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Comparison of Pericanalicular and Intracanalicular Fibroadenoma Mammae Growth Patterns in Various Age Ranges

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Abstract

Background: Fibroadenoma mammae are the most common type of benign breast tumor in women. Fibroadenoma mammae can occur at various ages. Not much data is recorded about anatomical pathology, especially regarding the distribution of fibroadenoma mammae growth patterns in Siaga Medika Purbalingga Hospital. Studies in Indonesia that focus on this topic also remain scarce.

Objective: To analyze the comparison between the growth patterns in fibroadenoma mammae patients aged 11-50 years.

Method: This is a cross-sectional study with data collected retrospectively based on medical records and histopathological examinations in Siaga Medika Purbalingga Hospital from January to December 2021. The statistical analysis was done using JASP 0.14.1.0.

Results: Most patients with fibroadenoma mammae were in the age range 21-30 years (48.9%) with a pericanalicular pattern (66%). The four groups had two different growth patterns ($p < 0.001$). The odds ratio showed 3.4, which means patients aged ≤30 years have a 3.4x higher chance of being diagnosed with pericanalicular fibroadenoma mammae than patients aged >30 years.

Conclusion: The incidence of pericanalicular and intracanalicular fibroadenoma mammae growth patterns in Siaga Medika Purbalingga Hospital patients can be affected by age.

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INTRODUCTION

Breast tumors often occur in women, caused by the growth of tissue in the breast, which can be benign or malignant. In Indonesia, 47% of breast cancers are detected in women under the age of 40.[1] The most common benign breast tumor is fibroadenoma mammae (FAM). According to the NSW Breast Cancer Institute, FAM occurs in women aged 21-25 years, and less than 5% occurs in those over 50 years[2].

FAM incidence can occur due to several risk factors, such as age, unhealthy lifestyle, obesity, hormonal influences, history of marriage, parity, and breastfeeding history.[3] Fibroadenoma is associated with a slightly increased risk of carcinoma[4]. Malignancy in FAM can occur if there are histopathological changes like adenosis, epithelial calcification, or papillary apocrine. These are associated with the possible presence of other lesions in the surrounding breast tissue, such as atypical hyperplasia, to become malignant[5,6].

A family history of breast cancer is significantly associated with an increased risk of benign breast tumors, including mammary fibroadenoma, fibrocystic lesions, and epithelial proliferation with or without atypical. On average, pre-menopausal women with a family history of breast cancer were at increased risk of developing benign breast tumors[6,7].

Fibroadenoma mammae consist of lobular stroma and epithelium associated with myoepithelial cells and have a pericanalicular or intracanalicular pattern[3]. A study suggested that pericanalicular was higher in adolescent patients, while the proportion of mucus in the stroma increased with age and the growth pattern of intracanalicular was commonly found in adult patients[9].

According to the early detection results in women aged 25-29 years in Purbalingga by health profile data in 2021, there were no beingn breast tumors especially fibroadenoma mammae, whereas there were many incidences in hospitals. Histopathological growth patterns in FAM related to age can increase breast cancer risk. It is necessary to examine the growth pattern associated with the patient's history in order to prevent the development of breast tumors[10].

METHODS

A cross-sectional study design is used in this form of observational research. From January to December 2021, medical data and histopathological investigations were used in this study. All patients diagnosed with fibroadenoma mammae in 2021 were included in the study. It was divided into four groups based on age and development trends.

With 47 respondents, this study employed a purposeful selection of patients, with data collected utilizing secondary data on age and two growth trends. Patients aged 11 to 50 with no mixed development pattern are eligible. JASP 0.14.1.0 was used for statistical analysis.

RESULTS

During the research, 112 samples were obtained, with only 47 samples meeting the requirements. As listed in Table 1, most respondents are 21-30 years old. Most types of pericanalicular FAM were at the age of 21-30

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years out of 31 people (66%), while the total number of intracanalicular FAM was 16 people (34%). The odds ratio (Table 4) showed 3.4, which means patients aged ≤30 years have a 3.4x higher chance of being diagnosed with pericanalicular fibroadenoma mammae than patients aged >30 years.

