A Correlative Study of Fine Needle Aspiration Cytology with Histopathology of Female Breast Lesions

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ABSTRACT

BACKGROUND
Breast lesions remain a major public health problem worldwide. Fine needle aspiration cytology (FNAC) has become one of the first-line investigations for the diagnosis of breast lumps. Although one of the major goals of FNAC is to differentiate benign from malignant lesions, in certain cases, this may not be possible due to a lack of uniformity with regards to the reporting terminology used in breast cytology by pathologists worldwide, resulting in poor communication of results among health-care providers. The present study aims to evaluate the role and diagnostic accuracy of FNAC in the evaluation of breast lesions using the National Cancer Institute (NCI) recommended terminology by correlating with histopathological examination (HPE) results.

METHODS
In this retrospective study conducted over a period of two years, a total of 382 female patients with breast lesions underwent FNAC and was categorized according to the NCI guidelines. Of these, 156 cases had histopathological follow-up and their FNAC diagnoses were compared. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) along with 95% confidence interval (95% CI) and accuracy of FNAC were calculated.

RESULTS
Among the 156 cases, none were unsatisfactory (C1); 105 (67.1%) were benign (C2); 7 (4.4%) were atypical but probably benign (C3); 2 (1.1%) were suspicious favouring malignancy (C4); 43 (27.4%) were malignant (C5). Cyto-histopathological correlation was carried out. Of categories C2 and C3 (total of 112 cases), 109 were confirmed as benign (true negative) and the remaining 3 cases turned out to be malignant (false negative). Of categories C4 and C5 (total of 45 cases), all cases were confirmed as malignant (true positive) and none were benign (false positive). The present study showed a sensitivity, specificity, PPV, NPV and accuracy of 93.62% (95% CI, 82.46%–98.66%), 100% (95% CI, 96.67%–100%), 100% (95% CI, 92.5%–99.6%), 97.32% (95% CI, 92.4%–99.09%) and 98.08% respectively.

CONCLUSIONS
Our study concluded that FNAC is a rapid and effective method, and reporting of smears using NCI guidelines highly correlated with the histopathological diagnosis.

KEY WORDS
Breast Lesions, Cytdiagnosis, Histopathologic Diagnosis, Fine-Needle Aspiration Cytology, Histopathological Examination, National Cancer Institute
Lesions of the breast constitute a major public health problem worldwide, both in developed as well as in developing countries.\(^1\) A palpable breast lump, whether benign or malignant, is a cause of great anxiety to the patient.\(^4\) Thus, the need arises to distinguish benign from malignant lesions, prior to definitive treatment. Fine needle aspiration cytology (FNAC) is a simple procedure that involves passing a fine (22-24 G) needle fitted to an air-tight syringe, through the skin, to sample fluid or tissue from a solid or cystic mass. The extracted material is skillfully smeared onto a glass slide and is air-dried or fixed, stained rapidly, studied and diagnosis rendered promptly.\(^5\)

Investigations like ultrasonography and mammography are used as an adjunct to FNAC, with biopsy as the standard procedure in the diagnosis of breast lesions. The triple test approach, which comprises clinical breast examination, radiological imaging (sonography and mammography), and pathological assessment with FNAC however remains an excellent tool in the initial assessment of palpable breast lumps as well as for screening asymptomatic patients.\(^6,7\) But each of these techniques have their own advantages and limitations.\(^6,8,9\)

Histopathologic studies still remain the gold standard or reference point for establishing the diagnostic accuracy of cytological smears. However, surgical biopsy (either core needle biopsy [CNB] or excision) results in a large burden of surgery with major preparations, high cost (as compared to FNAC), hospital reservations, medicolegal complications, technological complexities and a large staff, long tissue processing time, cumbersome, and time consuming results, complications, interpretations;\(^1,9\) patient discomfort such as pain, infection, bleeding and haematoma, and the risk of seeding of the tumour along the needle track in case of core biopsies.\(^6\) Hence, FNAC helps to determine when the surgical approach is warranted.

