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ORIGINAL ARTICLE

DIAGNOSTIC ACCURACY OF FNAC VERSUS OPEN BIOPSY IN DIAGNOSING CARCINOMA BREAST IN PALPABLE BREAST LESIONS IN ADULT FEMALE POPULATION OF KHYBER PAKHTUNKHWA, PAKISTAN

Mir Attaullah Khan[1], Hamidullah Shah[2], Khalid Javed[3]

Departments of Pathology, [1]Gajju Khan Medical College, Swabi, [2]Lady Reading Hospital, Peshawar, [3]Khyber Girls Medical College, Peshawar, Pakistan

ABSTRACT

Background: Fine needle aspiration cytology (FNAC) is usually considered as a reliable, easily performed and inexpensive test for diagnosing palpable lesions of breasts with a high degree of accuracy. The objective of this study was to compare the diagnostic accuracy of FNAC versus open biopsy in diagnosing carcinoma breast in palpable breast lesions in adult female population of Khyber Pakhtunkhwa, Pakistan.

Material and Methods: This cross-sectional study was conducted at Department of Pathology, Lady Reading Hospital, Peshawar, Pakistan from 1st January 2019 to 31st December 2019. Sixty (60) FNAC reports of palpable adult female breast lesions in definitive categories {(C2 (benign) and C5 (malignant)} with respective open biopsy reports were included in the study. Nine (9) FNAC reports of inconclusive categories (C1, C3 & C4) were excluded. Age in years was a single demographic variable. The data for "presence of carcinoma breast" for both the open biopsy and FNAC were placed in two-by-two table. Sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of FNAC were determined as percentages with confidence intervals at 95% confidence level.

Results: The mean age of the sample was 37 ± 17 (17-70, range 53) years. Out of 60 cases on open biopsy, 14 (23.33%) were confirmed as having and 46 (76.67%) as not having carcinoma breast and on FNAC, 12 (20%) were positive and 48 (80%) were negative for carcinoma breast. Two-by-two table showed 12 true positive (TP), 46 true negative (TN), two false negative (FN) and zero false positive (FP) cases. The sensitivity of FNAC was 85.71%, specificity 100%, PPV 100%, NPV 95.83% and accuracy was 96.67%.

Conclusion: FNAC is a reliable method in diagnosing carcinoma breast in palpable breast lesions in adult female population of Khyber Pakhtunkhwa, Pakistan.

KEY WORDS: Female; Breast; Carcinoma; Fine Needle Aspiration Cytology; Biopsy; Sensitivity; Specificity; Prevalence.

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INTRODUCTION

Diagnostic accuracy of a test is its ability to discriminate between the target condition and health. This discriminative ability can be measured quantitatively in the form of diagnostic accuracy such as sensitivity and specificity, predictive values, likelihood ratios, the area under the receiver operating characteristic (ROC) curve, Youden's index and diagnostic odds ratio.[1] In this context FNAC in spite of its limitations, has shown good results and thus has emerged as a simple, reliable and acceptable diagnostic test in palpable breast lumps.[2]

The technique of fine needle aspiration cytology (FNAC) started to be used from the mid of nineteenth century by clinicians. Lebert and Kun were the pioneers to use FNAC for diagnosing cancers. They used needles for obtaining tissue fragments

Corresponding Author:

Professor Dr. Mir Attaullah Khan
Department of Pathology
Gajju Khan Medical College, Swabi, Pakistan
E-mail: mirattaullah9@gmail.com

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and cells for the diagnosis of various malignancies.

Initially few of the pathologists were using this technique but in the current era it has become an important test in the field of diagnostic pathology. FNAC has taken almost one hundred years to be applied widely after its initial use.[3] Triple approach comprising clinical, radiological and pathological evaluation has been proved as an accurate approach for diagnosing palpable breast lumps.[4]

FNAC plays an important role in the diagnosis of breast lesions. Globally as well as regionally it has shown excellent results in terms of sensitivity, specificity, positive and negative predictive values and accuracy while assessing breast lesions preoperatively. Moreover it is simple, rapid, easy to perform and an inexpensive outpatient procedure.[5-8] Major goal of FNAC in breast is to differentiate between benign and malignant lesions.[4]

