Benign Breast Disease in Makkah, Saudi Arabia: A Retrospective Analytical Cross-Sectional Study

Mohammad I. Almatrafi 1, Mutlaq A. Almalki 2, Jumana A. Althagafi 3, Tala S. AlSindi 3, Roaa M. Masarit 3, Renad M. Almatrafi 3

1. College of Medicine, Umm Al-Qura University, Makkah, SAU 2. Breast Surgery, Al-Noor Specialist Hospital, Makkah, SAU 3. College of Medicine and Surgery, Umm Al-Qura University, Makkah, SAU

Corresponding author: Mohammad I. Almatrafi, mohammad.matrafi123@gmail.com

Abstract

Introduction

The most frequent reason for visiting breast clinics is benign breast disease (BBD), which accounts for 90% of all breast-related presentations globally [1,2]. BBD is widespread among women of childbearing age, peaking between the ages of 30 and 50 [3]. It is a range of histological entities that includes non-proliferative lesions, atypical hyperplasia, and proliferative lesions without atypia [4]. Although BBD is frequently benign, some cases do develop into cancer [1]. The patient’s medical history, clinical examination, and imaging modalities are all used to make the diagnosis [5].

Early menarche, regular short menstrual cycles, oral contraceptives, hormonal replacement therapy, nulliparity, pregnancy at an older age, and having a high postmenopausal body mass index (BMI) are risk factors linked to a higher risk of breast cancer, whereas having a high premenopausal BMI and nursing for a long time is linked to a lower risk [6-9]. Patients with BBD frequently exhibit mastalgia, a palpable tumor, and nipple discharge, necessitating biopsy in addition to targeted diagnostic imaging such as mammography, ultrasound, and magnetic resonance imaging (MRI) [5]. Up to 30% of women diagnosed with BBD will eventually need therapy [1]. Although some forms of BBD are linked to the development of later breast cancer, non-proliferative lesions with atypical hyperplasia are 3.9-15-fold more likely than proliferative lesions without atypia (1.3-1.9-fold greater risk) [10]. Between 70% and 79% of breast lumps in Uganda, Trinidad, and Nigeria are BBD, the majority of which are fibroadenoma (FA) and fibrocystic change (FCC) [11].

Similarly, the most common BBD in Saudi Arabia is FA, followed by FCC [12-14]. Owing to the lack of studies on BBD compared with breast cancer in Saudi Arabia, this study aimed to assess the common patterns of BBD and factors associated with the frequency of fibroadenoma (FA) occurrence.

Methodology

A retrospective analytical study was carried out at Al-Noor Specialist Hospital, Makkah, Saudi Arabia, from May to August 2022. The sample was all patients who attended the breast and endocrine unit from January 2015 to December 2020.

Results

This study included 222 of 367 patients who had BBD. Of them, 42.3% were aged 31-45 years, with a mean age of 36.71 ± 12.48 years. The mean body mass index (BMI) was 26.45 ± 6.69 kg/m², and the mean tumor size was 4.22 ± 4.9 mm.

Conclusion

Fibroadenoma among BBD types is the most common lesion in the studied population. This study established the baseline pattern of BBD in a specialized hospital in Makkah.
to assess the factors associated with the frequency of FA occurrence.

**Materials And Methods**

**Study design, setting, and time**

This retrospective cross-sectional study was carried out at Al-Noor Specialist Hospital, Makkah, Saudi Arabia, from May to August 2022.

**Study population**

The inclusion criteria were patients between 18 and 80 years who presented to the breast and endocrine unit of Al-Noor Specialist Hospital because of a breast complaint (mass, pain, swelling, and discharge) or for a screening mammogram from 2015 to 2020. The exclusion criteria were patients with malignancy, incomplete data, and pregnant or lactating women.

**Sample size**

The sample comprised all patients who attended the breast and endocrine unit from January 2015 to December 2020 and met the inclusion criteria.

