

ASSESSMENT OF DIAGNOSTIC ACCURACY OF FINE NEEDLE ASPIRATION CYTOLOGY IN BENIGN AND MALIGNANT BREAST LESIONS

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Abstract

Increasing awareness, associated anxiety & stress among women who perceive every lump in breast as carcinoma, compels the patient to seek the medical advice. It is sometimes difficult to determine whether a suspicious lump is benign or malignant simply from clinical assessment and fine needle aspiration cytology (FNAC) is helpful in reaching definitive diagnosis. Accuracy in the diagnosis can be increased by multiple sampling of appropriate sites by ultrasonography guidance and/or mammographic localization. Breast cancer is the most common cancer in women all over India. Due to lack of awareness and almost non-existent breast screening practices, patients present with palpable breast cancers. Hence based on above findings the present study was planned for Assessment of Diagnostic Accuracy of Fine Needle Aspiration Cytology in Benign and Malignant Breast Lesions.

The present study was planned in Department of Pathology, Indira Gandhi Institute of Medical Science, Patna, Bihar, India. The present study was planned from duration of march 2019 to August 2019. In the present study 50 females with breast lesion were included and evaluated in the present study. The FNAC was performed in each patient by the technique of Martin and Ellis using 21-22G needle attached to 20 ml disposable syringe and smear prepared both wet fixed in 95% ethanol and air dried. All cytology smears were stained by May Grunwald Giemsa, Papanicolaou, and hematoxylin and eosin stain.

It is highly useful in screening large population as it is simple, rapid, cost effective and reliable. FNAC has few limitations and biopsy is must in cases with suspicious and atypical lumps. FNAC serves as a compliment and not a substitute to the histopathology in such cases. So, it is concluded that FNAC should be used as a routine diagnostic procedure to maximize the availability of effective health care to patients with breast lesions.

Keywords: Diagnostic Accuracy, Fine Needle Aspiration, Cytology, Benign, Malignant Breast Lesions, etc.

Introduction

Breast masses are broadly classified as benign or malignant. Common causes of benign breast lesions include fibrocystic disease, fibroadenoma (see the image below), intraductal papilloma, and abscess. Malignant breast disease encompasses many histologic types that include, but are not limited to, in situ ductal or lobular carcinoma, infiltrating ductal or lobular carcinoma, and inflammatory carcinoma. The main concern of many women presenting with a breast mass is the likelihood of cancer. Reassuringly, most breast masses are benign.

Breast infections are divided into lactational and nonlactational infections and puerperal versus nonpuerperal, depending on their association with pregnancy. The process may be confined to the skin overlying the breast, or it may result from an underlying lesion (eg, sebaceous cyst), as in hidradenitis suppurativa. [1, 2, 3, 4]

The mammary glands arise from a caudal section of the ectodermal tissue known as the “milk lines,” which extend along the anterior surface of the developing fetus from the axilla to the groin. During puberty, pituitary and ovarian hormonal influences stimulate female breast enlargement, primarily owing to accumulation of adipocytes. Each breast contains approximately 15-25 glandular units know as breast lobules, which are demarcated by Cooper ligaments. Each lobule is composed of a tubuloalveolar gland and adipose tissue. Each lobule drains into the lactiferous duct, which subsequently empties onto the surface of the nipple. Multiple lactiferous ducts converge to form one ampulla, which traverses the nipple to open at the apex. [5]

Below the nipple surface, lactiferous ducts form large dilations called lactiferous sinuses, which act as milk reservoirs during lactation. [6] When the lactiferous duct lining undergoes epidermalization, keratin production may cause plugging of the duct, resulting in abscess formation. [7, 8] This may explain the high recurrence rate (an

estimated 39%-50%) of breast abscesses in patients treated with standard incision and drainage, as this technique does not address the basic mechanism by which breast abscesses are thought to occur.

Postpartum mastitis is a localized cellulitis caused by bacterial invasion through an irritated or fissured nipple. It typically occurs after the second postpartum week and may be precipitated by milk stasis. [9] There is usually a history of a cracked nipple or skin abrasion or failure to clean nipples after breastfeeding. [10] Sleeping position may also affect the progression of mastitis to breast abscess. [10] *Staphylococcus aureus* is the most common organism responsible, but *Staphylococcus epidermidis* and streptococci are occasionally isolated. Drainage of milk from the affected segment should be encouraged and is best achieved by continued breastfeeding or use of a breast pump. [3, 8, 4]

