D:/Biomedica Vol.26, Jul. – Dec. 2010/Bio-7.Doc P. 124 – 129 (WC)

ORIGINAL ARTICLE

ASSOCIATION OF FINE NEEDLE ASPIRATION CYTOLOGY WITH TUMOR SIZE IN PALPABLE BREAST LESIONS

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ABSTRACT

Introduction: Breast cancer is the most common type of cancer in women, age 40 – 50 years. It is the second leading cause of cancer deaths i.e about 250,000 women die of this disease every year.

Objective: The purpose of the study was to evaluate the accuracy, utility and feasibility of Fine Needle Aspiration Cytology (FNAC) in diagnosing breast lesions in association with palpable size of the tumour.

Material and Methods: It was a descriptive study conducted in the Department of Histopathology; Services Institute of Medical Sciences and Services Hospital Lahore. The study included 464 patients with palpable breast lesions undergoing fine-needle aspiration cytology during a period of three years from January 2006 to December 2008.

Results: Using $C_1 – C_5$ categories of FNAC smears, 281 out of 464 (60.6%) were categorized as C_2 followed by C_5 48 (10.3%), there was a significant ($P < 0.0001$) relationship between palpable size of the breast lesion and cytological category of the specimens. Fibroadenoma was the most frequent (161) (34.6%) benign tumour, C_3 accounted for 9.3% (43 out of 464).

Conclusion: The $C_1 – C_5$ grading system for FNAC is the most cost – effective and practical out patient procedure for early diagnosis of breast lesions. It is recommended that FNAC should be used as a routine diagnostic method to maximise availability of health care to patients with breast lesions.

Key Words: Fine-needle aspiration cytology. Fibroadenoma. Infiltrating Ductal Carcinoma.

INTRODUCTION

Breast cancer is the most common type of cancer in women, age 40 – 50 years. It is the second leading cause of cancer deaths i.e about 250,000 women die of this disease every year.[1] Breast cancer is also the most frequent malignancy in Pakistani females,[3-5] but patients in this country usually present late i.e with advanced disease, due to painless lump, fear of surgery and) non availability of female doctor.[6,7] The incidence of malignant neoplasia of the breast is on the rise. The statistical significance coupled with decreased morbidity and mortality associated with early detection of malignant tumours has prompted expensive screening programmes in the field of health care.[8] The apparent significant increase in the incidence is most probably attributable to an increase in screened cases and to increase awareness among women.[9] Self examination, clinical assessment, mammography and fine – needle aspiration cytology are proven pillars of screening programmes in different parts of the world.[10-12]

Fine needle aspiration cytology has been used as an initial investigative procedure for breast lesions, it is a rapid and non invasive procedure that has been increasingly used as an alternate to excision biopsy of palpable breast lesions.[13-15]

Increasing interest in the pre-operative prediction of breast cancer's aggressiveness led to the development of cytological grading system for FNA, and to their application to both air – dried, Romanowsky and alcohol fixed Papanicolau stained material. This grading system utilizes C1- C5 categories as recommended by the National Health Service (NHS) breast screening programme in the United Kingdom.[16,17]

Fine needle aspiration cytology is generally considered as a rapid, reliable, less traumatic and safe diagnostic tool to differentiate non–neoplastic from neoplastic breast lesions. This procedure is technically easy to apply in small breast lesions.[18, 19] FNAC is most accurate when experienced cytologists are available and when immediate assessment by professionals is performed for the evaluation of material adequacy, so that additional aspirations can be

performed when needed.[20]

The adequacy of the FNA of palpable breast lesions is based mostly upon factors such as confidence of needle placement, cell preservation and correlation with clinical and mammographic findings.[21] There is, however, no unanimity in the role of epithelial cell quantitation in determining the adequacy of FNA. The number of epithelial cell clusters (a total of six or more considered being adequate) as a parameter of adequacy could reduce the rate of false negative cytological diagnosis of palpable breast masses.[22]

The test has a high confidence level in the presence of two or more clinical factors like size and mobility of the breast mass, a definite decision regarding treatment can, therefore, be taken without a need of histological confirmation.[23]

In the presence of budget constraints and personnel shortage, hospitals are required to demonstrate even greater cost effectiveness in the diagnosis of breast lesions.[24] Accurate preoperative assessment of breast cancer is becoming increasingly important. Surgeons and pathologists are looking beyond the ability to diagnose invasive disease accurately. There is a constant search for tools that will allow earlier selection of patients for adjuvant chemotherapy or for more conservative surgical procedure.[25,26]

The purpose of the study was to determine the utility, feasibility and accuracy of FNAC and its continuing role in the diagnosis of palpable breast lesions; secondly to find association of cytological categories (C1 – C5) of FNA with palpable size of the breast lesions.