**Data collection**

A predesigned checklist was prepared to collect patients’ information: age, gender, comorbidities (hypertension, diabetes mellitus (DM), chronic obstructive pulmonary disease, chronic kidney disease, and ischemic heart diseases), medications, type of surgery (lumpectomy, incisional biopsy, and excisional biopsy), type of biopsy (true cut, fine needle aspiration, and open biopsy), type of lesion found (FA, intraductal papilloma, benign phylloid tumor, lobular carcinoma in situ, fat necrosis, tubular adenoma, juvenile FA, lipoma, FCC, fibroadenomatoid hyperplasia, sclerosing adenosis, and others), modality of choice (mammogram, ultrasound, and MRI), and type of abnormality detected (calcification, lymph node (LN) enlargement, inflammatory changes, and mass).

**Ethical considerations**

Ethical approval for the study was obtained from the Institutional Review Board (IRB) of Al-Noor Specialist Hospital, Makkah, Saudi Arabia.

**Data analysis**

Data were analyzed using Statistical Package for the Social Sciences (SPSS) version 26 (IBM SPSS Statistics, Armonk, NY, USA). The chi-squared test ($\chi^2$) was applied to qualitative data expressed as numbers and percentages to examine the relationship between the variables. The Mann-Whitney U test was used to analyze non-parametric variables and quantitative data presented as mean and standard deviation (mean ± SD). A p-value of less than 0.05 was regarded as statistically significant.

**Results**

This study included 222 patients who had BBD. Of them, 42.3% were aged 31-45 years, with a mean age of 36.71 ± 12.48 years. The mean BMI was 26.45 ± 6.69 kg/m$^2$, and the mean tumor size was 4.22 ± 4.9 mm. Of the participants, 92.3% were women, and 82.4% had Saudi nationality. Only 8.6% had chronic diseases, of whom 26.3% had iron deficiency anemia. Almost half of the participants (50.9%) were taking medications (Table 1). The most frequent diagnosis was FA (55.4%) (Table 2).
| Variable                        | Number (%) |
|--------------------------------|------------|
| **Age (years)**                |            |
| <30                            | 75 (33.8)  |
| 31-45                          | 94 (42.3)  |
| >45                            | 53 (23.9)  |
| **Mean age (years)**           | 36.71 ± 12.48 |
| **BMI**                        | 26.45 ± 6.69 |
| **Tumor size (mm)**            | 4.22 ± 4.9  |
| **Gender**                     |            |
| Female                         | 205 (92.3) |
| Male                           | 17 (7.7)   |
| **Nationality**                |            |
| Non-Saudi                      | 39 (17.6)  |
| Saudi                          | 183 (82.4) |
| **Chronic diseases**           |            |
| Yes                            | 19 (8.6)   |
| No                             | 203 (91.4) |
| **Chronic diseases in the studied population (number: 19)** | |
| Anxiety, depressive episodes   | 1 (5.2)    |
| CHD                            | 1 (5.2)    |
| Chronic adenotonsillitis       | 2 (10.5)   |
| Asthma                         | 1 (5.2)    |
| Infertility                    | 1 (5.2)    |
| DM                             | 3 (15.7)   |
| Hypothyroidism                 | 3 (15.7)   |
| Iron deficiency anemia         | 5 (26.3)   |
| Renal failure                  | 1 (5.2)    |
| Scoliosis                      | 1 (5.2)    |
| **Medication**                 |            |
| Yes                            | 113 (50.9) |
| No                             | 109 (49.1) |

**TABLE 1: Distribution of participants according to their demographics, BMI, tumor size, chronic diseases, and medications (total number: 222)**

BMI, body mass index; mm, millimeter; CHD, congenital heart defects; DM, diabetes mellitus
| Diagnosis            | Number (%) |
|----------------------|------------|
| Abscess              | 18 (8.1)   |
| Benign phylloides tumor | 9 (4.1)    |
| Fibroadenoma*        | 123 (55.4) |
| Fibrocystic changes  | 34 (15.3)  |
| Gynecomastia         | 12 (5.4)   |
| Hyperplasia          | 2 (0.9)    |
| Keratinous cyst      | 2 (0.9)    |
| Lipoma               | 7 (3.2)    |
| Mastitis             | 8 (3.6)    |
| Papilloma            | 1 (0.5)    |
| Schwannoma           | 2 (0.9)    |
| Sclerosing adenosis  | 1 (0.5)    |
| Sebaceous cyst       | 1 (0.5)    |
| Tubular adenoma      | 2 (0.9)    |

