Role of Fine Needle Aspiration Cytology in the Evaluation of Breast Masses in Pregnant and Lactating Women - A Retrospective Study in a Tertiary Health Care Center in North-East India

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ABSTRACT

BACKGROUND

Palpable breast lumps are a common presentation during pregnancy and lactation. The breast gland is a hormone responsive organ that undergoes physiologic changes due to hormonal stimulation. Fine Needle Aspiration Cytology (FNAC) is a rapid, simple, reliable and inexpensive diagnostic tool that has an important role in the diagnosis of breast masses during pregnancy and lactation.

METHODS

The present study is a retrospective analysis of 49 cases of breast masses during pregnancy and lactation period conducted at the Department of Pathology, RIMS over a period of 4 years (January 2014 to December 2018). We intend to evaluate the role of fine needle aspiration cytology in the interpretation of breast masses in pregnant and lactating women.

RESULTS

Around 49 breast masses were identified during pregnant and lactating period. Non–neoplastic breast lesions were the most common aetiology seen. Our study observed that among the benign breast lesions, galactocele was the most common pathology seen in 16 cases (32.65 %). Other benign breast lesions seen during this period included nine cases (18.37 %) of benign breast lesion with pregnancy and lactational changes, three cases (6.12 %) of benign proliferative breast lesion, two cases (4.08 %) of mastitis and three cases (6.12 %) of fat necrosis. Fibroadenoma was seen in 7 cases (14.29 %) constituting the most common benign tumour seen during this period. Two cases (4.08 %) of lactating adenoma were observed. Two cases (4.08 %) of pregnancy associated breast carcinoma (PABC) was also seen during this period.

CONCLUSIONS

FNAC plays an important role in evaluating the cytomorphological diagnosis of breast masses in pregnant and lactating women. However, the cytopathologist must be aware of the cytological features in FNA smears with atypical features to avoid a false positive diagnosis of breast cancer in pregnant and lactating women.

KEYWORDS

FNAC, Breast Masses, PABC, Pregnancy, Lactation

BACKGROUND

The breast gland is a hormone responsive organ. During pregnancy and lactation, the breast undergoes physiologic changes due to hormonal stimulation that increases breast size and water content. These changes can be attributed to various hormones, which may lead to ductal and lobular growth, increased vascularity and a decreased in stroma.[1,2] This usually results in significantly increased breast density and makes breast evaluation challenging in these patients.[3] Palpable breast lumps during pregnancy and lactation are common presenting symptoms. A breast disorder diagnosed during pregnancy, within one year of postpartum or during lactation is considered to be pregnancy – related. Malignancy occurring in breast up to one year after delivery is included in most studies as Pregnancy – associated – breast cancer (PABC).[3] It is important to recognize benign breast masses to avoid unnecessary biopsies while maintaining a high clinical suspicion as 20 % of palpable lumps during this period are malignant.[4]

Fine needle aspiration cytology is a rapid, simple, reliable and inexpensive diagnostic tool with minimal surgical intervention for diagnosis of breast masses during pregnancy and lactation.[5] Even though limitations and pitfalls do exist for this method like any other investigative procedure. A variety of specific aetiologies are observed in pregnant and lactating women. It can be categorized as non-neoplastic and neoplastic lesions. Non-neoplastic entities include galactocele, sub-areolar abscess, benign breast lesion or lactational changes, mastitis with or without abscess and benign proliferative breast lesion. Neoplastic lesions include fibroadenoma, lactating adenoma and pregnancy associated breast cancer (PABC).[6] The cytological interpretation in these benign breast diseases during pregnancy and lactation is challenging due to the atypia inherent to the secretory change in glandular epithelium.[7]

A definitive picture needs to be sorted out for each and every lesion that can be encountered in this specific period. One such lesion is galactocele. A galactocele is a retention cyst containing milk to form a large mass. It generally arises shortly after pregnancy, during lactation. Milk is aspirated and appearance of abundant granular, secretary material, numerous foamy macrophages and few acinar cells clinches the diagnosis. Certain changes inherent to the pregnancy and lactational state will be reflected on the aspiration smears. Cellularity is usually moderate with single and well dispersed cells in a lipid rich foamy or granular background. Large nuclei with abundant vacuolated or wispy cytoplasm are usually observed. In subareolar abscess, a tender mass is usually seen in this region. Numerous acute Inflammatory cell is the principle findings along with anucleatesquames, multinucleate giant cells, macrophages & reactive changes in the epithelium

A diagnosis of fat necrosis is given when the smear show normal as well as degenerated fatty tissue, foamy macrophages multi nucleated giant cells, few epithelial cell against a background of free lipid droplets and granular debris. Fibroadenoma will have the characteristic branching sheet of ductal epithelial cells and stromal fragments against a background of bipolar cells. Lactating adenoma usually seen during pregnancy and show as moderately cellular aspirates. Smears show single or small clusters in a foamy & lipid background. The cellular features are the changes characteristically seen during pregnancy. Pregnancy - associated breast cancer refer to breast cancer that is diagnosed during pregnancy or within the first post-partum year. It is an aggressive form of breast cancer and the patient is usually at an advanced stage at the time of diagnosis over and above the pathological means for confirmation, imaging examinations are indispensable.[8]

Objectives

The objective of the present study is to determine the cytological profile of breast masses by FNAC presenting during pregnancy and lactation, as there is lack of data in our country in general and our region in particular.