Every year, breast cancer is diagnosed in about one million females throughout the world.[9] Pakistan has 2.5 times higher incidence rate (one out of nine females) of breast carcinoma in females as compared to other Asian countries.[10,11] Due to this reason every palpable lesion of the breast is worrisome for both the patient as well as the treating clinician. To remove this anxiety and to treat the lesion accurately, an early diagnosis by FNAC is very crucial. If FNAC is augmented by other two methods of the triple approach i.e. radiological and clinical assessment, the diagnosis becomes accurate and reliable and the lesion can be managed properly.[12] If the three methods in triple approach agree about the nature of the lesion either to be benign or malignant, then the lesion can be treated accordingly.[13] If the diagnosis by these modalities differs from one another, then a needle biopsy or lumpectomy of the lesion is performed and examined histologically (gold standard) for confirmation of the diagnosis.[4] The issue of inadequacy in FNAC of breast can be minimized very much if procedure and reporting of FNAC are done by the same reporting pathologist.[14,15]

The objective of this study was to compare the diagnostic accuracy of fine needle aspiration cytology (FNAC) versus open biopsy in diagnosing breast carcinoma in palpable breast lesions in adult female population of Khyber Pakhtunkhwa, Pakistan.

MATERIALS AND METHODS

It was a record based cross-sectional study conducted at the Department of Pathology, Lady Reading Hospital, Peshawar, Pakistan from 1st January 2019 to 31st December 2019. This hospital is the oldest and largest tertiary care hospital of the province of Khyber Pakhtunkhwa in north-west of Pakistan.

The sample size[16] was calculated to be 60, using an online sample size calculator,[17] with expected sensitivity 90%, expected specificity 90%, prevalence of carcinoma breast 0.05% (50/ 100,000), precision (± expected) 0.34, confidence level 95% and expected dropout rate 0%.

Sixty nine (69) FNAC reports of palpable breast lesions and their subsequent open biopsy reports were available for the year 2019 in the laboratory archive. Sixty (60) FNAC reports of palpable adult female breast lesions in definitive categories {(C2 (benign) and C5 (malignant)} with respective open biopsy reports were included in the study. Nine (9) FNAC reports of inconclusive categories {C1 (inadequate or non-diagnostic aspirates), C3 (cellular atypia that is probably benign), C4 (suspicious for malignancies)} were excluded.

Age in years was a single demographic variable. We had one group and one research variable "presence of carcinoma breast" with two attributes of present and absent, and two tests/ methods for comparison. All the subjects had undergone two tests; FNAC, a screening test and open biopsy, a gold standard test for this one variable. The data for "presence of carcinoma breast" for both the open biopsy and FNAC were put up into a two-by-two contingency table. Sensitivity, specificity, precision/ positive predictive value, negative predictive value and diagnostic accuracy of FNAC were determined as percentages with estimated population parameters as "exact" Clopper-Pearson confidence intervals (CI) at 95% confidence level (CL) from this table (Table 1) by applying the following definitions and statistical formulas[18,19] using online statistical calculators.[20,21]

1. Sensitivity/ True Positive Rate (TPR) is the ability of a test to correctly categorize an individual as 'diseased' = [True positive (TP)/ True positive (TP) + False negative (FN)] × 100
2. Specificity/ True Negative Rate (TNR) is the ability of a test to correctly categorize an individual as 'disease-free' = [True negative (TN) / True negative (TN) + False positive (FP)] × 100
3. Precision/ Positive predictive value (PPV) is the percentage of individuals with a positive test who actually have the disease = [True positive / True positive + False positive] × 100
4. Negative predictive value is the percentage of individuals with a negative test who do not have the disease = [True negative / True negative + False negative] × 100
5. Accuracy of a test is its ability to differentiate the patient and healthy cases correctly = [True positive + True negative / True Positive + True Negative + False Positive + False Negative (Total Population)] × 100

RESULTS

A sample of 60 cases was selected. The mean age of the sample was 37 ± 17 (17-70, range 53) years. Out of 60 cases on open biopsy, 14 (23.33%)

Table 1: Two-by-two table for FNAC versus open biopsy for carcinoma breast in palpable breast lesions in adult female population of Khyber Pakhtunkhwa, Pakistan (n=60)

Total sample		Carcinoma breast confirmed on open biopsy (gold standard)		Total tests
		Present	Absent	
Carcinoma breast on FNAC (screening test)	Positive	True positive (TP) =12	False positive (FP) =0	Total positive tests =12
	Negative	False negative (FN) =02	True negative (TN) =46	Total negative tests =48
Total cases		Total diseased = 14	Total non-diseased =46	Total sample =60