TABLE 2: Distribution of patients according to their diagnosis (total number: 222)

*The most common diagnosis

For 37.8% of the patients, the tumor was either on the left or on the right side equally. One-third (33.3%) had bilateral benign-looking LN. Of the documented Breast Imaging Reporting and Data System (BI-RADS) scores, 12.1% had a score of 3. Over half (55%) of the patients had an excisional biopsy. Of the patients, 33.3%, 82.4%, and 9.9% underwent mammograms, ultrasounds, and MRI, respectively (Table 3).
| Variable                  | Number (%) |
|---------------------------|------------|
| **Tumor side**            |            |
| Left                      | 84 (37.8)  |
| Right                     | 84 (37.8)  |
| Both                      | 48 (21.6)  |
| Not available             | 6 (2.7)    |
| **Lymph node**            |            |
| Not available             | 129 (58.1) |
| Bilateral benign-looking  | 74 (33.3)  |
| Left axillary             | 5 (2.3)    |
| Right axillary            | 14 (6.3)   |
| 1                         | 4 (1.8)    |
| 2                         | 8 (3.6)    |
| 3                         | 27 (12.1)  |
| 4                         | 24 (10.8)  |
| Not available             | 159 (71.7) |
| **Bi-RADS score**         |            |
| Not available             | 43 (19.4)  |
| Excision                  | 123 (55)   |
| Fluid needle aspiration   | 3 (1.4)    |
| Incision and drainage     | 5 (2.3)    |
| Lumpectomy                | 11 (5)     |
| US-guided true-cut biopsy | 37 (17)    |
| Not done                  | 148 (66.7) |
| Done                      | 74 (33.3)  |
| **Mammogram**             |            |
| Not done                  | 39 (17.6)  |
| Done                      | 183 (82.4) |
| **US**                    |            |
| Not done                  | 200 (90.1) |
| Done                      | 22 (9.9)   |

**TABLE 3: Distribution of patients according to clinical data and investigations (total number: 222)**

Bi-RADS, Breast Imaging Reporting and Data System; US, ultrasound; MRI, magnetic resonance imaging

*The most common diagnostic imaging technique used

Figure 1 illustrates that 55.4% of the studied patients were diagnosed with FA. Additionally, FA was significantly higher among patients aged under 30 years (p ≤ 0.05) (Figure 2). Table 4 shows a significantly higher rate of FA among patients in their 30s (p ≤ 0.05).
FIGURE 1: Percentage of patients according to FA (total number: 222)

FA, fibroadenoma

FIGURE 2: Relationship between FA and patients’ age (total number: 222)

FA, fibroadenoma

χ²: 19.61, p-value ≤ 0.001
| Variable                  | Fibroadenoma | | | | | |
|---------------------------|--------------|----------------|----------------|----------------|----------------|----------------|
|                           | Yes (number (%)) | No (number (%)) | χ² | p-value |          |          |
| Age (years) (mean ± SD)   | 33.55 ± 12.28 | 40.64 ± 11.65 | 1* | <0.001 |          |          |
| BMI                       | 26.08 ± 7.03  | 26.97 ± 6.2   | 1.23* | 0.218 |          |          |
| Tumor size (mm)           | 4.48 ± 5.68   | 3.77 ± 3.01   | 0.53* | 0.596 |          |          |
| Gender                    |              |               | 14.19 | <0.001 |          |          |
| Female                    | 121 (98.4)    | 84 (84.8)     |          |          |          |          |
| Male                      | 2 (1.6)       | 15 (15.2)     |          |          |          |          |
| Nationality               |              |               | 0.85 | 0.355 |          |          |
| Non-Saudi                 | 19 (15.4)     | 20 (20.2)     |          |          |          |          |
| Saudi                     | 104 (84.6)    | 79 (79.8)     |          |          |          |          |
| Chronic diseases          |              |               | 0.05 | 0.819 |          |          |
| Yes                       | 11 (8.9)      | 8 (8.1)       |          |          |          |          |
| No                        | 112 (91.1)    | 91 (91.9)     |          |          |          |          |
| Medication                |              |               | 0.83 | 0.36  |          |          |
| Yes                       | 66 (53.7)     | 47 (47.5)     |          |          |          |          |
| No                        | 57 (46.3)     | 52 (52.5)     |          |          |          |          |