Nonlactating infections may be divided into central (periareolar) and peripheral breast lesions. Periareolar infections consist of active inflammation around nondilated subareolar breast ducts—a condition termed periductal mastitis. Peripheral nonlactating breast abscesses are less common than periareolar abscesses and are often associated with an underlying condition such as diabetes, rheumatoid arthritis, steroid treatment, granulomatous lobular mastitis, trauma, and smoking. [1, 11, 12] Primary skin infections of the breast (cellulitis or abscess) most commonly affect the skin of the lower half of the breast and often recur in women who are overweight, have large breasts, or have poor personal hygiene. [3]

Breast masses can involve any of the tissues that make up the breast, including overlying skin, ducts, lobules, and connective tissues. Fibrocystic disease, the most common breast mass in women, is found in 60%-90% of breasts during routine autopsy. Fibroadenoma, the most common benign tumor, typically affects women aged 30 years or younger and accounts for 91% of all solid breast masses in females younger than 19 years. [5] Infiltrating ductal carcinoma is the most common malignant tumor; however, inflammatory carcinoma is the most aggressive and carries the worst prognosis. Mammary Paget disease, or adenocarcinoma of the nipple epidermis, is relatively rare but may be misdiagnosed as a benign dermatosis if care is not taken. [13, 14]

Statistics provided refer to populations in the United States. After skin cancer, breast cancer is the most commonly diagnosed cancer in women, accounting for roughly 1 in 4 cancers diagnosed and affecting 12.4% of women during their lifetime. [15] Breast infections occur in as many as 10%-33% of lactating women. [16, 17] Lactational mastitis is seen in approximately 2%-3% of

lactating women, [6, 18, 4] and breast abscess may develop in 5%-11% of women with mastitis. [18, 4]

Morbidity and mortality depends on etiology (benign vs malignant) and stage of malignant lesions. Approximately 2.1%-3.6% of women die of breast cancer. In 2009, approximately 40,170 women were expected to die from breast cancer, [15] remaining stable at 40,610 in 2017, just behind lung and colon cancer. Despite significant differences in sociodemographic and clinical characteristics, overall and disease-free survival rates are similar for men and women with breast cancer.

Associated morbidity may include scarring, disfigurement, lymphedema, and psychologic stress. Mastitis is usually seen in lactating women, but the presence in a nonlactating woman should spur evaluation for an inflammatory carcinoma, newly onset diabetes, infection with *Mycobacterium tuberculosis*, and other idiopathic causes. [3, 12]

Abscess formation complicates postpartum mastitis in fewer than 10% of cases. Neonatal mastitis usually occurs in term or near-term infants, is twice as common in females, and progresses to development of a breast abscess in approximately 50% of cases. While white women have a higher incidence of breast cancer than African American women after age 40 years, African American women have a higher incidence of early breast cancer (before age 40 years) and are more likely to die of breast cancer at every age.

African American women have been variably reported to have an increased incidence of developing a primary breast abscess. Approximately 99% of breast cancers are found in women. Up to 1% of breast cancers occur in men, but numbers have been increasing. Men with changes in breast size should undergo as aggressive of a diagnostic workup as women. Fibroadenoma, a benign condition, is the most common cause of breast mass in women younger than 35 years. [5]

In 2017, women aged 40 years or older accounted for nearly 96% of new breast cancer diagnoses and 98% of breast cancer deaths. The median age at breast cancer diagnosis is 62 years. Breast infections most commonly affect women aged 18-50 years.

Nonpuerperal breast masses encompass a wider range of ages, from the late second to eighth decade of life. Peak incidence is often in the fourth decade of life. Ninety-five percent of these infections occur in women. [8]

Puerperal breast abscesses and mastitis are commonly found in women of childbearing age (mean age of 32 years). [1] Women who reside in rural settings may be more likely to present with a more advanced cancer stage than women in urban settings. This may partly result from

the availability of and access to effective screening tools and primary care.

Breast mass: Prognosis varies from excellent in patients with a fibroadenoma to poor in those with inflammatory breast cancer. Influencing factors include tumor size, histology, nodal involvement, distant metastases, and comorbid conditions.

Breast abscess: Unfortunately, the recurrence rate of breast abscess is high (39%-50%) when treated with standard incision and drainage, and studies have shown even higher recurrence rates in women undergoing fine-needle aspiration. Nonpuerperal abscesses recur more frequently, especially when associated with non-staphylococcal species (>50% recurrence rate). [8] Studies of patients with fistulectomy show lower recurrence rates. **Mastitis:** Most patients experience resolution within 2-3 weeks. All patients with symptoms that have not resolved within 5 weeks should be evaluated for resistant infection or malignancy.

