


Characteristics, Clinical Features, And Management Of Fibroadenoma Mammae Patients At Dustira Hospital Cimahi

Ris Kristiana¹, Salsha Regina Syakira², Endah Hamidah¹, Endry Septiadi³, Fitriardi Sejati⁴, Tatang Bisri⁵

¹Department of Anatomical Pathology, Faculty of Medicine, University of General Ahmad Yani, Cimahi, West Java, Indonesia, ²Medical Study Program, Faculty of Medicine, University of General Ahmad Yani, Cimahi, West Java, Indonesia, ³Department of Nutritional Sciences, Faculty of Medicine, University of General Ahmad Yani, Cimahi, West Java, Indonesia, ⁴Department of Surgery, Faculty of Medicine, University of General Ahmad Yani, Cimahi, West Java, Indonesia, ⁵Department of Anesthesia and Intensive Care, Faculty of Medicine, University of General Ahmad Yani, Cimahi, West Java, Indonesia

Article Info	ABSTRACT
<p>Keywords: Age, body mass index, FAM, management, topography</p>	<p>Fibroadenoma mammae (FAM) is the most common benign breast tumor that occurs at the age of 14-35 years. About 10% of the female population has FAM. FAM manifests as solitary masses that are easily movable, well-defined, with a smooth surface. The aim of this study was to determine the characteristics, clinical features, and management of FAM patients at Dustira Hospital using secondary data from medical records. A total of 68 FAM patients were selected as samples during the period 2018-2023. The research variables consisted of the number of cases, age, body mass index(BMI), location, topography, size, quantity, and management of FAM. Univariate analysis was used in this study and the results were presented in narrative and tabular forms. The results of the study showed that the highest number of FAM cases occurred in 2018, reaching 28 (41.1%). Characteristics of FAM patients included 49 individuals (72%) in the 16-30 age group, 32 individuals (47%) with normal body mass index. Clinical features of FAM were found in 31 individuals (45.6%) on the right breast, 24 individuals (35.3%) in the upper medial quadrant, with a size of 3-5 cm in 24 individuals (35.3%), and 49 individuals (72.1%) limited solitary masses. Management included surgery in all 68 individuals (100%), with 67 individuals (98.5%) underwent excision, while 1 individual (1.5%) underwent incision. Age and BMI are suspected to play a role in FAM formation related to estrogen hypersensitivity and mutations in the mediator complex subunit 12 (MED12). Lesion size is influenced by estrogen exposure. Management of fibroadenoma depends on the patient's preferences and clinical conditions. Women at risk or suspecting breast masses are advised to perform self-breast examination (BSE) and efficiently consult with healthcare professionals.</p>
<p>This is an open access article under the CC BY-NC license</p> 	<p>Corresponding Author: Ris Kristiana Department of Anatomical Pathology, Faculty of Medicine, University of General Ahmad Yani, Cimahi, West Java, Indonesia ris.kristiana@lecture.unjani.ac.id</p>

INTRODUCTION

Fibroadenoma mammae (FAM) is the most common benign breast tumor in women aged 14-35 years. ¹ Less than 5% occur in those over 50 years of age. ² It is estimated that around 10% of the world's female population experiences fibroadenoma once in their lifetime. ³ In 2019, Indonesia had 28,910 cases of breast tumors with West Java Province ranking first with 6,109 cases, followed by Jakarta with 4,610 cases. ⁴ The nature of this tumor is a well-defined and movable mass. The tumor is composed of loose stroma and glands lined with epithelium.