We obtained the histopathology of FAM in every respondent with the same pattern, so we only provided representatives for each group, as shown in Table 2. Figure 1 shows a simple cuboidal epithelial structure in the lactiferous ducts, which is tubular or wheel-like. In the pericanalicular type, the epithelium is proliferating rather than the stroma, as shown in Figure 2. Figure 3 shows the stroma, or dense fibrous connective tissue, surrounding the epithelium of the lobular ducts of the breast. Figure 4 shows interlobular stroma that experienced proliferation that exceeded normal.

Glands in a pericanalicular are separated by an expanded stroma. Figure 5 shows that the epithelium in intracanalicular FAM does not proliferate but is compressed by the stroma, branch-like. Intracanalicular pattern is usually called fibromyxoid degeneration. Glands are compressed into linear branching structures by proliferating stroma. Stromal elements like adipose and smooth muscle are rare. Figure 6 shows that stromal components are generally uniform in cellularity, with elongated stromal cells. Both pericanalicular and intracanalicular cells have no mitotic activity or stromal atypia.

Table 1. Characteristics of Respondents

Characteristics		Frequency	Presentation
Age (years old, y.o)	11-20	15	31,9%
	21-30	23	48,9%
	31-40	7	14,9%
	41-50	2	4,3%
Growth Pattern	Pericanalicular	31	66%
	Intracanalicular	16	34%
	Total	47	100%

Table 2. Growth Pattern by Age

Age (y.o)	Growth Pattern	Frequency	Presentation
11-20	Pericanalicular	14	29,8%
	Intracanalicular	1	2,1%
21-30	Pericanalicular	16	34%
	Intracanalicular	7	14,9%
31-40	Pericanalicular	1	2,1%
	Intracanalicular	6	12,8%
41-50	Pericanalicular	0	0%
	Intracanalicular	2	4,3%
	Total	47	100%

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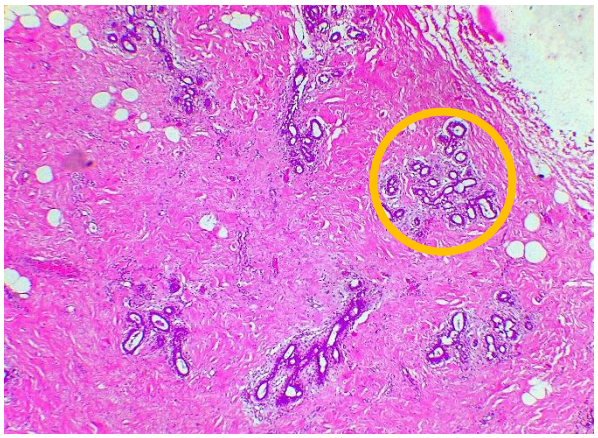


Figure 1. Pericanalicular pattern in 11-20 y.o patients (40x magnification).

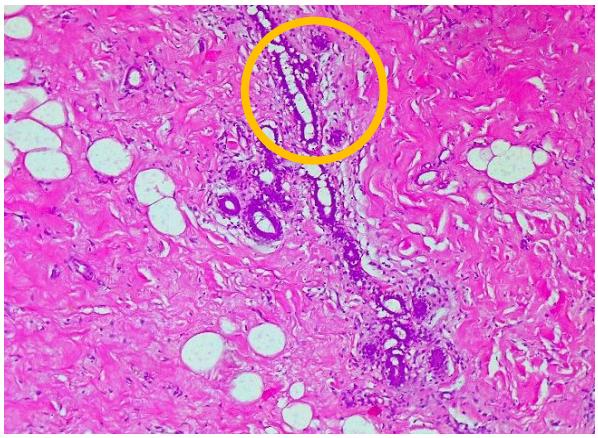


Figure 2. Pericanalicular pattern in 11-20 y.o patients (100x magnification).

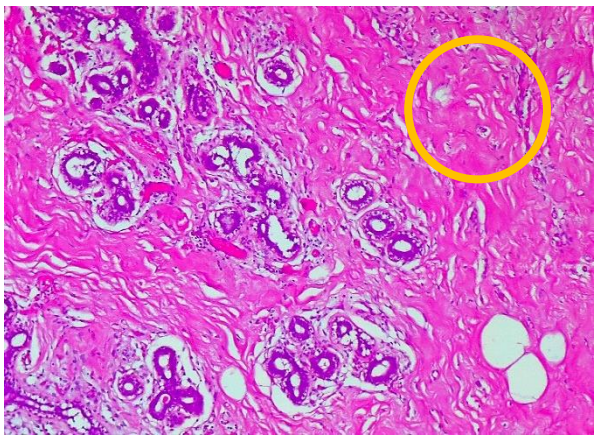


Figure 3. Pericanalicular pattern in 21-30 y.o patients (100x magnification)