Table 2: Parameters of FNAC versus open biopsy for carcinoma breast in palpable breast lesions in adult female population of Khyber Pakhtunkhwa, Pakistan (n=60)

S. No.	Characteristics of FNAC	Sample Statistics (Values)	95% CI for Population	
			Lower	Upper
1	Sensitivity %	85.71%	57.19	98.22
2	Specificity %	100%	92.29	100.00
3	Precision/ Positive predictive value (PPV) %	100%	73.53	100.00
4	Negative predictive value %	95.83%	86.44	98.81
5	Accuracy %	96.67%	88.47	99.59

were confirmed as having carcinoma breast and 46 (76.67%) were confirmed as not having carcinoma breast. Out of 60 cases on FNAC, 12 (20%) were positive for carcinoma breast and 48 (80%) were negative for carcinoma breast.

The data from both the methods were put into a two-by-two contingency table (confusion matrix). It showed 12 true positive (TP), 46 true negative (TN), two false negative (FN) and zero false positive (FP) cases. (Table 1)

The diagnostic accuracy of FNAC test versus open biopsy was measured by five parameters as sensitivity, specificity, precision/ positive predictive value, negative predictive value and accuracy by using online statistical calculators.[20,21] The values are given in percentage for sample and as 95% CI for the population. (Table 2)

DISCUSSION

Our study showed promising results in terms of sensitivity, specificity, PPV, NPV and accuracy which are 85.71%, 100%, 100%, 95.83% and 96.67% respectively. Diagnostic accuracy of FNAC in palpable breast lesions can be more than 99% if it is used in combination to other two parameters (radiological and clinical examination) of the triple approach for evaluation of palpable breast lumps.[22-24] Similarly when diagnosed early, to be possible by FNAC, a patient of breast cancer has more than 90% chance of survival. Regrettably it is not the case in our set up as here patients come for testing their breast lumps in an advanced stage when they have become incurable. This late presentation is attributed to poor socioeconomic conditions and high illiteracy level in our country. These factors attribute to the highest mortality rate from breast carcinoma in Pakistan as compared to any other Asian country. Here in this country, approximately 90,000 cases of breast cancer are diagnosed annually with a death toll of 40,000 patients among them.[25]

A study conducted by Bukhari, et al.[26] in Lahore, Pakistan has shown sensitivity, specificity, accuracy, negative predictive value, and positive predictive value of FNAC in breast lumps to be 98%, 100%, 98%, 100%, and 97%, respectively. Another study conducted in Telangana state of India by Sundar, et al.[27] reveled sensitivity and specificity of FNAC in comparison with histopathology of breast lesions to be 87.5% and 97.10% respectively while positive predictive value (PPV) and negative predictive value (NPV) were calculated to be 97.51% and 97.3% respectively. These results correlate well with the results of our study.

Similarly various other local and global studies have shown sensitivity of FNAC from 83% to 97% and specificity of 99 % to 100% in evaluation of breast lesions.[23-25] The results of these studies are similar to those of our study as sensitivity 85.71% and specificity 100% of FNAC in our study is correlated to the sensitivity 83-97% and specificity 99-100% of FNAC in these studies.

Similarly the diagnostic accuracy 96.7%, PPV 100% and NPV 95.8% of our study also correlated closely with those obtained from these studies i.e. 97-98%, 99-100% and 95-99% respectively.

In our study there was no false positive case while

there were two false negative cases. These two cases were reported falsely negative by an error due to inevitable factors. These errors are not due to malpractice. Several of them arise inherently and made even by experienced practitioners.[28] Pathologists are more susceptible to subjective distractions and errors as compared to other medical practitioners.[29]

Although false positive diagnosis by FNAC in breast lesions is rare, still such results are reported even from centers of excellence like Royal Marsden Hospital in UK, where four out of 1,104 cases were given the diagnosis of breast carcinoma which were proved benign by subsequent excisional biopsy and histopathologic examination. The four benign lesions which were falsely diagnosed as malignant in this center were actually granulomatous mastitis, radiation induced changes and fibroadenoma.

Similarly the French Cancer Institute of Curie has reported 23 false positive cases by FNAC in breast lesions in its published series of 44 years.[30] As far as our study is concerned, there was no false positive case reported. It may be attributed to the small sample size of our study or due to the reason that both FNAC and histopathology of the lesions were performed by the same pathologist.