MATERIALS AND METHODS

It was a descriptive study conducted in the Department of Histopathology, Services Institute of Medical Sciences / Services Hospital, Lahore. The study included 464 subjects coming to the out – patient department with palpable breast lesions during a period of three years from January 2006 to December 2008. The patients included in the study were males and females of any age presenting with palpable breast lesions. On the other hand patients already diagnosed to have breast cancer, or have fungating and inflammed tumour including those in pregnant females.

The FNA procedure was performed in the Department of Histopathology, Services Institute of Medical Sciences / Services Hospital, Lahore. The physical examination was performed, tumor size was assessed and divided into four groups i.e. ; < 1 cm., 1 – 2 cm., 2 – 5 cm. and > 5 cm as already described.[27] Aspirates were taken under aseptic conditions using 22 gauge needle on a disposable syringe with application of vacuum. For each mass two to four passes were made in accordance with the recommendations of American Consensus Meeting on breast needle procedures.[27] The smears were prepared and routinely processed for cytological examination according to standard practice. The smears were stained with haematoxylin and eosin, Giemsa and Papanicolau stains. Each smear was numbered, labeled properly, mounted and examined under the microscope. Results of FNAC were reported according to the diagnostic categories from $C_1 – C_5$ as recommended by NHS breast screening programmes.[16]

Statistical Analysis

Data was analysed descriptively and analytically. In analytical section mean tumour size and (±) SD in various breast lesions was calculated and compared by t-test at 5% level of significance, while Chi-square test was applied to compare the distribution of different categories of aspirates in different breast lesions in association with tumour size.

RESULTS

The study included 464 patients presenting with palpable breast lesion. There were 457 (98.4%) females and 7(1.6%) males presenting with palpable breast lump. Out of 464 fine needle aspirates 63 (13.6%) were categorized as C_1, 281 (60.6%) C_2, 29 (6.2%) C_3, 43 (9.3%) C_4 and 48 (10.3%) C_5 (Table 1, Figure 1).

Sixty – three (13.6%) of the 464 aspirates from breast masses with mean palpable size 1.9 cm. (range 0.5 – 7 cm) were found to be inadequate. Whereas significant (P < 0.02) number 401 (86.4%) from masses with mean size 2.28 cm. (range 0.5 – 15 cm) were adequate for making a categorical diagnosis.

Table 1: *Distribution of FNA categories according to the tumor size in palpable breast lesions.*

FNAC Categories		Number of Cases (%)	Size Range (cm)	Mean (cm)
C_1 – Insufficient or Inadequate		63 (13.6%)	0.5 – 7	1.9 ± 1.42
C_2 – Benign/ inflammatory	Adequate n = 401 (86.4) Mean = 2.28 Range = 0.5 – 15 cm.	281 (60.6%)	0.5 – 7	2.2 ± 2.27
C_3 – Atypical, probably benign		29 (6.2%)	1 – 5	2.3 ± 1.14
C_4 – Suspicious		43 (9.3%)	0.5 – 14	3.9 ± 3.33
C_5 – Malignant		48 (10.3%)	1 – 15	4.0 ± 3.00

Among the adequate aspirates maximum number 281 (60.6%) from masses of mean size 2.2 cm. were categorized as C_2. Aspirates graded as C_3 (6.2%), C_4 (9.3%) and C_5 (10.3%) were aspirated from masses with palpable size 2.3 cm. 3.9 cm. and 4 cm, respectively (Table 1).