METHODS

The present study is a retrospective analysis of palpable breast masses in pregnant and lactating women presenting to out-patient department (OPD) for FNAC. We collected the data from the records of the Department of Pathology, Regional Institute of Medical Sciences (RIMS), Imphal, India over a period of 4 years (January 2014 to December 2018). FNAC was done after taking an informed consent following a short clinical history and thorough clinical examination and evaluation of other related investigation findings. A cytopathologist performed the FNAC using a 23 - 24 gauge needle attached to a 20 mL syringe and Franzen handle. Aspirations were performed using multiple passes in the lesion maintaining negative pressure. The aspirate was then smeared on a minimum of five slides, four were air dried and one was fixed in 95 % ethanol.

The air-dried smears were routinely stained with Giemsa stain. Papanicolaou (PAP) stain was done from the alcohol fixed smear. All the stained smears were studied, analyzed and appropriate diagnosis was given based on the cytomorphological features and in correlation with clinical findings.

The cytological diagnosis could be classified into the following main groups:
1. Non–neoplastic lesions - Galactocele, mastitis, breast lesions with pregnancy or lactational changes, subareolar abscess, benign proliferative lesions and fat necrosis.
2. Neoplastic lesions - Fibroadenoma, lactating adenoma and pregnancy associated breast carcinoma.
3. Smears that have scanty ductal cells, poor cell presentation and too much blood were discarded as unsatisfactory smears and a repeat aspiration was carried out.

Statistical Analysis

It's a retrospective descriptive study of cases with breast mass during pregnancy and lactation. In the present study, data has been entered and analysed using IBM SPSS statistic

24. Here, we have studied the age range, mean age and the frequency distribution of the cases in percentage according to the cytological diagnosis.

RESULTS

A total number of 49 cases of breast masses in pregnant and lactating women were aspirated during a period of 4 years. On analysis of the data, we observed that of all the benign breast lesions, galactocele was the most common presentation constituting a total of 16 cases (32.65 %). Benign breast lesions with pregnancy and lactational changes comprised of 9 cases (18.37 %) constituting the 2nd most common presentation. Other benign breast lesions reported in our study included 2 cases (4.08 %) of mastitis, 3 cases (6.12 %) of fat necrosis, 5 cases (10.21 %) of subareolar abscess and 3 cases (6.12 %) of benign proliferative breast disease. Fibroadenoma was the most common neoplastic lesion and was reported in 7 cases (14.29 %).

Lactating adenoma was seen in 2 cases (4.08 %) during lactational period. Further, two cases (4.08 %) of PABC was reported during postpartum period. The above data is presented in Table 1. In our study, the age ranged from 18 to 39 years. The mean age of the study population was 26.08 years. The maximum number of cases was recorded in the age group of 26 - 30 years (30.61 %) and least number of cases in the age group of 36 - 40 years (10.20 %) as shown Table 2. Of the total 49 cases, 11 FNACs (22.45 %) were observed in pregnant women and 38 FNACs (77.55 %) were seen in lactation or post–partum period as shown in Table 3.