There were only two (3.33%) false negative cases in our study. Several other studies conducted by Saleh, et al.[28], Yu, et al.[31] have also shown similar results with a false negative result rate of less than 5%. Age of both these false negative cases in our study was in 6th decade. Both had single palpable lumps (one measuring 3.5 cm and the other 4 cm in maximum diameter) in their right breasts. FNAC reports of both these cases showed hypo cellular aspirates with scattered neutrophils and histiocytes. Same cytologic findings were reported in studies by Saleh, et al.[28] and Yu, et al.[31] The diagnosis on the basis of these findings should not have been given. Rather repeat FNAC should have been performed. Second opinion was also not sought due to the availability of a single histopathologist/ cytopathologist in the department.

At this point it is worth quoting the lines written by Stephen S. Sternberg in the preface to the first edition of a book named Sternberg's Diagnostic Surgical Pathology. "We speak of the loneliness of the long distance runner, but there may be no one lonelier than a surgical pathologist working solo" and "Knowing when and what one does not know is of singular importance".[32] This highlights the importance of second opinion in the cases of surgical pathology bearing diagnostic doubt.

CONCLUSION

FNAC is a reliable method in diagnosing carcinoma breast in palpable breast lesions in adult female population of Khyber Pakhtunkhwa, Pakistan.

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REFERENCES

1. Šimundić AM. Measures of Diagnostic Accuracy: Basic Definitions. EJIFCC 2009 Jan 20; 19(4):203-11.
2. Biren P, Alam KP, Jagdish H. Comparison of the diagnostic accuracy of FNAC and biopsy in the diagnosis of a palpable breast lump. Global J Research Analysis 2016; 5(12):73-4.
3. Hamdani RA, Shaheen N, Rathore MU, Anjum S, Amin MS, Qadir A, et al. Fine needle aspiration cytology in breast lesions- its concordance with histopathological examination of excised lesion. J Rawalpindi Med Coll 2015; 19(1): 41-3.
4. Chandanwale S, Rajpal M, Jadhav P, Sood S, Gupta K. Pattern of benign breast lesions on FNAC in consecutive 100 cases: A study at tertiary care hospital in India. Int J Pharm Biol Sci 2013; 3(4):129-38.
5. Sachin B, Ingle1, Chitra RH. Fine needle aspiration cytology [FNAC]. Int J Cur Res Rev 2018; 10 (15):20-4. https://doi.org/10.31782/IJCRR.2018.10155
6. Soderstrom N. Punctures of goitre for aspiration biopsy. A preliminary report. Acta Med Scand 1952; 144 (13): 23-44.
7. Einhorn J, Franzen S. Thin needle biopsy in diagnosis of thyroid disease. Acta Radiol 1962; 58 (14):321-36. https://doi.org/10.3109/00016926209169574
8. Lowhagen T, Willens JS, Lundell G. Aspiration biopsy cytology in diagnosis of thyroid cancer. World J Surgery 1981; 5 (15):61-73. https://doi.org/10.1007/BF01657837
9. Menhas R, Umer S. Breast Cancer among Pakistani Women [letter to editor]. Iran J Public Health 2015; 44 (4):586-7.
10. Asif HM, Sultana S, Akhtar N, Rehman JU, Rehman RU. Prevalence, risk factors and disease knowledge of breast cancer in Pakistan. Asian Pac J Cancer Prev 2014; 15(11): 4411-16. https://doi.org/10.7314/APJCP.2014.15.11.4411
11. Bray F, McCarron P, Parkin DM. The changing global patterns of female breast cancer incidence and mortality. Breast Cancer Res 2004; 6:229-39. https://doi.org/10.1186/bcr932
12. Kocjan G, Bourgain C, Fassina A, Hagmar B. The role of breast FNAC in diagnosis and clinical management: a survey of current practice. Cytopathology 2008; 19:271-8. https://doi.org/10.1111/j.1365-2303.2008.00610.x
13. Kocjan G. Needle aspiration cytology of the breast: current perspective on the role in diagnosis and management. Acta Med Croatica 2008; 62:391-401.
14. Yamaguchi R, Tsuchiya SI, Koshikawa T. Diagnos-

tic accuracy of fine-needle aspiration cytology of the breast: Japanese Society of Clinical Cytology. Oncol Rep 2012; 28 (9):1606-12. https://doi.org/10.3892/or.2012.2014

