Cytomorphological patterns of palpable breast lesions diagnosed on fine needle aspiration cytology in females

Aamir Sharif¹, Tahira Tabassum¹, Muhammad Riaz², Muhammad Akram³ and Naveed Munir⁴

Abstract
Breast cancer is the most common malignant tumor and is a leading cause of death worldwide. This study was planned to find out the frequencies of various types of lesions from palpable breasts of female patients through fine needle aspiration cytology. This retrospective study was carried out during December 2017 to May 2018 on 100 female patients presenting with palpable breast mass at University Medical Complex & Research Center, Sargodha, Pakistan. Following written informed consent from patients, a detailed history, patient age, and clinical examination were recorded. The fine needle aspiration cytology was performed and aspirates were processed following the standard methods for cytopathological examination. The cases were grouped according to the five tier reporting format for breast lesion (C1–C5) laid down by the International Academy of Cytologists (IAC) in 2016. The spectrum of breast lesions on cytomorphological interpretation was 54% benign (C2), 2% atypia/suspicious probably benign (C3), 3% suspicious probably malignant (C4) and 41% malignant (C5). Inadequate/insufficient material (C1) was not included in the study. In this study, the specificity, sensitivity, negative and positive predictive value, and diagnostic accuracy of fine needle aspiration cytology were 100%, 91.11%, 98.18%, 100%, and 98.96%, respectively. In benign lesions, maximum cases were of fibroadenoma (24%) followed by fibrocystic disease (4%), lipoma (3%) while benign phyllodes tumor and galactoceles were only 1% each. Breast mass was the chief presenting complaint. Breast cancer was commonest among all the morphological patterns of breast lesions followed by fibroadenoma. This study supports that cytological examination using fine needle aspiration cytology is an economical, rapid, easy and valuable diagnostic tool.

Keywords
breast cancer, cytological examination, fine needle aspiration cytology

Introduction
Breast cancer is one of the most common cancers worldwide in females and is an important cause of mortality and morbidity.¹,² In developed countries like Australia, Western Europe, and North America, the breast cancer mortality rate is decreased due to the development of modern techniques for early diagnosis and improved therapy³ whereas developing countries are now experiencing an increase in the registration of new cases of breast cancer. In Asia, Pakistan ranked fifth where majority of the
females are suffering from breast cancer and the number of patients is increasing each year.\textsuperscript{4} Pakistan also has the highest standardized death rates (25.2/100,000) due to breast cancer.\textsuperscript{5} Patients are being reported in advanced stage of disease due to low socio-economic status, existing social circumstances, and lack of screening facilities. Absence or lack of female doctors in rural areas is also a contributing factor as women are hesitant to be examined by the male physician for breast pathology.\textsuperscript{5} Globally, triple assessment is done for the investigation of breast mass which includes clinical examination, imaging studies, that is, ultrasound and mammography and above all fine needle aspiration cytology (FNAC). Muddegowda et al.\textsuperscript{7} in their study assessed the diagnostic accuracy of FNAC on patients presented with palpable breast and showed a very high accuracy (97%), specificity (98%) and sensitivity (94.5%). FNAC is cost-effective, reliable and can prevent unwanted surgery as well.\textsuperscript{7} Aker et al.\textsuperscript{8} conducted a study on the diagnostic accuracy of FNAC and found 95.97% accuracy in preoperative diagnosis of breast cancer in combination with clinicocytological examination. The use of frozen section histology had been reduced up to 80% as FNAC became much reliable for malignancy detection.\textsuperscript{9} Therefore, this study was planned to find out the frequency of various types of lesions in palpable breasts of female patients and to get insights into the morphological patterns of breast lesions through FNAC.

**Materials and methods**

This retrospective study was carried out on female patients visiting the University Medical Complex & Research Center (UMC & RC), Sargodha, Punjab, Pakistan, during December 2017 to May 2018 for examination of suspected palpable breast lesions through FNAC. The study was approved by the Health Research Ethics Committee of Sargodha Medical College (approval no. MSC101). Written informed consent was taken from all the study subjects prior to inclusion in the study. A total of 100 patients presenting with palpable breast mass were included in this study based on inclusion and exclusion criteria. Only female patients of age group 15–60 years with clinical diagnosis of breast lump were included. Female patients having history of previous trauma to the breast, and with recurrent malignancy, or on chemotherapy/radiotherapy were excluded from the study. A total of 100 patients visiting the UMC & RC for FNAC examination of their palpable breast lesions and meeting the inclusion criteria as defined for this study were included while other patients were excluded from the study. After informed consent and before performing FNAC, a detailed history, general physical, and clinical examination were carried out. FNAC was performed by injecting the needle into the palpable lesion on breast mass using 5 or 10 mL disposable syringe from Becton and Dickinson (BD) Malaysia for each patient collecting the lesion from the palpable mass. The procedure was repeated twice or thrice in some cases depending upon the size and gross appearance of the palpable mass or nodule. Cellular component was aspirated into a syringe and spread onto the glass slides for smear preparation. For each patient, 6–12 smears on slides were prepared. Each slide was positioned on the table and on its frosted end a small- or medium-sized drop of aspirated material was placed and spread it with the help of a glass spreader to prepare the smear of the aspirate. The prepared smears were air dried and stained with the Hematoxylin & Eosin (H&E) staining technique. The stained slides were observed under the microscope using high power objective lens. Cytologically, the lesions were categorized into five-tier reporting format for breast lesions laid down by The International Academy of Cytology (IAC) in 2016, that is, C1: inadequate/insufficient material, C2: benign, C3: atypical probably benign, C4: suspicious of malignancy, and C5: malignant.\textsuperscript{10}