With the obvious advantages of ease, simplicity, rapidity, inexpensive and virtually painless procedure and with a high percentage of sensitivity, specificity, accuracy and virtually no complications, FNAC has become a standard tool and one of the first-line investigations for the diagnosis of breast lumps.\(^1,6,8,10,11\) Moreover, FNAC is a relatively safe procedure in certain circumstances like very small lesions, superficial lesions, or lesions very close to the chest wall as compared to biopsies. In addition, FNAC maintains tactile sensitivity, allows multi-directional passes allowing a broader sampling of lesion, and immediate reporting whenever necessary.\(^1\)

FNAC is not only useful in diagnosis and further planning of treatment without need for biopsy, but also helpful in prognostication of the tumour factors such as nuclear grading, mitotic index, hormone receptor status and DNA contents.\(^2\) Especially in developing countries and countries with limited resources, majority of breast malignancies are advanced\(^7\) and an unequivocal pre-operative diagnosis of malignancy is frequently required by surgeons in order to justify a more intense medical evaluation for metastatic disease. In such settings, FNAC serves as a cost-effective alternative to open surgical biopsy. However, successful FNAC demands high specimen quality and experience on part of both the aspirator and the cytopathologist.\(^9\)

Accurate pathological diagnosis is crucial for further treatment and estimation of an outcome. One of the major goals of FNAC is to differentiate benign from malignant lesions. However, in certain instances, differentiation of benign from malignant lesion is not possible due to significant overlap on smears and also when there is a paucity of cells. To address these cytomorphologic uncertainties and to bring a higher degree of uniformity to the reporting terminology so as to limit false positive or false negative results, the National Cancer Institute (NCI) proposed five diagnostic categories, based on the National Health Services Breast Screening Programme (NHSBSP) of Britain proposed in 1996 namely, C1, C2, C3, C4 and C5.\(^1,4\)

In the present study, we aim to evaluate the role and diagnostic accuracy of FNAC in the evaluation of breast lesions using the NCI recommended terminology by correlating with histopathological results.

**METHODS**

Ethical clearance was applied for and obtained from the Institutional Ethics Committee before the commencement of the present study. A retrospective study was conducted over a period of two years, i.e., between the period of January 2011 to December 2012. The data of all patients presenting with breast lump who underwent FNAC in the Cytology division of Pathology Department, JNIMS, Manipur, during this period were retrieved and reviewed. Only the female breast cases were further analysed. Details concerning age, laterality and site of the breast lesions were recorded. Available cytopathologic reports and slides were retrieved and the cytomorphological features of all the lesions were further studied.

Informed consent had been taken. All patients had been made to lie down on the examination bed and all breast lump aspirates had been performed using 22-24-gauge needle and 10 mL syringe by the cytopathologist under aseptic precautions. The aspirated material was then smeared onto a minimum of 5 clean, dry and grease-free slides. One slide was rapidly stained with Leishman stain for a minute and examined for sample adequacy. Three slides were air dried and stained with May-Grunwald-Giemsa stain. One slide was wet-fixed in 95% ethyl alcohol and subsequently stained with Papanicolaou stain. The stained smears were then classified into five major diagnostic categories after screening and interpretation by applying the probabilistic approach;\(^4\) These were C1, Non diagnostic/unsatisfactory/unremarkable; C2, Benign; C3, Atypical; C4, Suspicious for malignancy; and C5, Malignant.

Records of subsequent excisional biopsies or mastectomies were also retrieved from the Histopathology division of Pathology Department. Specimens had been fixed in 10% formalin solution, routinely processed, sectioned and stained with haematoxylin and eosin staining methods for microscopic examination. The histopathologic examination (HPE) reports and slides were retrieved and reviewed. Comparison was made with the corresponding cytopathology...
The present study showed a sensitivity of 93.62% (95% CI, 82.46%–98.66%), specificity of 100% (95% CI, 96.67%–100%), PPV of 100% (95% CI, 92.5%–99.6%), NPV of 97.32% (95% CI, 92.4%–99.0%), and accuracy of 98.08% for FNAC in the diagnosis of malignant lesions. The false positive and false negative rate was 0% and 6.4%, respectively.