Breast disease is one of the common clinical problem in India with cancer of breast being second most common cancer in the women. [16] The most common presentation of breast disease is a palpable mass; although breast diseases can also present as inflammatory lesion, nipple secretion and imaging abnormalities. [17] Increasing awareness, associated anxiety & stress among women who perceive every lump in breast as carcinoma, compels the patient to seek the medical advice. It is sometimes difficult to determine whether a suspicious lump is benign or malignant simply from clinical assessment and fine needle aspiration cytology (FNAC) is helpful in reaching definitive diagnosis. Accuracy in the diagnosis can be increased by multiple sampling of appropriate sites by ultrasonography guidance and/or mammographic localization. [18-19]

Breast cancer is the most common cancer in women all over India. Due to lack of awareness and almost non-existent breast screening practices, patients present with palpable breast cancers. Hence based on above findings the present study was planned for Assessment of Diagnostic Accuracy of Fine Needle Aspiration Cytology in Benign and Malignant Breast Lesions.

Methodology:

The present study was planned in Department of Pathology, Indira Gandhi Institute of Medical Science, Patna, Bihar, India. The present study was planned from duration of March 2019 to August 2019. In the present study 50 females with breast lesion were included and evaluated in the present study. The FNAC was performed in each patient by the technique of Martin and Ellis [20] using 21-22G needle attached to 20 ml disposable syringe and smear prepared both wet fixed in 95% ethanol and air

dried. All cytology smears were stained by May Grunwald Giemsa, Papanicolaou, and hematoxylin and eosin stain.

All the patients were informed consents. The aim and the objective of the present study were conveyed to them. Approval of the institutional ethical committee was taken prior to conduct of this study.

Following was the inclusion and exclusion criteria for the present study.

Results & Discussion:

Breast cancer is the leading cause of morbidity and mortality. [21-22] Fine needle aspiration cytology (FNAC) is widely accepted as a reliable technique in the initial evaluation of breast lumps. The procedure is simple, safe, cost effective, minimally invasive, rapid and can be carried out at outpatient department. [23-24] It is highly sensitive, specific and diagnostically accurate. A breast mass is generally palpable when it exceeds 2cm in size. The likelihood of a palpable mass of being malignant increases with age. Only 10% of breast masses under the age of 40 are malignant compared to 60% of masses over the age of 50 years. [25] Investigation of a palpable breast lump involves "Triple test" which analyses clinical and radiological findings in conjunction with pathologic features (FNAC) for the diagnosis as well as to reduce the risk of missed diagnosis to < 1%. [26]

FNAC is highly sensitive, specific, rapid, easy to perform, cost effective and can be carried out at OPD level. Molecular ancillary techniques for example progesterone receptor & estrogen receptor, proliferation antigen & DNA pattern analysis can be applied on aspirated material. FNAC is also useful as a follow-up procedure for post-mastectomy or lumpectomy⁶ and in diagnosis of primary breast lymphomas so that an option of breast conservation can be offered. It can also be used to diagnose lesions of male breast such as gynaecomastia, accessory axillary breast tissue & carcinoma and to access status of axillary lymph nodes. [27-28]

FNAC of breast lump is an accepted and established method to determine the nature of breast lump with high degree of accuracy. [29-30] The application of Fine needle aspiration (FNA) for the diagnosis of palpable breast masses was first introduced by Martin and Ellis [31] in 1930, and since then, it has been established as an important tool in the evaluation of breast lesions. Most of the patients with breast lump are in a state of anxiety. To reduce unnecessary surgical procedures as well as at the same time to minimize delay in the diagnosis & to institute prompt treatment, FNAC plays an important role.

Fine needle aspiration cytology (FNAC) is an established procedure and has been used for more than four decades for the diagnosis of palpable breast masses. [32-33] The

advantages of FNAC include simplicity, accuracy, low morbidity, minimal patient discomfort, relatively low cost and immediate availability as an office procedure without anaesthesia. Prompt diagnosis relieves patient's anxiety and allows time to plan definitive treatment. Many benign conditions can be diagnosed accurately and surgery avoided, also the need for frozen section diagnosis is reduced. The reported sensitivities of FNAC range from 43.8% to 95%, specificities from 89.8% to 100%, positive predictive values from 76.2% to 100% and negative predictive values from 46.3% to 98.8%. [34] If skilled cytopathologists are provided with adequate material, the diagnostic accuracy of FNAC is high.