**TABLE 4: Relationship between FA and patients’ demographics, BMI, tumor size, chronic diseases, and medications (total number: 222)**

FA, fibroadenoma; SD, standard deviation; BMI, body mass index; mm, millimeter

*Mann-Whitney U test

**Discussion**

The present study was carried out to investigate the patterns of BBD and its associated risk factors in Makkah. Our findings showed that among the 222 participants, FA was the most common BBD, followed by FCC, abscesses, and gynecomastia. Furthermore, the prevalence of FA was higher in young women than in other subjects.

Compared with previous studies, FA remains the most frequently reported type of BBD (55.4%). Similar observations were reported by Albasri [12], Chiedozi et al. [15], and Jamal [13], at 44.3%, 27.5%, and 47%, respectively. These findings align with most of the literature, including the studies of Malik et al. [16] and Aslam et al. [17].

In this study, FA was highly prevalent in the third decade, with a mean age of 33.55 years, similar to the research of Razik et al. [18] and higher than the study of Albasri [12]. However, other variables, such as residence in Saudi Arabia and chronic diseases, were not significantly associated with FA, which disagrees with the study of Razik et al. [18].

The similarity of our result with those mentioned above is consistent with national studies regardless of the level of care. Our research was carried out in a specialized center, whereas the study of Albasri [12] was in a tertiary hospital, the study of Razik et al. [18] was a multicentric study, and Jamal [13] was in a teaching hospital.

In our study, FCC was the second most commonly reported lesion, accounting for 15.3% of all BBD types. This finding is in line with the findings of Albasri [12], Alamri et al. [19], and Amr et al. [20]. They found an FCC frequency of 23.4%, 18.8%, and 21.1%, respectively.

In our cohort, abscesses were the third most commonly reported BBD type, accounting for 8.1%, which is
comparable to the study of Alami et al. (5.9%) [19] and higher than the study of Ahmad Mohammed (0.8%) [21]. In the present study, benign phylloid tumor was found in 4.1% of the study population, while Aslam et al. [17] and Masciardi and Ferranti [22] reported a lower rate. Other BBD types, such as gynecomastia, epithelial hyperplasia, lipoma, and mastitis, were found to be low in our cohort; similar rates were also reported in the studies of Albasi [12] and Razik et al. [18].

Limitations
The study has some limitations, notably its retrospective design and sample size affected by poor recording systems, which limited data collection to a five-year period. The lower rate of benign breast disease in our study compared with the Makkah population may result from many variables such as the distribution of patients across city hospitals. However, other reasons could explain our findings such as a lack of awareness of such conditions, hesitancy to seek medical care due to social difficulties, and ignorance of these issues.

Conclusions
In conclusion, fibroadenoma is the most common lesion of benign breast disease in the studied population. This study established the baseline pattern of benign breast disease in a specialized hospital in Makkah, which provides valuable information to local physicians.

Additional Information
Disclosures
Human subjects: Consent was obtained or waived by all participants in this study. The Institutional Review Board (IRB) of Al-Noor Specialist Hospital, Makkah, Saudi Arabia, issued approval H-02-K-076-0222-664.
Animal subjects: All authors declare that this study did not involve animal subjects or tissue.
Conflicts of interest: All authors have confirmed that this study did not involve animal subjects or tissue.
Payment/services info: All authors declare that no financial support was received from any organization for the submitted work.
Financial relationships: All authors declare that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work.
Other relationships: All authors declare that there are no other relationships or activities that could appear to have influenced the submitted work.