Table 1. Age Distribution of Female Breast Lesions

| C | FA | Abs | Bas | FCD | Gal | Lacta | Granulosa | Atypical | Suspicious | Malignant | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 11-20 | 46 | 2 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 52 |
| 21-30 | 70 | 2 | 14 | 1 | 3 | 1 | 5 | 0 | 2 | 126 | 33.0 |
| 31-40 | 27 | 9 | 17 | 1 | 0 | 0 | 12 | 1 | 2 | 20 | 103 | 27.0 |
| 41-50 | 5 | 2 | 8 | 5 | 21 | 0 | 0 | 8 | 1 | 4 | 22 | 72 | 18.0 |
| 51-60 | 2 | 0 | 1 | 0 | 4 | 0 | 1 | 1 | 17 | 24 | 63 |
| 61-70 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 4 |
| 71-80 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 1 | 0.3 |
| Total | 161 | 47 | 23 | 51 | 2 | 4 | 22 | 6 | 4 | 66 | 382 | 100.0 |
| % | 42.1 | 12.3 | 6.0 | 13.4 | 1.0 | 0.5 | 5.8 | 1.0 | 13.7 | 17.0 | |

Table 2. Laterality and Quadrant

| Laterality | UO | UI | LO | LI | Total | % |
|---|---|---|---|---|---|---|
| Right | 152 (39.8%) | 34 (9.0%) | 18 (4.7%) | 9 (2.4%) | 213 | 55.8% |
| Left | 111 (29.1%) | 33 (8.6%) | 16 (4.2%) | 9 (2.4%) | 169 | 44.2% |
| Total | 263 | 67 | 34 | 18 | 382 | 100% |
| % | 68.0% | 17.5% | 9.0% | 4.7% | |

Table 3. Comparison of the Distribution of Various National Cancer Institute Guidelines Comparison of Present Study with Published Studies

| Study | Year of Publication | Total Number of Cases | Malignant | Abs. | Suspicious | Atypical | Atypical | Benign | FA |
|---|---|---|---|---|---|---|---|---|---|
| Ukah and Oluwasola | 2005 | 1401 | 38 (2.7) | 803 (57.3) | 6 (0.4) | 107 (7.6) | 447 (31.9) |
| Challa et al | 2010 | 812 | 8 (0.9) | 314 (38.6) | 27 (3.3) | 12 (1.4) | 451 (55.5) |
| Sankeye et al | 2012 | 215 | 13 (5.6) | 121 (55.2) | 8 (3.6) | 8 (3.5) | 65 (29.0) |
| Singh et al | 2014 | 102 | 2 (2.0) | 200 (19.7) | 1 (0.1) | 8 (7.8) | 70 (68.6) |
| Arul and Masilamani | 2015 | 523 | 14 (2.7) | 253 (47.7) | 18 (3.5) | 75 (14.3) | 99 (18.7) |
| Madiobogwu et al | 2017 | 110 | 17 | 46 | 5 | 4 | 38 |
| Veena et al | 2017 | 178 | 4 (2.2) | 134 (75.28) | 14 (7.8) | 6 (3.3) | 29 (16.2) |
| Present study | 2019 | 382 | 0 | 290 (75.9) | 22 (5.8) | 4 (1.0) | 66 (17.3) |

Table 4. Comparison of the Distribution of Various National Breast Cancer Institute Guidelines Comparison of Present Study with Published Studies

| Study | Year of Publication | Total Number of Cases | Malignant | Abs. | Suspicious | Atypical | Atypical | Benign | FA |
|---|---|---|---|---|---|---|---|---|---|
| Ukah and Oluwasola | 2005 | 1401 | 38 (2.7) | 803 (57.3) | 6 (0.4) | 107 (7.6) | 447 (31.9) |
| Nguansangiam et al | 2006 | 102 | 56 (55.6) | 80 (44) | 182 |
| Sankoye and Dvange | 2012 | 31 (40.0) | 54 (9.2) | 76 |
| Yusuf and Aranda | 2012 | 117 | 58 (50.8) | 83 (41.5) | 200 |
| Arul and Masilamani | 2015 | 196 (49.2) | 88 (20.8) | 286 |
| Daramola et al | 2015 | 398 (91.3) | 30 (7.6) | 436 |
| Madiobogwu et al | 2017 | 58 | 52 (72.7) | 52 (72.7) | 110 |
| Veena et al | 2017 | 112 | 79 (70.5) | 30 (26.6) | 142 |
| Present study | 2019 | 109 | 70 | 47 (43) | 156 |