15. Guidelines for non-operative diagnostic procedures and reporting in breast cancer screening. National Coordinating Group for Breast Screening Pathology. NHSBSP Publication 2001; 50:15-20.
16. Buderer NM. Statistical methodology: I. Incorporating the prevalence of disease into the sample size calculation for sensitivity and specificity. Acad Emerg Med 1996 Sep; 3(9):895-900. https://doi.org/10.1111/j.1553-2712.1996.tb03538.x
17. Arifin WN. Sample size calculator (web) [Internet]. 2017-2020 [cited 2019 Aug 02]. Available at: https://wnarifin.github.io/ssc/sssnsp.html
18. Wikipedia. Sensitivity and specificity [internet]. San Francisco, USA: Wikimeida Foundation Inc. [accessed 2020 Jan 25]. Available at: https://en.wikipedia.org/wiki/Sensitivity_and_specificity
19. Parikh R, Mathai A, Parikh S, Chandra Sekhar G, Thomas R. Understanding and using sensitivity, specificity and predictive values. Indian J Ophthalmol 2008 Jan-Feb; 56(1): 45-50. https://doi.org/10.4103/0301-4738.37595
20. MEDCALC®. Diagnostic test evaluation calculator [internet]. Ostend Belgium: MedCalc Software Ltd; 2020 [accessed 2020 Jan 25]. Available at: https://www.medcalc.org/calc/diagnostic_test.php
21. Statistics Kingdom. Proportion confidence interval calculator [internet]. Melbourne, Australia: Statistics Kingdom; 2007 [accessed 2020 Jan 25]. Available at: http://www.statskingdom.com/41_proportion_confidence_interval.html
22. Tiwari M. Role of fine needle aspiration cytology in diagnosis of breast lumps. Kathmandu Univ Med J 2007; 5(2):215-17.
23. Aziz M, Ahmad N, Zahid J, Faizullah. Comparison of FNAC and open biopsy in palpable breast lumps. J Coll Physicians Surg Pak 2004; 14(11): 654-6.
24. Hussain MT. Comparison of fine needle aspiration cytology with excision biopsy of breast lump. J Coll Physicians Surg Pak 2005; 15(4):211-14.
25. Qingqing HE, Fan X, Yuan T. Eleven years of experience reveals that FNAC is still a useful method for preoperative diagnosis of carcinoma. Breast 2007; 16 (3): 303-6. https://doi.org/10.1016/j.breast.2006.12.006
26. Bukhari MH, Arshad M, Jamal S, Niazi S, Bashir S, Bakhshi IM, et al. Use of the fine-needle aspiration in the evaluation of breast lumps. Pathol Res Int 2011; 2011:689521. https://doi.org/10.4061/2011/689521
27. Sunder KS, Aruna T. Sensitivity and specificity of fine-needle aspiration cytology (FNAC) in diagnosis of breast lesions. Sch J App Med Sci 2017; 5(2C):465-9.
28. Sharif MA, Hamdani SNR. Second opinion and discrepancy in the diagnosis of soft tissue lesions at surgical pathology. Indian J of Pathol Microbiol 2010; 53: 466-70. https://doi.org/10.4103/0377-4929.68277
29. Rosai J. Introduction. In: Rosai J, editor. Rosai and Ackerman's Surgical Pathology. London, UK: Mosby; 2004.p.1-24.
30. Powles TJ, Trott PA, Cherryman G. Fine needle aspiration cytodiagnosis as a pre-requisite for primary medical treatment of breast cancer. Cytopathology 1991; 2 (1):7-12. https://doi.org/10.1111/j.1365-2303.1991.tb00378.x
31. Saleh FM, Ansari NP, Alam O. Comparison between fine needle aspiration with histopathology to validate diagnosis of breast lump. Mymensingh Med J 2012; 21: 450-5.
32. Mills SE, Carter D, Greenson JK, Reuter VE, Stoler MH. Sternberg's Diagnostic Surgical Pathology. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2010.

CONFLICT OF INTEREST
Authors declare no conflict of interest.
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AUTHORS' CONTRIBUTION

The following authors have made substantial contributions to the manuscript as under:

Conception or Design:	MAK, HS, KJ
Acquisition, Analysis or Interpretation of Data:	MAK, HS, KJ
Manuscript Writing & Approval:	MAK, HS, KJ

All the authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.