**Statistical analysis**

The data were collected and analyzed for statistical significance using statistical package for social sciences (SPSS) 17.0. Data were presented as mean, range, and percentages. Qualitative data were presented as percentages frequency distribution. Percentages of specificity, sensitivity, negative predictive value (NPV), positive predictive value (PPV), diagnostic accuracy, and false negative and false positive rate of FNAC were also calculated.

**Results**

Among 100 female patients presenting with breast mass, the spectrum of breast lesions on cytomorphological interpretation was 54% benign (C2),
2% atypia/suspicious probably benign (C3), 3% suspicious probably malignant (C4), and 41% malignant (C5). Among the benign (C2) cases, 21% were inflammatory and 33% benign. Inadequate/insufficient materials (C1) were not included in the study. Among the total studied cases of breast lesions, FNAC diagnosis of 54% cases was reported as benign and 41% cases as malignant by FNAC followed by confirmation with histopathology representing true negative (TN) and true positive (TP) cases, respectively. In this study, specificity, sensitivity, NPV, PPV, and diagnostic accuracy of FNAC were also calculated and found 100% specificity, 91.11% sensitivity, 98.18% NPV, 100% PPV, and 98.96% diagnostic accuracy of FNAC. The false negative rate was 1.81% with 0% false positive rate.

In inflammatory lesions, majority of the cases were of acute pyogenic mastitis (12%) followed by tuberculous mastitis (9%). In benign lesions, the maximum cases were of fibroadenoma (24%) followed by fibrocystic disease (4%), lipoma (3%), while benign phyllodes tumor and galactocele were only 1% each. Among all these lesions, carcinoma was the most common lesions constituting 41% as given in Table 1. Cytological picture of representative H&E stained smears of FNAC aspirates is shown in Figure 1.

The age of patients recruited for the study ranged from 15 to 60 years with mean age of 33.11 years. The most affected patients belonged to 31–35 years age group (47%) followed by the age group 41–45 years (37%). All the malignant cases were under the age of 22–60 years with mean age of 41.48 years. The most common age group affected being 31–40 years (39.02% cases) followed by the age groups 41–50 and 51–60 years (24.39%) each. The patients affected with fibroadenoma fall under 16–39 years of age with mean age of 21.37 years and the most affected (53.57%) patients were under the age of 15–20 years. The most affected patient with acute pyogenic mastitis belonged to 26–30 years age (33.33%) while the majority of the patients affected with tuberculous mastitis were under 21–25 years age (33.3%). There were four cases of fibrocystic disease and three cases each of breast lipomas and suspicious for malignancy with mean age of 22, 32.66, and 47 years, respectively. The frequency distribution of various lesions in different age groups under study is given in Table 2. Correlation of cytological and histopathological study of breast lesions of the study population is given in Table 3.

Usually patients with breast pathology presenting with history of palpable breast mass, breast pain, nipple discharge or retraction. In this study, among all cases (100 patients) presenting with palpable breast, 17% of the cases has breast pain and 10% with nipple discharge. Other modes of presentation include axillary lymphadenopathy, nipple retraction, and peau d’orange seen in 8%, 7%, and 3% cases, respectively.