The present study focuses on most common differential diagnosis for palpable breast masses in pregnant and lactating women and the cytomorphologic features as observed in various diagnosis are summarized as follows - One third of the total cases (32.6 %) were confirmed to be galactocele and smears showed scattered macrophages and clusters of benign ductal cells in a background of lipid droplets. Aspirate smears showing evidence of increased cellularity, dispersed acinar cell population having abundant fragile vacuolated cytoplasm with round vesicular nuclei, prominent nucleoli and lack of bipolar nuclei against a dirty proteinaceous background were given a diagnosis of benign breast lesions with pregnancy or lactational changes (Fig. 1) and there were nine such cases.
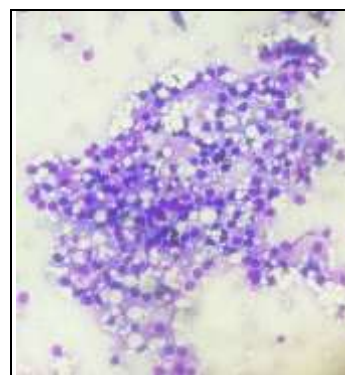
Figure 1.
FNA Smear Showing Clusters of Acinar Cells Having Abundant Vacuolated Cytoplasm in a Foamy Background Consistent with Features of Lactational Change. Giemsa 400x
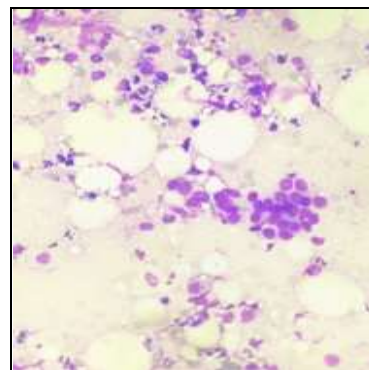
Figure 2.
FNA Smear Showing Acute Mastitis with Lactational Change. Giemsa 400x
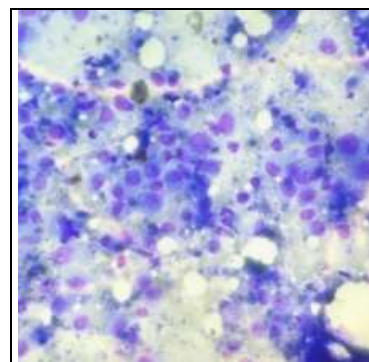
Figure 3.
FNA Smear Showing Highly Cellular Pleomorphic Malignant Cells in Ductal Carcinoma. Giemsa 400x

Breast Lesions during Pregnancy and Lactation	No. of Cases	Percentage (%)
Non – neoplastic lesions	38	77.55
Galactocele	16	32.65
Benign breast lesions or lactational changes	9	18.37
Subareolar abscess	5	10.21
Benign proliferative breast lesion	3	6.12
Fat necrosis	3	6.12
Acute mastitis	1	2.04
Chronic mastitis	1	2.04
Neoplastic lesions	11	22.45
Lactating adenoma	2	4.08
PABC (Ductal carcinoma)	2	4.08
Fibroadenoma	7	14.29
Total	49	100
Table 1. Observation of FNA Cytology (N = 49)		

*PABC - Pregnancy associated breast cancer

| Age Group (in years)	No. of Cases	Percentage (%)
15 - 20	9	18.37
21 - 25	13	26.53
26 - 30	15	30.61
31 - 35	7	14.29
36 - 40	5	10.20
Total	49	100
Table 2. Distribution of Cases According to Age (N = 49)		

Gestational Age (in years)	No. of Cases	Percentage (%)
No. of breast masses that arose during pregnancy (16 - 32 weeks)	11	22.45
No. of breast masses that arose during post–partum period or lactation	38	77.55
Total	49	100
Table 3. Distribution of Cases According to Gestational Age (N = 49)		

Another nine cases (18 %) revealed evidence of cohesive sheets and clusters of benign ductal cells without significant nuclear overlapping and regular cellular spacing having finely granular chromatin pattern against the background of naked bipolar nuclei, was given a diagnosis of benign proliferative breast lesion. Aspirate smears which revealed benign bimodal population of ductal cells in a background of acute inflammatory cells, a diagnosis of acute mastitis were

given (Fig. 2) and there was a case with these features. When the smears showed mainly mature or anucleate squamous cells against a background of acute inflammatory cells, a diagnosis of subareolar abscess was given and five of them presented with these findings.

Smears showing evidence of fragments of adipose tissues, macrophages, multinucleated giant cells and dirty necrotic background were given a diagnosis of fat necrosis. When the smears showed dispersed cell population, highly cellular pleomorphic cells with high N : C ratio, hyperchromasia and prominent nucleoli, a diagnosis of breast ductal carcinoma was given (Fig 3). Lack of proteinaceous background and naked bipolar nuclei in such cases is a clue to the diagnosis.

DISCUSSION

FNAC provides an easy, inexpensive, reliable and rapid diagnostic tool for evaluating the aetiology of breast masses during pregnancy and lactation thereby reducing the surgical intervention to a minimum. In our study, we presented the cytomorphologic diagnosis of 49 cases of breast masses during pregnancy and lactation over a period of 4 years, i. e., January, 2014 to December, 2018. The patterns of lesions included benign breast lesions with pregnancy and lactational changes, benign proliferative breast lesions, acute and chronic mastitis, fat necrosis, subareolar abscess, galactocele, fibroadenoma, lactating adenoma and PABC (ductal carcinoma).

The cellularity, loss of cell cohesion, lack of bipolar nuclei and prominent nucleoli in smears from breast lesion with pregnancy and lactational changes may be misinterpreted as carcinoma in the absence of clinical information.[7] In order to avoid false positive diagnosis, the nuclear chromatin which is bland, granular and evenly distributed should be carefully examined. The milky background is the principle key to diagnosis.[9] On the other hand, a malignant lesion could be under called due to fear of over diagnosis of lactational changes as malignancy.[9] Hence, it is important that the cytopathologist should be aware of the typical changes expected in FNAC smear.