Table 2: *Association of tumour size with FNA cytology of palpable breast lump.*

Tumour Size (cm)	FNAC Categories					Total n (%)
	C_1 n (%)	C_2 n (%)	C_3 n (%)	C_4 n (%)	C_5 n (%)	
< 1	10 (2.15)	16 (3.45)	0	1 (0.21)	1 (0.21)	28 (6%)
1 – 2	35 (7.54)	167 (35.99)	16 (3.45)	10 (2.15)	14 (3.01)	242 (52%)
2 – 5	15 (3.2)	93 (20.04)	13 (2.8)	27 (5.82)	22 (4.74)	170 (37%)
> 5	3 (0.7)	5 (1.07)	0	5 (1.07)	11 (2.37)	24 (5%)
Total n = 464 (100%)	63 (13.6)	281 (60.6)	29 (6.2)	43 (9.3)	48 (10.3)	464 (100%)

n = number of cases

Maximum number of palpable breast lesions 242 (52.1%) out of464 were 1 – 2 cm. in size followed by the ones 2 – 5 cm in size 170 (37%). There was a significant ($P < 0.0001$) relationship between the size of the lesion and cytological category of FNAC, as shown in our study where category C_4 and C_5 were mostly from masses 2–5 cm, or more in size (Table 2).

Among the 232 (50%) benign epithelial and intralobular biphasic stromal lesions, fibroadenoma was the most frequent 157 (67.6%) with 4 (1.7%) out of these found to be suspicious (C_3) for malignancy (Table 3).

The proliferative and neoplastic lesions 329 (71%) accounted for the major diagnostic category. Fibroadenoma was found to be the most common benign lesion 161 out of 329 (48.9%) with frequent palpable size ranging from 1 – 2 cm. Infiltrating ductal carcinoma 88 out of 329 (26.7%) mostly presented in the palpable size ranging from 2–5 cm (Figure 2).

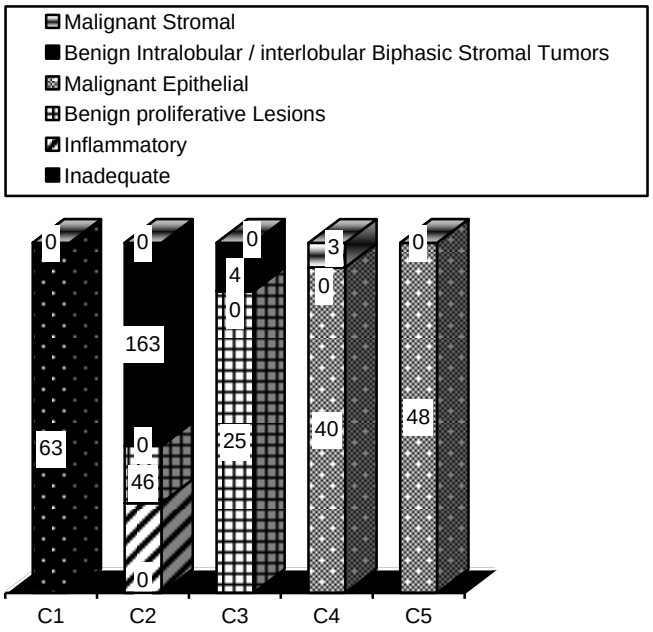


Fig. 1: *Cytological patterns in FNAC of palpable breast masses.*

DISCUSSION

Fine needle aspiration of the breast is a rapid, relatively atraumatic and accurate method for the diagnosis of breast disease.[16] The real challenge for FNA cytologist is in their ability to tra-nslate cytological patterns into histological ones that have diagnostic meaning.[30]

Early diagnosis of cancer is crucial, a delay in the diagnosis of breast cancer is unfortunately common because of economic and social reasons in our society, with a poor impact on the management of such patients, it is therefore, important that a reliable cost – effective and easy to perform investigation like FNAC should be done in such circumstances.[2]

A definite diagnosis sometimes cannot be made by FNAC either due to inherent limitations of cytological examination or by inability to obtain adequate material for diagnosis. The rate of sampling error and inadequacy for