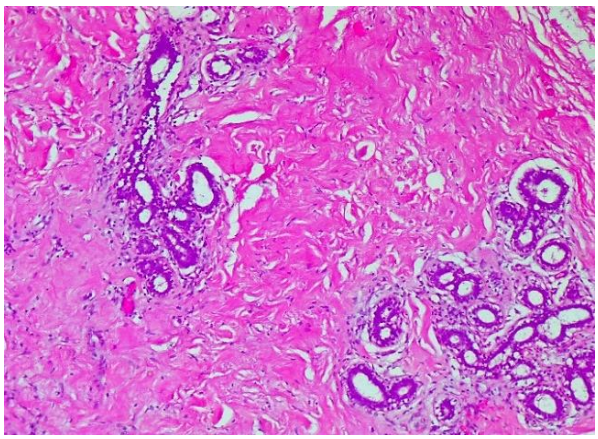
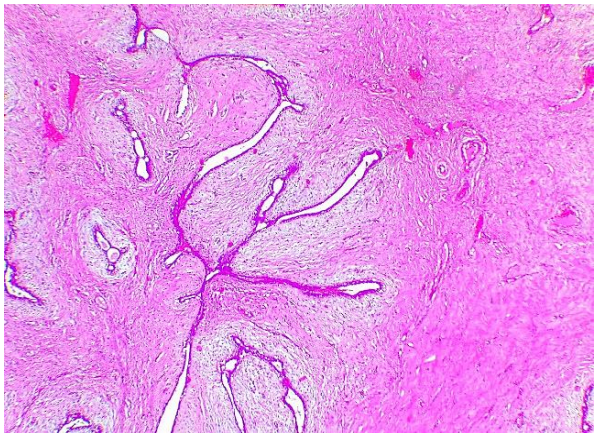


Figure 4. Pericanalicular pattern in 21-30 y.o patients (100x magnification)



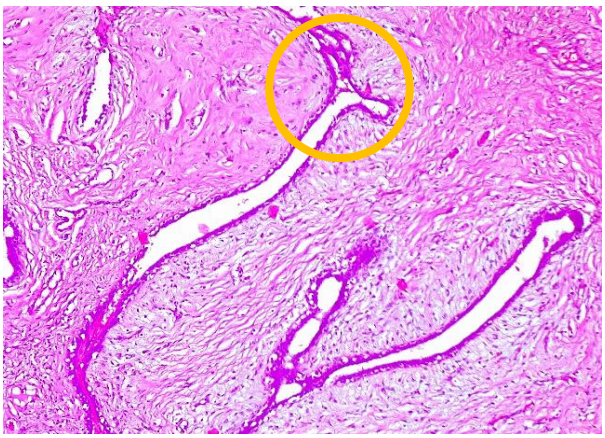


Figure 5. Intracanalicular pattern in 31-40 y.o patients (magnification, left 40x, right 100x)

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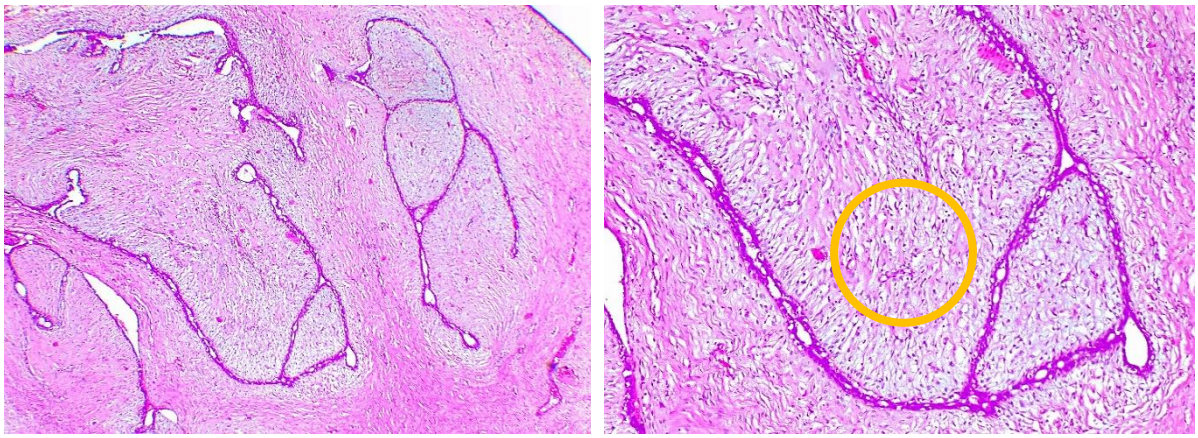