Table 5. Comparison of Histopathological Cases of the Present Study with Published Studies

| Study | Year of Publication | Total Number of Cases | Malignant | Abs. | Suspicious | Atypical | Atypical | Benign | FA |
|---|---|---|---|---|---|---|---|---|---|
| Ukah and Oluwasola | 2005 | 1401 | 38 (2.7) | 803 (57.3) | 6 (0.4) | 107 (7.6) | 447 (31.9) |
| Nguansangiam et al | 2006 | 102 | 56 (55.6) | 80 (44) | 182 |
| Sankoye and Dvange | 2012 | 31 (40.0) | 54 (9.2) | 76 |
| Yusuf and Aranda | 2012 | 117 | 58 (50.8) | 83 (41.5) | 200 |
| Arul and Masilamani | 2015 | 196 (49.2) | 88 (20.8) | 286 |
| Daramola et al | 2015 | 398 (91.3) | 30 (7.6) | 436 |
| Madiobogwu et al | 2017 | 58 | 52 (72.7) | 52 (72.7) | 110 |
| Veena et al | 2017 | 112 | 79 (70.5) | 30 (26.6) | 142 |
| Present study | 2019 | 109 | 70 | 47 (43) | 156 |
In the present study, benign breast lesions were more common in 21–30 years, which was similar to studies by Veena et al. Malignant breast lesions were most common in 41–50 years, which were comparable to studies by Arul et al.

The present study shows that benign lesions are common in the younger age group and malignancy rates increase with increasing age of patients. The right breast (213, 55.8%) was found to be more commonly involved in the present study, which was in contrast to some published findings; however, the upper outer quadrant (263, 68.8%) was the most common location which is similar to findings by the same researchers.

The distribution of the FNAC diagnoses of breast lesions using NCI guidelines (1996) in our institution as compared with published studies is shown in Table 4. Categories C2 to C5 of our study were comparable to frequencies found in most published studies. In the present study, there were no C1 categories, since rapid stain was conducted for all cases to determine specimen adequacy; Categories C2 and C5 are straightforward and has been associated with a high degree of diagnostic accuracy as was observed in the present study (99% and 100% respectively). However, the interpretation of C3 and C4 are difficult and confusing because they do not have strict criteria for diagnosis. Some researchers have suggested clubbing of C3 and C4 as a single term called equivocal/suspicious category as they believe that a Core needle biopsy (CNB) or surgical biopsy should be done for this combined category, as the incidence of malignancy is significant in both subgroups. In the present study, benign and malignant outcome of C3 was 71.4% and 28.6%, while malignant outcome of C4 was 100%, which is comparable to large-scale studies with histopathological correlation. Since the current study showed 71.4% benign lesions with C3 and 100% malignancy with C4, we feel that it is still useful to maintain the categories C3 and C4 separately.

On HPE of the 156 cases, benign cases (69.9%, 109/156) were more common as compared to malignant cases (30.1%, 47/156). This finding was similar to various studies. The most common benign and malignant breast lesions on HPE were fibroadenoma and IDC-NOS respectively. These findings were comparable to various published studies. One case of ILC was under-diagnosed as fibroadenoma in C2, one case of IDC-NOS and papillary misdiagnosed as C3 on FNAC, contributing to false negative results. Factors contributing to false negative results may include the small size of the lesion, hypocellularity, and inadequate sampling during aspiration, histological tumour types such as low nuclear grade in ILC, and well-differentiated intracystic papillary carcinoma. All cases from C4 and C5 was diagnosed as malignant on HPE. These results were considered as true positive. Both false negative and false positive diagnoses can be reduced by good sampling technique, proper tumour localization, triple assessment, and more importantly availing expert second opinions for doubtful cases.

The present study showed a sensitivity of 93.62% (95% CI, 82.46%–98.66%), specificity of 100% (95% CI, 96.67%–100%), PPV of 100% (95% CI, 92.5%–99.6%), NPV of 97.32% (95% CI, 92.4%–99.09%), and accuracy of 98.08% for FNAC in the diagnosis of malignant lesions, comparable to other published studies as in Table 6.

**DISCUSSION**

**CONCLUSIONS**

Fine-needle aspiration cytology is a rapid and effective method for the primary categorization of palpable breast lumps into benign, malignant, atypical, suspicious, and unsatisfactory categories. Benign breast lesions are common than malignant lesions, fibroadenoma is the most common benign breast lesion, whereas IDC accounts for the highest number of malignant lesions. Histological correlation indicated FNAC to be a good diagnostic tool.

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