5

The exact etiology of fibroadenoma mammary is unknown. However, hypersensitivity to estrogen and mutations *in mediator complex subunit 12* (MED12) play an important role in the development of fibroadenoma mammary. ^{6,7,8} Risk factors associated with FAM include age, family history, contraception, age at *menarche*, body mass index (BMI), and lifestyle. ⁹⁻¹²

Fibroadenomas can grow unilaterally or bilaterally. More than 50% of fibroadenoma cases are found unilaterally, namely on the right side of the breast with the most common topography in the superior lateral quadrant followed by the inferior medial quadrant. ¹³ As many as >70% of fibroadenomas arise as a solitary mass and about 10-25% are *multiple masses*. Although fibroadenomas often appear as solitary lesions, in some cases, *multiple lesions* can appear on the same side of the breast or even bilaterally. ¹⁴ The diameter of FAM is most often 1-4 cm, but it is possible for FAM to develop >5 cm which is called *giant fibroadenoma*. ¹⁵

All breast masses should be tested with *a triple test* involving physical examination, mammography, and biopsy. Given that not all areas are equipped with mammography facilities, and ultrasound is relatively more accessible, breast ultrasound may be a viable alternative. ¹⁶

Management options for fibroadenoma mammary cases consist of conservative therapy and surgery. Excisional surgery is the best option for fibroadenoma and can be performed as early as possible. ¹⁷ The risk of malignant transformation in FAM is very low, estimated at 0.0125-0.3%, but the risk of malignancy increases 2.17 times in patients with FAM and 3.10 times in patients with complex FAM. ¹⁸

Based on the description above, this problem is important to be studied further because of the many cases of breast tumors, especially fibroadenoma mammae, both globally and in Indonesia. Although FAM is a benign tumor, there is still a possibility of it turning into a breast malignancy that will cause higher morbidity and mortality rates. This study was conducted to find out more about the characteristics, clinical features, and management of fibroadenoma mammae patients at Dustira Hospital Cimahi for the period 2018-2023.

METHODS

This study uses a descriptive observational method. The purpose of this study is to provide an overview and description of the characteristics, clinical features, and management of fibroadenoma mammae patients at Dustira Cimahi Hospital for the period 2018-2023 using secondary data from medical records.

The inclusion criteria in this study were all patients diagnosed with fibroadenoma mammae based on histopathological examination at Dustira Cimahi Hospital during the period 2018-2023. The exclusion criteria were patients diagnosed with breast carcinoma, breast abscess, or breast abnormalities other than fibroadenoma.

The sampling method used *total sampling* until the number of samples was equal to the number of populations that met the criteria. The study began with the preparation of a proposal, request for permission, and research ethics. After approval, the researcher recorded and processed medical record data using *the Statistical Package for Social Science* (IBM SPSS). *Statistics 26*. The research was conducted from October-November 2023. It has been approved by the Research and Research Ethics Committee of Dustira Level II Hospital with the number Etik.RSD/157/X/2023 .

RESULTS AND DISCUSSION

Number of Cases of Fibroadenoma Mammae

The number of cases of fibroadenoma mammae is described in the following table:

Table 1. Number of FAM Cases

Year	Frequency (N)	(%)	Percentage
2018	28		41.1
2019	0		0
2020	0		0
2021	8		11.8
2022	14		20.6
2023	18		26.5
Total	68		100

Based on table 1, the number of FAM cases occurred in 2018 (41.1%), 2023 (26.5%), 2022 (20.6%), and 2021 (11.8%). In 2019 and 2020, no medical records of fibroadenoma mammae were found at Dustira Cimahi Hospital (0%).

Characteristics of Fibroadenoma Mammae Patients

Characteristics of FAM patients were divided based on age and body mass index.

The results can be seen in the following table:

Table 2. Frequency Distribution based on FAM Patient Age

Age (Year)	Frequency (N)	Percentage (%)
0-15	1	1,5
16-30	49	72,0
31-45	11	16,2
≥ 46	7	10,3
Total	68	100

Based on table 2, it can be concluded that the majority of FAM cases are in the 16-30 age group (72.0%). This is related to estrogen levels that peak in women in the 2nd to 3rd

decade, then decrease by 50% at the age of 50 years and decrease rapidly after menopause.

9

Estrogen has a physiological role in proliferation and ductal morphogenesis. However, when estrogen exposure is excessive, the pro-proliferative effects of steroids can cause the accumulation of replication errors. There are 3 main mechanisms of tumorigenesis due to high estrogen levels. The first mechanism occurs because cells that proliferate due to estrogen stimulation have higher energy needs, resulting in the production of by-products of cellular respiration, namely *Reactive oxidative species* (ROS). The second mechanism occurs because estrogen is metabolized into quinones which are mutagenic and can interact directly to cause DNA damage.