In this study, galactocele was found to be the most common presentation (32.65 %), which was in concordance with the findings of Sharma M et al.[10] who also showed the highest incidence of galactocele during pregnancy and lactation constituting about 35.5 %. They are true cuboidal epithelium lined cysts that contain milk like fluid, often accompanied by inflammatory or necrotic debris. The reason for galactocele being the most common presentation in our study may be because of mammary duct obstruction due to milk stagnation when breast feeding ceases.

Benign breast lesion with pregnancy and lactational changes was seen in 18.37 %, which was in concordance with the findings of Rai et al.[3]

Fibroadenoma was the most common benign breast neoplastic lesion in pregnancy and lactation in our study (14.29 %) as reported in a few studies.[4,11] These are hormone sensitive benign tumours and are therefore expected to grow during pregnancy and breast feeding due to increase hormone levels, resulting in detection of a previously unnoticed lump.

Lactating adenoma was another common benign breast tumour presented during lactation in our study (4.08 %). It consists of proliferation of epithelial component only compared to fibroadenoma where there is proliferation of both stromal and epithelial components.[10] Lactating adenoma regresses spontaneously at the end of lactational period. FNAC is an adequate method of diagnosing lactating adenoma as core biopsy may possibly lead to formation of milk fistula.[12] However, the cytopathologist should be aware of the differentiating features between fibroadenoma and carcinoma from lactating adenoma.

Mastitis and abscess formation seen in our study were the common benign diseases reported during pregnancy and lactation. In our study, mastitis was seen in 4.08 % and subareolar abscess was seen in 10.21 %, which was comparable with the findings of Rai et al.[3] where 18.75 % was reported. This is believed to be due to the entry of common pathogens (Staphylococcus, Streptococcus) from the infant's nose or throat into the breast through the damaged epithelial cells of nipple areolar complex.[10] Fat necrosis was seen in 14.29 % and benign proliferative breast lesions in only 6.12 %.

Pregnancy associated breast carcinoma is defined as the breast carcinomas which occur during pregnancy or within one year post-delivery.[8] We reported 4.08 % of PABC which was comparable to the findings of Tina Rai et al.[3] who also reported 6.25 % of PABC. The reported cases in our study were seen in post–partum period. The increasing incidence of PABC over the past several years may be because more women are becoming pregnant in their 30s and 40s and the incidence of breast cancer increases with age.[13]

The age of common presentation in our study was seen in the age group of 26 - 30 years (30.61 %) which was comparable to the findings of Lubab et al.[12] This may be because the above age group is the main age of fertilization.

Majority of the breast masses were presented during post–partum or lactational period (77.55 %) which was comparable to the findings observed in Tina Rai et al.[3]

We need to explore other reliable methods to diagnose breast masses relatively quickly & also accurately. One such study is comparison of conventional FNAC smear finding and thin prep (TP). Though thin prep slide preparation following breast FNA has practical advantages as we don't need to make smears immediately, certain cytomorphologic findings inherent to this technique needs to be considered e.g. cell appear differently, nuclei are more pronounced in TP, so, the threshold for cytologic atypia should be higher.

Another technique to be considered, over and above the breast FNAC is core needle biopsy (CNB). As reported by Saha et al.[14] if initial FNAC is inadequate, core needle biopsy is another alternative method to be tried so, that diagnosis is not missed.

Another interesting technique that is coming up in the study of any tumour is cell block study along with immunocytochemistry (ICC). One study done on lung masses using CB & ICC has been found to have distinct advantages over FNAC alone.[15]

In our study, FNAC was the only technique used for the diagnosis. Cell block along with ICC would be another technique that can be added in future studies for more confirmative diagnosis without resorting to surgical procedure.

CONCLUSIONS

Palpable breast lumps during pregnancy and lactation are a common clinical presentation. FNAC has an important role in the diagnosis of breast masses during pregnancy and lactation and it decreases the delay in diagnosis of breast cancer, which are on the rise due to increase in child bearing age group. Based on our study, we concluded that FNAC is a safe first line of investigation in the diagnosis of breast diseases compared to surgical open biopsy which pose a risk in pregnant and lactating women. This will rule out unnecessary surgical biopsy in benign breast lesions in pregnant and lactating women. However, the cytopathologist must be aware of the characteristic cytological features in FNA smears with atypical features to avoid a false positive diagnosis of breast cancer in pregnant and lactating period.

In our study, we presented the role of FNAC in the cytomorphological diagnosis of various patterns of breast diseases during pregnancy and lactation ranging from benign breast lesions to fatal malignant lesions.

Limitations
The study period was short and was done in a single centre. As a result, the total number of cases were small and hence, the findings cannot be generalized to all the lesions seen in breast masses during pregnancy and lactation in the population.

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