Breast self-examination (BSE) is recommended to detect or identify the palpable breast mass at an early stage of breast diseases. But unfortunately only a small proportion (7%) of patients found their palpable breast mass by BSE while in majority (64%) of patients, breast mass was an incidental finding identified during medical checkup of the patients by the physician. In 17% of the patients,

| FNAC categories | Diagnosis | Number of cases | Percentage | Overall percentage |
|----------------|-----------|----------------|------------|--------------------|
| C1             | Inadequate or insufficient | – | 0 | 0% | 0% |
| C2             | Inflammatory breast lesions | Acute pyogenic mastitis | 12 | 12% | 54% |
|                |           | Tuberculous mastitis | 09 | 09% |    |
|                | Benign breast lesions | Fibroadenoma | 24 | 24% |    |
|                |           | Fibrocystic disease | 04 | 04% |    |
|                |           | Lipoma | 03 | 03% |    |
|                |           | Galactocele | 01 | 01% |    |
|                |           | Benign phyllodes | 01 | 01% |    |
| C3             | Atypical probably benign | – | 02 | 02% | 02% |
| C4             | Suspicious for malignancy | – | 03 | 03% | 03% |
| C5             | Malignant breast lesion | Breast carcinoma | 41 | 41% | 41% |
| Total          |           |               | 100 |    | 100% |

FNAC: fine needle aspiration cytology.
Figure 1. Cytological picture of H&E stained smear of FNAC aspirates (400×): (a) tuberculous mastitis, (b) acute pyogenic mastitis, (c) fibroadenoma, (d) atypical probably benign, (e) suspicious for malignancy, and (f) carcinoma.

Table 2. Distribution of various lesions in different age groups.

| FNAC category | Diagnosis                        | Age group (years) | Total |
|---------------|----------------------------------|------------------|-------|
|               |                                  | 15–20 21–25 26–30 31–35 36–40 41–45 46–50 51–55 56–60 |       |
| C1            |                                  | – – – – – – – – – 00 | 00    |
| C2            | Inflammatory lesions             | – 02 04 03 03 – – – – 12 | 12    |
| C2            | Tuberculous mastitis             | – 04 03 01 01 – – – – 09 | 09    |
| C2            | Acute pyogenic mastitis          | 14 07 01 01 01 – – – – 24 | 24    |
| C2            | Fibroadenoma                     | – 01 01 01 01 – – – – 04 | 04    |
| C2            | Fibrocystic disease              | – 01 01 – – 01 – – – 03 | 03    |
| C2            | Lipoma                           | – – – – 01 – – – – 01 | 01    |
| C2            | Galactocele                       | – – – – – – – – – 01 | 01    |
| C3            | Atypical probably benign         | – – – – 01 01 – – – 02 | 02    |
| C4            | Suspicious for malignancy        | – – – – 01 – – 01 – 03 | 03    |
| C5            | Malignant breast lesion          | 01 04 09 07 07 03 05 05 41 | 41    |
| Total         |                                  | 14 16 14 17 14 09 05 05 06 100 | 100   |

FNAC: fine needle aspiration cytology.

Duration from discovery to presentation of palpable breast mass ranged from 6 days to 11 years. 38% of the patients presented during 1–3 months, whereas 12% presented within 1–3 months, and palpable breast mass was discovered by the patient’s husband as shown in Figure 2.
followed by 23% who presented in 4–6 months duration.

Among all the studied cases, left breast was involved in 54% of the patients, right breast in 40% while both breasts were involved in 6% of the cases.

**Discussion**

Lump in the breast may be either benign or malignant; however, fear of malignancy is the main reason to compel the patients report to the clinician. Thus, to relieve the stress of the patients, it is necessary to investigate these patients according to standard protocols. FNAC is extensively recognized as a reliable procedure for the initial examination of palpable breast masses. It is minimally invasive, cost-effective, safe, simple, rapid and sensitive as compared to biopsy. The main objective of FNAC is to distinguish malignant lesions from benign lesions in order to plan for the treatment protocol and follow-up.

In this study, the spectrum of breast lesions on cytomorphological interpretation was benign (33%), inflammatory (21%), suspicious probably benign (2%), suspicious probably malignant (3%), and malignant (41%). Bukhari et al. also reported 31% malignant cases in their study which are in agreement to our study findings. In Nigeria, similar findings were found by Egwuonwu et al. and Mayun et al. who reported 47.3% and 40% malignant lesions in their study patients, respectively. Ahmed et al. reported 30.5% cases of malignancy in their study conducted in Sudan. This study results are also consistent with the findings of Siddiqui et al. and Lakhana and Khalid who found breast cancer as the most commonly encountered lesion.

Previous studies reported fibroadenoma as the commonest finding in breast lesions followed by breast cancer and fibrocystic disease. Comparison of cytomorphological findings of this study to various literature reports is given in Table 4. These differences might be attributed to geographical, socioeconomic, cultural, and religious variations.

The age of studied population ranged from 15 to 60 years with mean age of 33.11 years. Similar findings were reported by Goyal et al. who conducted a study in India and found most of the breast cancer patients belong to 15–70 years age.