DNA damage coupled with cellular oxidative stress due to ROS will disrupt the replication process. The latter mechanism occurs because estrogen not only triggers damage DNA, but also has the potential to inhibit the repair of actively proliferating cells, resulting in the formation of tumor masses.⁶

MED12 mutations are also found most frequently at age 30. MED12 is a gene located on chromosome X which encodes the complex mediator.¹⁹ Research conducted by Piscuoglio et al (2016) found that 60% of fibroadenoma cases have MED12 mutations, especially in codon 44 of axon 2.⁷ MED12 mutations cause estrogen signals to become irregular by interacting with *estrogen receptor α* (ERα) and *estrogen receptor β* (ERβ) directly, which increases the sensitivity of breast tissue estrogen receptors to estrogen.^{9,20}

Excessive estrogen stimulation accompanied by increased sensitivity of estrogen receptors causes accumulation and replication errors, resulting in mutations and tumor cell development.⁶

Table 3. Frequency Distribution based on BMI of FA M Patients

IMT	Frequency (N)	Percentage (%)
<i>Underweight</i>	8	11.8
Normal	32	47.0
<i>Overweight</i>	18	26.5
<i>Obese I</i>	8	11.8
<i>Obese II</i>	2	2.9
Total	68	100

Based on table 3, it can be seen that the majority of FAM cases occurred in the group with normal BMI, namely 32 cases (47%). A study conducted by Iyengar et al. (2017) on 72 women with a median BMI of 21.9 kg/m² showed that women with normal BMI may experience biochemical changes, such as increased insulin and triglyceride levels due to inflammation in the white adipose tissue of the breast.²¹ Leptin has been shown to regulate aromatase in adipose stromal cells, so that increased leptin levels correlate with increased aromatase expression in the breast. Local estrogen production in the breasts of women with inflammation of this white adipose tissue may contribute to the development of fibroadenoma.²¹

Compared to BMI, lifestyle and diet are more significant risk factors for FAM. ²² Research conducted by Dafriani et al. (2021) on fibroadenoma patients with a p value <0.05 showed that dietary habits were associated with fibroadenoma. The study stated that 71% of fibroadenoma patients had risky dietary habits such as consuming high-cholesterol foods, including fast food, canned food, drinks containing artificial sweeteners, bread, and preserved foods. ²³ Fast food contains high levels of salt, fat, and calories including cholesterol which reaches 70%. ²³ Foods with the highest cholesterol content include beef brain, eggs, broiler chicken, beef liver, squid, and shrimp. ²⁴

Features of Fibroadenoma Mammae Patients

The clinical picture of FAM patients consists of the location, topography, size, and number of FAM masses. The results can be seen in the following table:

Table 4. Frequency Distribution based on Clinical Features of FAM Patients

Variable	Frequency (N)	Percentage (%)
FAM Location <i>Dextra</i>		
	31	45.6
<i>Sinister</i>	29	42.6
<i>Bilateral</i>	8	11.8
Total	68	100
Topography FAM		
<i>Superior Lateral</i>	17	25.0
<i>Superior Medial</i>	24	35.3
<i>Inferior</i>	7	10.3
<i>Lateral inferior</i>	10	14.7
<i>Media</i>		
<i>Multiple</i>	10	14.7
Total	68	100
Size		
FAM (cm)	31	
<3		45.6
3-5	24	35.3
>5	13	19.1
Total	68	100
Amount		
FAM	49	
1		72.1
>1	19	27.9
Total	68	100