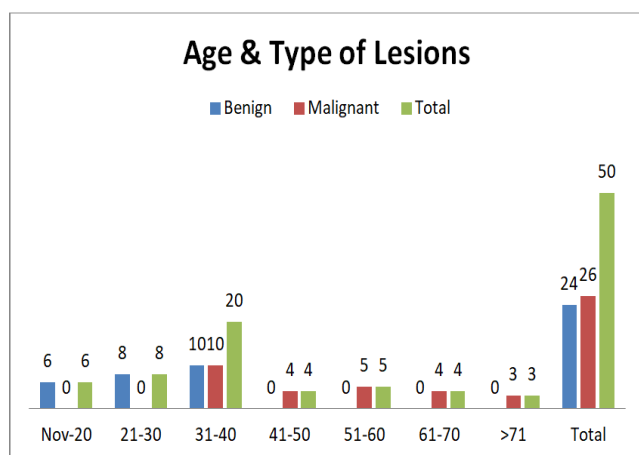


Figure 1: Age Distribution for Cases

Table 1: Size of the tumor in benign and malignant lesions

Size (cms)	Benign	Malignant
Less than 5 cms	16	3
5-10 cms	8	21
More than 10 cms	0	2
Total	24	26

Table 3: Diagnosis of breast lump lesions (Fine needle aspiration cytology).

Diagnosis	No. Patients with Prediction
Benign	20(False negative-2)
Suspicious	3 (Malignancy Confirmed with HP)
Malignant	27 (False Positive-0)
Total	50

The findings of Mahmood et al [35] who also reported maximum incidence in the 3rd decade. The findings of Hussain MT et al [36] varies who reported a maximum incidence of 30% of breast lumps in the age group of 31-40 years followed by 20% in 15- 20 years. These studies as well as the present work indicate that the major burden of breast lesions is on the active and economically productive young age group. Thus, there is the need for early and accurate diagnosis and management of these patients. Breast cancer is the second most common cancer among Indian females next only to cervical cancer. In experienced

hands, FNA is highly accurate diagnostic procedure with sensitivity and specificity over 95% for palpable breast lesions. [37-38]

Singh A et al also reported that invasive ductal carcinoma is the commonest breast malignancy. In the present study, there were 215 cases diagnosed under the benign category from which 92 cases were available for histological follow up. [39]

The diagnosis of carcinoma breast on cytology during lactation is difficult as it may sometimes be presented as obstructed galactophoreic duct may be the reason of false negative diagnosis. Hypercellular lesions such as cellular fibroadenoma, proliferative breast disease, phyllodes tumor and post radiation induced atypical changes can have findings such as nucleomegaly, mild pleomorphism and presence of nucleoli which may sometimes erroneously report malignancy in benign lesions. [40]

Carcinoma of the breast is a leading cause of death in women and needs to be evaluated at an early stage. FNAC helps in rapid diagnosis of breast lesions and their management. The technique of FNAC was described by Kun in 1847 and was introduced into clinical practice by Ellis and Martin in 1930. Pre-operative diagnosis of breast carcinoma helps in early institution of the neo-adjuvant therapy. The objective of the study is to study the diagnostic efficacy of Fine needle aspiration cytology in breast lesions and to recognize diagnostic difficulties and pitfalls related to FNAC diagnosis. [41]

Fine-needle aspiration cytology is a patient friendly, easy, reliable, repeatable and simple diagnostic test. When performed by an expert pathologist, the diagnostic accuracy of FNAC is very high. A high sensitivity and a high positive predictive value proved that a positive FNAC in the breast means a definite diagnosis of the concerned pathology if compared with the final histology report. The high specificity and a high negative predictive value for malignancy illustrated the high accuracy of FNAC in the diagnosis of malignancy in the breast. Very importantly, a report negative for malignancy was highly accurate (>98%) in predicting an absence of malignancy. Thus, we conclude that FNAC is a very important preliminary diagnostic test in palpable breast lumps.

In spite of its few limitations, FNAC has high levels of diagnostic accuracy when it is performed by an experienced pathologist. The high specificity and high negative predictive value for malignancy illustrated the high accuracy of FNAC in the diagnosis of malignancy in the breast. Therefore, we conclude that the diagnosis of breast lesions based on FNAC should be practiced as a routine procedure as there is high degree of correlation with histopathological findings.

Conclusion:

It is highly useful in screening large population as it is simple, rapid, cost effective and reliable. FNAC has few limitations and biopsy is must in cases with suspicious and atypical lumps. FNAC serves as a compliment and not a substitute to the histopathology in such cases. So, it is concluded that FNAC should be used as a routine diagnostic procedure to maximize the availability of effective health care to patients with breast lesions.

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