References
1. Santen RJ, Mansel R: Benign breast disorders. N Engl J Med. 2005, 353:275-85. 10.1056/NEJMra055492
2. Hughes LE, Mansel RE, Webster DJ: Aberrations of normal development and involution (ANDI): a new perspective on pathogenesis and nomenclature of benign breast disorders. Lancet. 1987, 2:1516-9. 10.1016/0140-6736(87)91204-9
3. Orr B, Kelley IL 3rd: Benign breast diseases: evaluation and management. Clin Obstet Gynecol. 2016, 59:710-26. 10.1097/GRF.000000000000233
4. Hartmann LC, Sellers TA, Frost MH, et al.: Benign breast disease and the risk of breast cancer. N Engl J Med. 2005, 353:229-37. 10.1056/NEJMoa044383
5. Stachs A, Stubarb I, Reiner T, Hartmann S: Benign breast disease in women. Dtsch Arztebl Int. 2019, 116:565-74. 10.3238/arztebl.2019.0565
6. Collaborative Group on Hormonal Factors in Breast Cancer: Breast cancer and hormonal contraceptives: collaborative reanalysis of individual data on 53 297 women with breast cancer and 100 239 women without breast cancer from 54 epidemiological studies. Lancet. 1996, 347:1713-27. 10.1016/s0140-6736(96)90806-5
7. Breast cancer and hormone replacement therapy: collaborative reanalysis of data from 51 epidemiological studies of 52,705 women with breast cancer and 108,411 women without breast cancer. Collaborative Group on Hormonal Factors in Breast Cancer. Lancet. 1997, 350:1047-59.
8. Huang Z, Hankinson SE, Colditz GA, et al.: Dual effects of weight and weight gain on breast cancer risk. JAMA. 1997, 278:1407-11.
9. Kelsey JL, Gammon MD, John EM: Reproductive factors and breast cancer. Epidemiol Rev. 1993, 15:36-47. 10.1093/oxfordjournals.epirev.a056115
10. Schmitt SJ, Connolly J: Diseases of the breast. Lippincott, Williams & Wilkins, Philadelphia, PA; 2004.
11. Olu-Eddo AN, Ugiagbe EE: Benign breast lesions in western Saudi Arabia. An 8-year histopathological review of 603 cases. Saudi Med J. 2011, 52:211-6. 10.4103/0300-1652.95790
12. Albasi AM: Pattern of benign breast diseases in western Saudi Arabia. An 8-year histopathological review of 603 cases. Saudi Med J. 2014, 35:1517-20.
13. Jamal AA: Pattern of breast diseases in a teaching hospital in Jeddah, Saudi Arabia. Saudi Med J. 2001, 22:110-3.
14. Amin TT, Al-Mulhim AR, Chopra R: Histopathological patterns of female breast lesions at secondary level care in Saudi Arabia. Asian Pac J Cancer Prev. 2009, 10:1121-6.
15. Chiedozi LC, El-Hag IA, Kollur SM: Breast diseases in the Northern region of Saudi Arabia. Saudi Med J. 2005, 24:623-7.
16. Malik N, Sahlahuddin O, Azhar M, et al.: Breast diseases; spectrum in Wah Cantt; POF hospital experience. Professional Med J. 2010, 17:566-72.
17. Aslam HM, Saleem S, Shahid N, Mughal A, Umah R: Clinical- pathological profile of patients with breast diseases. Diagn Pathol. 2013, 8:77.
18. Razik MA, Alsubaie AM, Alsetri HM, Albassam KA, Alkhurayyif AO, Altamimi MM, Alnanzi SM: Clinical and histopathological features of breast tumors in women: a cross-sectional study at three hospitals in
Kingdom of Saudi Arabia. Pan Afr Med J. 2021, 39:267. 10.11604/pamj.2021.39.267.30341
19. Alamri A, Alsharei S, Al-Wadei H, et al.: Epidemiological pattern of breast diseases among females in the south-western region, Saudi Arabia. Int J Clin Med. 2020, 11:257-69. 10.4236/ijcm.2020.115027
20. Amr SS, Sa’di AR, Ilahi F, Sheikh SS: The spectrum of breast diseases in Saudi Arab females: a 26 year pathological survey at Dhahran Health Center. Ann Saudi Med. 1995, 15:125-52. 10.5144/0256-4947.1995.125
21. Ahmad Mohammed A: Benign breast disorders in female. Rev de Senol y Patol Mamar. 2022, 35:42-8. 10.1016/j.senol.2021.01.005
22. Masciadri N, Ferranti C: Benign breast lesions: ultrasound. J Ultrasound. 2011, 14:55-65. 10.1016/j.jus.2011.03.002