The results of the study attached to table 4 are clinical descriptions of FAM patients. The results of the study showed that FAM mostly occurred on the *right side* with 31 cases (45.6%). This result is in line with research by Nurprilinda et al. (2023) which also stated that the most lateralization of FAM masses was on the right breast side (44.3%).²⁵ There has been no explanation regarding the comparison of the number of FAM cases on the *right* and *left sides* because fibroadenoma can be found on the right or left side or even on both sides.^{15,25} Unlike fibroadenoma, breast malignancy is more often found on the *left side of the breast due to higher expression of breast cancer genes (BRCA1) and BRCA2 on the left side.*²⁶

Based on table 4, the most FAM topography occurred in the *superior medial quadrant* with a total of 24 people (35.3%). This is not in accordance with the research of Laxman et al. (2018) which stated that 17 people (34%) had fibroadenoma masses in the *superior lateral quadrant.*²⁷ Fibroadenoma is abnormal proliferation of glands and connective tissue of the breast. FAM can be found in various quadrants of the breast due to the structure of the lobules that spread in the breast. However, the dominant lymphatic drainage towards *the axilla* causes the most cases of FAM in the *superior quadrant lateral.*^{16,25}

The description of FAM size presented in table 4 shows that the majority of FAM patients have masses measuring <3cm. This result is in line with the research of Nurprilinda et al (2023) which stated that the majority of FAM sufferers have a mass size of 1.12 cm (30.9%) and the lowest frequency with a mass measuring > 4 cm (17.0%).²⁵ Increasing public awareness of the importance of conducting breast self-examination (SADARI) is useful for early detection so that FAM masses can be identified when they are still small.²⁵

Giant fibroadenoma is the rarest variant of fibroadenoma with an incidence of 0.5%-2% and is the most common cause of unilateral macromastia in women.²⁸ This tumor has a diameter of >5 cm with a weight of >500 grams. *Giant fibroadenoma* shows characteristics similar to malignancy, such as breast skin changes, nipple inversion, and enlargement of superficial veins. However, *giant fibroadenoma* remains a benign lesion that will not develop into malignancy.^{28,29}

The majority of FAM patients had solitary lesions as shown in table 4, which was 49 cases (72.1%). This is in accordance with Soltanian's (2015) study which stated that 70% of fibroadenoma cases were solitary masses with 10-25% of cases referring to more than one tumor.²⁸

Overview of FAM Patient Management

Management of FAM patients is divided into conservative and surgical management. The results can be seen in the following table:

Table 5. Frequency Distribution based on Management of FAM Patients

Variables	Frequency (N)	Percentage (%)
Governance		
Conservative	0	0
Surgery	68	100
Total	68	100
Type		1.5

Variables	Frequency (N)	Percentage (%)
Surgery	1	
Incisional Biopsy		
Excisional Biopsy	67	98.5
Lumpectomy	0	0
Mastectomy	0	0
Cryoblation	0	0
Total	68	100

The management of FAM presented in table 5 shows that all patients underwent surgery (100%). This is in line with the research of Sidauruk et al. (2013) on fibroadenoma patients who were hospitalized at the Hospital Santa Elisabeth Medan which showed that 101 patients (98.1%) chose to undergo surgery while 2 patients (1.9%) chose conservative measures.³⁰

The management options for FAM cases can be conservative or surgical intervention. Asymptomatic masses measuring <3cm in individuals <40 years old can be managed conservatively.³¹ Conservative management includes observation of the FAM mass for 2 years interspersed with radiological examinations every 6 months.²⁸

Surgical intervention is performed in all women aged >40 years even if the *triple test result shows a benign lesion, because the risk for breast malignancy increases with age. All fibroadenoma masses with a diameter of >3-4 cm should be considered for mass removal, regardless of the triple test result and the patient's age.*³²

Table 5 shows that 67 patients (98.5%) underwent excisional biopsy and 1 patient (1.5%) underwent incisional biopsy. Excisional biopsy has both diagnostic and therapeutic purposes, providing a definitive diagnosis while removing the fibroadenoma. This surgical procedure involves removing the entire fibroadenoma along with the surrounding normal tissue.³³

The advantages of excisional biopsy are the larger tissue sample, providing more comprehensive information for pathological evaluation. This procedure also involves the removal of the entire lesion or suspicious area, resulting in more precise results in determining the nature and characteristics of the lesion, including the lesion boundaries. In addition, excisional biopsy can provide clearer and more controlled surgical margins, assisting in the complete removal of the lesion and reducing the risk of recurrence.³³

Research data shows that 1 person (1.5%) underwent an incisional biopsy procedure. An incisional biopsy is a diagnostic procedure that involves taking a portion of the tumor mass as a sample to establish a histopathological diagnosis.³⁴ This may be due to the suspected malignancy of the patient's mass, so an incisional biopsy was performed as an initial step for further histopathological examination.