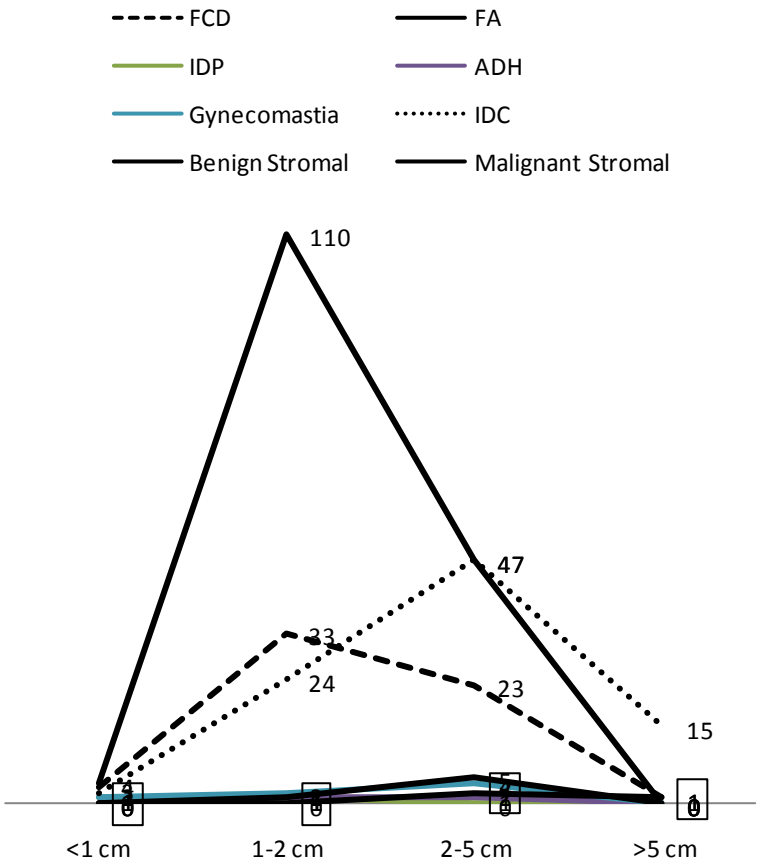
Table 3: *Frequency of C_2 and C_3 Aspirates in Various Benign and Suspicious Breast Lesions.*

Benign Breast Lesions	C2 (n)	%	C3 (n)	%
Fibrocystic Disease	38	16.37	22	9.48
Fibroadenoma (Intralobular Biphasic Stromal Tumor)	157	67.67	04	1.72
Intraductal Papilloma	01	0.43	01	0.43
Atypical Ductal Hyperplasia	0	0	2	0.86
Gynecomastia	07	3.01	0	0
Total n= 232 (100%)	203	87.5	29	12.5

n= number of cases

lesion < 1 cm can be attributed to deep location of the lesions. The lower diagnostic accuracy of FNAC for lesions smaller than 1 cm reported by other authors were identified in our study.[27] Where 63 out of 464 (13.6%) were categorized as inadequate, due mostly to deep location of the lesion or due to fault in the technique a finding consistent with a study conducted on 4,367 aspirates where 15.1% aspirates were found to be inadequate, especially in suspicious collagenous lesions and in specimens submitted by inexperienced sampling procedures.[21]Another study also reported 114 out of 507 (22.5%) aspirates as inadequate.[28]

A comparison of palpation size of the breast lesions in adequate and inadequate specimens of our study showed a significant (P<0.02) difference in the mean palpation size of the lesions 2.28cm vs. 1.90 cm (Table 1), indicating that cytological diagnoses must be correlated with clinical findings to reduce the rate of false negative cases. Our findings are in contrast to a study conducted in the University of Texas cancer Center where no significant difference was found on comparison between adequate and inadequate palpation size of the breast lesion (2.8 vs. 2.9).[22]



FCD = Fibrocystic disease, FA = Fibroadenoma, IDP = Intraductal papilloma, ADH = Atypical, ductal hyperplasia, IDC = Infiltrating ductal carcinoma

Fig. 2: *Distribution of proliferative and neoplastic breast lesions and their association with tumour size.*

The mean palpable size of breast lesions in our study was found to be 2.28 cm (range 0.5 – 15 cm) which was comparable to a study including 213 patients having 3.7 cm (range 1 – 13 cm) mean tumour size.[23] Majority of the masses aspirated in our study 242 (52%) were 1 – 2 cm. in size and categorized as C_2 followed by 170 out of 464 (37%) 2 – 5 cm., and 24 out 464 (5%) > 5 cm. in size (Table 2). The aspirates categorized as C_4 and C_5 were 49 (10.5%) and were 2 – 5 cm in size, our findings are in contrast to a retrospective study on 193 breast cancer patients in Agha Khan University, Karachi, majority (75%) of the patients presented with lumps > 6 cm in size, due probably to late presentation.[7] In this study aspirates of C_2 category 281 (60.6%) they were comparable with a study where 26 of 50 (52%) specimens were categorised as C2.[2]