Figure 6. Intracanalicular pattern in 41-50 y.o patients (magnification, left 40x, right 100x)

Table 3. Chi-square Test

	Value	df	*p*
X^2	17,339	3	< 0,001
N	47		

Table 4. Odds Ratio

	Log Odds Ratio	95% Confidence intervals		*p*
		Lower	Upper	
Odds ratio	3,4	1,2	5,6	< 0,001
Fisher's exact test	3,3	1,1	7,2	

DISCUSSION

Most incidences of fibroadenoma occur in the 2nd and 3rd decades, although they can occur in all age groups. FAM is known as a biphasic tumor consisting of epithelial and stromal components[11]. It can be influenced by estrogenic factors, especially in adolescents[12]. Hypersensitivity to estrogen in the breast lobules is considered a trigger for nodules at 15-30 years old[13].

The highest estrogen levels in women are at ovulation and puberty, while estrogen levels will decrease after menopause, which can increase the incidence of FAM in women <30 years old[14]. According to the study of Tumidi et al., the average age of women affected by FAM was 23 years old[15].

A study showed that about 60% of fibroadenomas have MED12 mutations, mostly at codon 44 of exon 2, related to estrogen regulation and extracellular matrix organization[16]. Excessive estrogen stimulation, increased sensitivity of estrogen receptors, or decreased sensitivity of estrogen antagonists are considered to be the main factors causing the emergence of FAM during adolescence[17].

Most of the respondents in this study were <30 years old with 38 respondents (80.6%) and nine respondents (19.4%) aged >30 years. Saadaat et al. stated that the average age of diagnosis of FAM was between 20 and 30 years old[18]. Most cases of fibroadenoma occur

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before menopause, suggesting FAM is the most common breast mass in young women.

A total of 31 respondents (66%) with pericanalicular FAM growth patterns and intracanalicular FAM growth patterns participated in this study, 16 respondents (34%). The condition is probably caused by the hormone estrogen, which affects the proliferation of the breast lobular ductal epithelium[19]. Laxman et al. found that the most common type of FAM encountered, or around 84%, is pericanalicular[20].

Another influence that causes pericanalicular FAM most often appears because most of the histopathological features of FAM will appear as round or oval-shaped ducts. The connective tissue in intracanalicular FAM experienced more proliferation than canalicular FAM, so the gland was irregularly shaped with a narrow, star-like lumen[21]. Another characteristic of intracanalicular FAM that can be found is that the stroma compresses the ducts, and the ductal epithelium proliferates only slightly and produces a branching appearance[22].

According to Ansari et al., the incidence of fibroadenoma declines with age and is more likely to present as a complex or mixed histological hallmark of FAM (pericana-licular and intraarticular).[23] The condition was predicted due to changes in the FAM stroma to hyaline, myxoid degeneration, and ductal epithelial proliferation in most cases.

The pericanalicular pattern was the dominant pattern in 36 cases (65%), 11 other cases belonged to the intracanalicular pattern, and the remaining 8 cases were mixed growth patterns[11]. The proportion of mucus in the stroma increases with age, and hyperplasia in the ductal epithelium decreases; therefore, the intracanalicular type is rare in adolescents with FAM.

CONCLUSION

There is a significant difference in the incidence between pericanalicular and intracanalicular FAM in various age range, as shown in Table 3 (p <0,001). The incidence of pericanalicular and intracanalicular FAM in Siaga Medika Purbalingga Hospital patients in 2021 was obtained with a ratio of 31:16, or 66% pericanalicular FAM and 34% intracanalicular FAM, from a total of 47 patients. A further study must explain how external estrogen affects the incidence of FAM, especially in adolescents.

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