CONCLUSION

Based on research on fibroadenoma mammae patients at Dustira Hospital Cimahi for the period 2018-2023, it can be concluded that the number of FAM cases was 68 cases. The

characteristics of the most patients were aged 16-30 years as many as 49 patients (72%) with a normal body mass index category of 32 patients (47.0%). The clinical features of FAM patients include the location of the mass found most on the *right side* as many as 31 patients (45.6%). The majority of FAM masses were in the *superior medial quadrant* as many as 24 patients (35.3%). Most FAM masses were <3cm in size, namely 31 patients (45.6%) and 49 patients (72.1%) had solitary masses. All patients underwent surgery (100%) with the most mass removal technique being excisional biopsy as many as 67 cases (98.5%).

REFERENCES

1. Adaming SFS, Lufiyati A. Gambaran tingkat pengetahuan tentang fibroadenoma mammae dan perilaku SADARI pada wanita usia subur. *JPKM* 2022; 3(2): 101-10.
2. Westmead Breast Cancer Institute. Fibroadenoma. BCI. Australia. 2014
3. Salati SA. Breast fibroadenomas: a review in the light of current literature. *POL PRZEGL CHIR* 2021; 93(1): 1-9.
4. Kementerian Kesehatan Republik Indonesia. Profil kesehatan Indonesia tahun 2019. Kemenkes RI. Jakarta. 2020.
5. Kumar V, Abbas AK, Aster JC. Robbins basic pathology. 9th ed. Canada: Elsevier Saunders; 2013.
6. Bhardwaj P, Au CC, Martin AB, Ladumor H, Oshchepkova S, Moges R, et al. Estrogens and breast cancer: mechanisms involved in obesity- related development, growth and progression. *J Steroid Biochem Mol Biol* 2019; 189: 161-70.
7. Piscuoglio S, Murray M, Fusco N, Marchiò C, Loo FL, Martelotto LG, dkk. MED12 somatic mutations in fibroadenomas and phyllodes tumours of the breast. *Histopathology* 2015; 67(5): 719-29.
8. Loke BN, Md Nasir ND, Thike AA, Lee JYH, Lee CS, Teh BT, et al. Genetics and genomics of breast fibroadenomas. *J Clin Pathol* 2018;71(5):381-7.
9. Tan WJ, Chan JY, Thike AA, Lim JCT, Md Nasir ND, Tan JSY, et al. MED12 protein expression in breast fibroepithelial lesions: Correlation with mutation status and oestrogen receptor expression. *J Clin Pathol* 2016; 69(10): 858-65.
10. Li R, Cui J, Shen Y. Brain sex matters: Estrogen in cognition and Alzheimer's disease. *Mol Cell Endocrinol* 2014; 25(389): 13-21.
11. Ahsani RF, Machmud PB. Hubungan riwayat reproduksi dengan tumor payudara pada perempuan usia muda di Indonesia (Analisis Riset PTM 2016). *Media Kesehatan Masyarakat Indonesia* 2019; 15(3): 237.
12. O'brien S, Kowdley GC. Benign breast diseases and body mass index: is there a correlation?. *Am Surg* 2014; 80(5): 461-5.
13. Abhishek V, Ajitha MB, Shivaswamy BS, Srinivasan N. A systematic study on fibroadenoma of the breast. *Eur J Surg Sci* 2012; 3(3): 80-5.
14. Guray M, Sahin AA. Benign breast diseases: classification, diagnosis, and management. *Breast Cancer The Oncologist* 2006; 11(5): 435-49.