A definite diagnosis of malignancy in this study was made in 48 of 464 (10.3%) aspirates, whereas 43 (9.3%) were found to be suspicious of malignancy, these findings were in contrast to a study conducted on 382 aspirates, with 98 (25.6%) diagnosed to be malignant and only 4 (1%) were found to be suspicious for malignancy.[20] The present study, showed similar results to another study categorising 20 out of 231 (9%) aspirates as suspicious.[29] False positive diagnosis may result from atypical epithelial proliferation, fibroadenoma and inflammatory lesions, as indicated in the present study (Table 3).

It was also observed in our study that with increasing size of the tumour, the surety of picking up the malignant lesion in higher cytological grades also increased. In feasibility study of FNAC in the diagnosis of breast lesions with special aim to evaluate extra cost and delay in surgical treatment due to unsuccessful preoperative biopsies, it was found that FNA was able to correctly diagnose malignant lesions in 194 out of 289 (67%) aspirates as compared to our study where 48 (10.3%) malignant and 43 (9.3%) suspicious were identified (Figure 2), thus avoiding delays in cancer surgery due to multiple biopsies.[26]

It is **concluded** that in this era of economic constraints, low allocation of health budgets in deve

loping countries, lack of screening programmes and increasing cost of diagnostic procedures, patients are invariably at a disadvantage and present late for medical assistance. It is, therefore recommended that FNAC should be used as a routine diagnostic procedure due to its cost effectiveness, thus maximising the availability of health care to patients with breast lesions. Palpable breast lesions can definitely be diagnosed by a combination of physical examination and FNAC which when performed by a dedicated cytopathologist should be an integral part of a breast screening service. The C_1 – C_5 categorising system for aspiration cytology is practical and gives greater degree of freedom of expression / opinion to cytopathologist and easily interpreted by the clinician.

