounced, nucleoli in LBC.[12]

Thus, the present study shows that LBC is superior to conventional FNAC in terms of cellularity, clean background and monolayers while the cytoplasmic and nuclear details in LBC are not as well preserved as in conventional smears. The present study points out that although the conventional FNAC and LBC have their own advantages and shortcomings, they have comparable diagnostic accuracy and a combination of these methods can be practiced to achieve a higher diagnostic rate.

II. SUMMARY

- This study includes a total of 30 FNAC proven cases of carcinoma breast.
- The cellularity in Liquid based cytology is found to be higher than that in conventional FNAC.
- Combined use of Liquid based cytology and conventional FNAC has better diagnostic value in carcinoma breast.
- The background blood debris is lower in Liquid based cytology than that in conventional smears.
- Monolayering of cells is more common in Liquid based cytology.
- The cytoplasmic and nuclear details is better preserved in conventional FNAC than in Liquid based cytology.
- In LBC, there are smaller clusters of cells and cellular dissociation is present.

III. CONCLUSION

In our study, it is concluded that although FNAC and LBC has its own merits and demerits, they have comparable diagnostic accuracy and the use of combination of these methods has superior value in diagnosing breast malignancy than either of them alone

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