Age is the strongest risk factor for breast cancer. It is proportional to risk, that is, the older the age, the higher the risk, but chances are increased markedly

| Cytological diagnosis | Histopathological diagnosis | Total |
|-----------------------|----------------------------|-------|
|                       | Benign | Malignant | |
| Benign (54)           | 54     | 1         | 55  |
| Malignant (41)        | 0      | 41        | 40  |
| Total (95)            | 54     | 41        | 95  |

a: true negative; b: false negative; c: false positive; d: true positive.

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**Figure 2.** Percent palpable breast mass discovery.
in postmenopausal years, that is, age >50 years.32 In this study, majority of the cases were between the age of 30–45 years. This indicates that females at their early ages are presenting with breast cancer in our setup and the results are consistent with the findings of previous studies conducted elsewhere in Pakistan.

Regarding fibroadenoma, similar findings were reported in previous studies with a slight variation in the age ranges. Study population’s age ranged from 13 to 51 years age. The 71 (44.93%) and 54 (34.17%) cases were in the age group of <20 and 21–30 years age, respectively. According to Prajapati,33 the fibroadenoma patients belonged to 18–39 years with mean age of 23.2 years which is in agreement to our study.

Regarding inflammatory lesions of the breast, our study results are supported by the findings of previous studies.10,20 This reflected the burden of tuberculosis in this region due to malnutrition, poor hygiene, and overpopulation. Regarding fibrocystic disease of breast, our study is in accordance with Rahman and Islam34 who found 210 (11.81%) cases with highest incidence rate (37.14%) in the age group of 21–30 years and second highest in 30–40 years of age (30%). With respect to suspicious cases for malignant cells, the findings of this study are in line with the findings of Rahman and Islam34 who reported 1.12%. They suggested core biopsy for the confirmation of malignancy.

One (1%) case of galactocele revealed milk during aspiration and that patient was under the reproductive age (31–35 years) having history of breast feeding. Majority of the patients (64%) found lump accidentally. These results are low as compared to previous studies of Akhtari-Zavare et al.35 who reported 36.7% of their patients who performed BSE, respectively. In this study, the lesions presented in the left breast were 54% and 40% had right breast involvement while both breasts were involved in 6% of the cases.

This study has the limitations of small sample size and not including the insufficient material of breast lesions in detailed cytological examination. Future studies will be carried out on large sample population from wide geographical distribution.

**Conclusion**

Commonest presenting complaints were breast lump with a wide variety of diagnosis. Nearly all patients accidently found breast lump and were not familiar with BSE. Delay in seeking medical treatment was another noteworthy finding. This study supports that cytological examination using FNAC is economical, rapid, easy and valuable diagnostic tool. It can provide information about the type of lesion which helps in planning the treatment modalities.

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**Availability of data and material**

Data sharing is not applicable to this article as no data sets were generated or analyzed during this study.

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**Table 4. Cytological comparison of this study with the literature reports.**

| Studies                  | Inadequate or insufficient (%) | Benign/inflammatory (%) | Atypical/suspicious probably benign (%) | Suspicious for malignancy (%) | Malignant (%) | Total cases |
|--------------------------|--------------------------------|-------------------------|----------------------------------------|-----------------------------|---------------|-------------|
| Panjvani et al.21        | 0                              | 68.18                   | 0.45                                    | 0.90                        | 31.08         | 222         |
| Khan et al.22            | 0                              | 32.4                    | 4.1                                     | 8.1                         | 55.4          | 74          |
| Yusuf and Atanda23       | 0                              | 54.5                    | 10                                      | 13.5                        | 22            | 200         |
| Singh et al.24           | 5                              | 51                      | 02                                      | 3                           | 39            | 100         |
| Chauhan et al.25         | 4.9                            | 73.07                   | 1.5                                     | 2.35                        | 18.16         | 468         |
| Rehan et al.26           | 11.1                           | 64.5                    | 9.8                                     | 4.2                         | 10.5          | 287         |
| Montezuma et al.27       | 5.77                           | 73.38                   | 13.74                                   | 1.57                        | 5.54          | 3625        |
| Rioki and Rogena28       | 15.2                           | 78.1                    | 1.8                                     | 4.1                         | 0.8           | 768         |
| Gorasiya and Jhaveri29   | 0                              | 9.38                    | 60                                      | 0                           | 30.62         | 160         |
| Khattak et al.20         | 0                              | 72.72                   | 3.4                                     | 4.54                        | 19.31         | 88          |
| Present study            | 0                              | 54                      | 02                                      | 3                           | 41            | 100         |

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Consent for publication
There is no identifying information.

Declaration of conflicting interests
The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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ORCID iDs
Aamir Sharif https://orcid.org/0000-0002-1115-8589
Muhammad Riaz https://orcid.org/0000-0002-5524-7735
Naveed Munir https://orcid.org/0000-0003-0380-1332

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