REFERENCES

1. Fatima S, Faridi N, Gill S. Breast Cancer: Steroid Receptors Prognostic and other Prognostic Indicators. JCPSP 2005; 15 (4): 230 – 233.
2. Hussain MT. Comparison of Fine Needle Aspiration Cytology with Excision Biopsy of Breast Lump. JCPSP 2005; 15 (4): 211 – 214.
3. Riaz S, Jalil S, Shakoor A, Suleman BA. Frequency and distribution of different types of breast carcinoma. Esculapio 2008; 4 (3): 29-31.
4. Malik I, Khan W, Khan Z. Pattern of malignant tumors observed in a university hospital : a retrospective analysis. J Pak Med Assoc 1998; 48 (5): 120 – 2.
5. Khan S, Gillani J, Nasreen S, Zai S. cancer in north west Pakistan and Afghan refugees. J Pak Med Assoc 1997; 47 (4): 122 – 4.
6. Farid G, rasool MI. Locoregional Recurrence After Management of Carcinoma Breast. JCPSP 2005; 15 (4): 218 – 20.
7. Hussain MM, Ansari AK. Late Presentation of Carcinoma Breast in Pakistani Women. Pak Armed Forces Med J 1996; 46 (2): 11 – 5.
8. Zafar N, Jamal S, Mamoon N, Luqman M, Anwar M. Typing and Grading of Cytological Category C5 Breast Lesions. JCPSP 2005; 15 (4): 221 – 224.
9. Putti TC, Pinder E, Elston CW, Lee AHS, Ellis IO. Breast pathology practice: most common problems in a consultation service. Histopathology 2005; 47: 445 – 457.
10. Clarke D, Sudhakaran N, Gateley CA. Replace fine needle aspiration cytology with automated core biopsy in the triple assessment of breast cancer. Ann R Coll Surg Engl 2001; 83 (2): 110 – 2.
11. Zafar N, Jamal S, Mamoon N, Luqman M. Cytohistological Correlation of C_3 and C_4 Breast Lesions. JCPSP 2005; 15 (4): 196 – 199.
12. Ahmed I, Nazir R, Chaudharey MY, Kundi S. Triple assessment of breast lump. J Coll Physicians Surg Pak 2007; 17 (9): 535 – 8.
13. Nggada HA, Tahir MB, Musa AB, Gali BM, Mayun AA, Pindiga UH et al. Correlation between histopathalogic and fine needle aspiration cytology diagnosis of palpable breast lesions : a five years review. Afr J Med Sci 2007; 36 (4): 295-8.
14. Oyama T, Koibuchi Y, McKee G. Core needle biopsy (CNB) as a method for breast lesions; comparison with fine needle aspiration cytology (FNA). Breast Cancer 2004; 11 (4): 339-42.
15. O'Neil S, Castelli M, Gattuso P, Kluskens L, Madsen K, Aranha G. Fine-needle aspiration of 697 palpable breast lesions with histopathological correlation. Surgery 1997; 122 (4): 824-8.
16. McManus DT and Anderson NH. Fine – needle aspiration cytology of the breast. Current Diagn Pathol 2001; 7: 262-271.
17. Mehmood A, Ahmed M, Jamal S. Role of cytological grading in the management of breast lump. J Coll Physicians Surg Pak 2003; 13 (3): 150 – 2.
18. Zagorianakou P, Fiaccavento S, Zagorianakou N, Makredima G, Stefanou D, Agnantis NJ. FNAC : its role, limitations and perspective in the preoperative diagnosis of breast cancer. Eur J Gynaecol Oncol 2005; 26 (2): 143-9.
19. Ishikawa T, Hamaguchi Y, Tanabe M, Momiyama N, Chishima T, Nakati Y et al. False – positive and false-negative cases of fine-needle aspiration cytology for palpable breast lesions. Breast Cancer 2007; 14 (4): 388-92.
20. Berner A, Davidson B, Sigstad E, Risberg B. Fine-needle aspiration cytology vs core biopsy in the diagnosis of breast lesions. Diagn Cytopathol 2003; 29 (6): 344-8.
21. Eckert R, Howell LP. Number, size, and composition of clusters as related to breast FNA adequacy. Diagn Cytopathol 1999; 21 (2): 105-11.
22. Boerner S, Sneige N. Specimen adequacy and false-negative diagnosis rate in fine – needle aspirates of palpable breast masse. Cancer 1998; 84 (6): 344-8.
23. Carrillo JF, Mendivil MF, Domínguez JR, de Obaldía GE, Esparcyza R. Accuracy of combined clinical findings and fine needle aspiration cytology for the diagnosis in palpable breast tumors. Rev Invest Clin 1999; 51 (6): 333 – 9.
24. Vimpeli SM, Saarenmaa I, Huhtala H, Soimakallio S. Large – core needle biopsy versusfine – needle aspiration biopsy in solid breast lesions: comparison of costs and diagnostic value. Acta Radiol 2008; 49 (8): 863-9.
25. O'Leary R, Hawkins K, Beazley JCS, Lansdown MRJ, Hanby AM. Agreement between preoperative core needle biopsy and postoperative invasive breast cancer histopathology is not dependent on the amount of clinical material obtained. J Clin Pathol 2004; 57: 193- 195.
26. Hukkinen K, Kivisaari L, Heikkilä PS,Von Smitten K, Leidenius M. Unsuccessful preoperative biopsies, fine needle aspiration cytology or core needle biopsy, lead to increased costs in the diagnostic workup in breast cancer. Acta Oncol 2008; 47 (6): 1037 – 45.
27. Barra AdeA, Gobbi H, Rezende de la CA, Gouvêa AP, Murta de Lusana CE, Reis JHP et al. A comparison of aspiration cytology and core needle biopsy according to tumor size of suspicious breast lesions. Diagn Cytopathol 2008; 36 (1): 26-31.
28. Joshi A, Kapila K, Verma K. Fine needle aspiration cytology in the management of male breast masses.

Nineteen years of experience. Acta Cytol 1999; 43 (3): 334 – 8.
29. Ariga R, Bloom K, Reddy VB, Kluskens L, Francescatti D, Dowlat K, et al. Am J Surg 2002; 184 (5): 410 – 3.
30. Tariq GR, Haleem A, Zaidi AH, Afzal M, Abbasi S. Role of FNA Cytology in the Management of Carcinoma Breast. JCPSP 2005; 15 (4): 207 – 210.