15. Mulia IGBLP, Dewi IGASM, Sumadi IWJ. Karakteristik klinikopatologi pasien fibroadenoma mammae di RSUP Sanglah Denpasar tahun 2017- 2018. *Jurnal Medika Udayana (JMU)* 2021; 10(4): 75-9.
16. Fadjari H. Pendekatan diagnosis benjolan di payudara. *CDK* 2012; 39(4): 308-10.
17. Gupta AK, Agarwal DK. Fibroadenoma of breast: our experience. *IJRR* 2018; 5(7): 87.
18. Wu YT, Wu HK, Chen ST, Chen CJ, Chen DR, Lai HW. Fibroadenoma progress to ductal carcinoma in situ, infiltrating ductal carcinoma and lymph node metastasis? Report an unusual case. *J Surg Case Rep* 2017; 5: 1-4.
19. Chang HY, Koh VCY, Nasir ND, Ng CCY, Guan P, Thike AA, *et al.* MED12, TERT and RARA in fibroepithelial tumours of the breast. *J Clin Pathol* 2020; 73(1): 51-6.
20. Maharani NU. Gambaran penderita tumor payudara berdasarkan usia biologis. *Jurnal Medika Utama* 2022; 3(2): 1851-3.
21. Iyengar NM, Brown KA, Zhou XK, Gucalp A, Subbaramaiah K, Giri DD, *et al.* Metabolic obesity, adipose inflammation and elevated breast aromatase in women with normal body mass index. *Cancer Prevention Research* 2017; 10(4): 235-43.
22. Putri KD, Hardini N, Dewi SY, Supartono B. The relationship of age and obesity with the histopathological profile of mammae fibroadenoma patients in pasar minggu hospital 20182019. *SENSORIK* 2022; 3(1): 1-9.
23. Dafriani P, Nur SA, Delfitri R. The risk factors of fibroadenoma: cross sectional study in Solok Selatan Hospital, Indonesia. *Atlantis Press* 2021; 39: 246-8.
24. UCSF Medical Center. Cholesterol Content of Foods. 2024.
25. Nurprilinda M, Gultom FL, Sanjaya SJ. Profile of fibroadenoma mammae patients at MRCCC Siloam Semanggi Hospital 2019-2020. *Asian Journal of Medicine and Health* 2023; 21(7): 90-100.
26. Abdou Y, Gupta M, Asaoka M, Attwood K, Mateusz O, Gandhi S, *et al.* Left sided breast cancer is associated with aggressive biology and worse outcomes than right sided breast cancer. *Sci Rep* 2022;12(1).
27. Laxman S, Sangolgi P, Jabshetty S, Bhavikatti A, Uttam A. Clinical profile of patients with fibroadenoma of breast. *International Surgery Journal* 2018; 5(3): 1057.
28. Soltanian HT, Lee M. Breast fibroadenomas in adolescents: current perspectives. *Adolesc Health Med Ther* 2015;6: 159-63.
29. Eleftheriades A, Tsarna E, Toutoudaki K, Paschalidou E, Christopoulos N, Georgopoulos I, *et al.* Giant juvenile fibroadenoma: Case report and review of the literature. *Journal of Clinical Medicine* 2023; 12(5): 2-13.
30. Sidauruk HA, Rasmaliah, Hiswani. Karakteristik penderita fibroadenoma mammae (FAM) rawat inap di RS Santa Elisabeth Medan tahun 2007-2011. *Garuda* 2013.
31. Suyatno. Peran pembedahan pada tumor jinak payudara. *Majalah Kedokteran Andalas* 2015; 38(1): 1- 16.
32. Brennan M, Houssami N, French J. Management of benign breast conditions. *Australian Family Physician* 2005; 34(4): 253-5.
33. Ramala SR, Chandak S, Chandak MS, Annareddy S. A comprehensive review of breast fibroadenoma: correlating clinical and athological findings. *Cureus* 2023; 15(12): 2-13.