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Relationship between Breast Cancer Subtypes and Serum CA 15-3 Levels with the Incidence of Pleural Effusion in Breast Cancer Patients at Dr. M. Djamil General Hospital, Padang, Indonesia

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ABSTRACT

Background: Breast cancer is a disease that has a high incidence rate worldwide. Serum CA 15-3 levels have been used extensively as a tumor marker in breast cancer and can assist in early detection, monitoring of response to therapy, and monitoring of recurrence. This study aimed to evaluate whether there is a relationship between breast cancer subtypes and serum CA 15-3 levels with the incidence of pleural effusion in breast cancer patients at this hospital. **Methods:** This study was a cross-sectional observational study. A total of 176 research subjects participated in this study. Analysis of the relationship between breast cancer and CA 15-3 levels with pleural effusion was carried out univariate and bivariate using SPSS version 25. **Results:** The results showed that there was a significant relationship between CA 15-3 serum levels and the incidence of pleural effusion in breast cancer patients (p-value = 0.0001). There was no statistically significant relationship between breast cancer subtypes and the incidence of pleural effusion (p-value = 0.105). There was no relationship between serum CA 15-3 levels and the incidence of pleural effusion in breast cancer patients based on breast cancer subtype (p-value > 0.005). **Conclusion:** There is a significant relationship between serum levels CA 15-3 serum with the incidence of pleural effusion in breast cancer patients at Dr. M. Djamil General Hospital, Padang, Indonesia.

1. Introduction

Breast cancer is one of the most common types of cancer among women worldwide, including in Indonesia. Breast cancer is a disease that has a high incidence rate worldwide. The incidence of breast cancer can differ between countries, depending on factors such as the level of public awareness, accessibility of health services, and the risk factors present in a particular population. According to data from the International Agency for Research on Cancer

(IARC), in 2020, it is estimated that there will be around 2.3 million new cases of breast cancer worldwide. This number makes breast cancer the most common type of cancer suffered by women, both in developed and developing countries. In Indonesia, breast cancer is also a significant health problem. According to Globocan 2020, it is estimated that there were around 71,280 new cases of breast cancer in Indonesia that year. This figure places breast cancer as the most common type of cancer suffered by women

in Indonesia. The incidence of breast cancer also tends to increase over time.¹⁻⁵

Breast cancer can be classified into several subtypes based on their biological and molecular characteristics. This classification is important because each subtype has different characteristics, including response to treatment and prognosis. In addition, in the treatment of breast cancer, various parameters are also used to monitor disease progression and response to therapy. One such parameter is the serum CA 15-3 level, which is a tumor antigen that can be measured in the patient's blood. Serum CA 15-3 levels have been used extensively as a tumor marker in breast cancer and can assist in early detection, monitoring of response to therapy, and monitoring of recurrence. Pleural effusion, namely the accumulation of fluid in the pleural space surrounding the lungs, is one of the complications that can occur in patients with breast cancer. Pleural effusion can be a sign of the spread of cancer to other organs, including the lungs. The incidence of pleural effusion in breast cancer patients can affect the prognosis and patient management. Given the importance of understanding the relationship between breast cancer subtypes and serum CA 15-3 levels with the incidence of pleural effusion in breast cancer patients, this study was conducted at Dr. M. Djamil General Hospital, Padang, Indonesia.⁶⁻⁹ This study aimed to evaluate whether there is a relationship between breast cancer subtypes and serum CA 15-3 levels with the incidence of pleural effusion in breast cancer patients at this hospital.

2. Methods

This study was an analytic observational study with a cross-sectional approach and used secondary data sourced from the medical record installation of Dr. M. Djamil General Hospital, Padang, Indonesia. A total of 176 research subjects were included in this study, and the research subjects met the inclusion criteria. The inclusion criteria in this study were medical record data of patients diagnosed with breast

cancer at Dr. M. Djamil General Hospital, Padang, Indonesia, from 2020-2023 and complete data on medical records. This study was approved by the medical and health research ethics committee of the Faculty of Medicine, Universitas Andalas, No. 226/UN.16.2/KEP-FK/2023.

This study observed the sociodemographic data of the research subjects, including age, body mass index, history of contraception, and history of breastfeeding. This study also observed pathological data on the type of breast cancer cells, cancer stage, and the incidence of pleural effusion in the study subjects. Data analysis was carried out using SPSS software version 25. Data analysis was performed using univariate and bivariate methods. Univariate analysis was performed to present the frequency distribution of each data variable. Meanwhile, bivariate analysis was carried out to determine the relationship between the test variables, with a p-value <0.05.

3. Results

Table 1 shows the characteristics of the research sample. The results of the analysis showed that most age groups were ≥ 45 years (76.1%), normal BMI (44.9%), injectable birth control (36.4%), lactation (91.5%), and clinical stage IV (59, 7%). Based on molecular subtypes, the most common subtype, namely luminal B (49.4%), was followed by HER-2 positive (29%), TNBC (13,6%), and luminal A (8%). Percentage of patients with levels CA 15-3 serum normal (<30 U/mL) is 65.9%, and high serum levels (≥ 30 U/mL) is 34.1%. Then the results showed that patients with pleural effusion were 25.6%, while those without pleural effusion were 74.4%.

Table 2 shows that the incidence of pleural effusion was more in the subtype group TNBC (33.3%), followed by subtypes luminal B (28,7%), HER- 2+ (23.5%), and there was no incidence of pleural effusion in luminal A (0%). Statistical test results obtained p-value=0,105, meaning that there is no relationship between breast cancer subtypes and the incidence of pleural effusion at Dr. M. Djamil General Hospital, Padang, Indonesia

Table 1. Characteristics of breast cancer patients at Dr. M. Djamil General Hospital, Padang, Indonesia.

Characteristics	Frequency (f)	Percentage (%)
Age (years)		
<45 Years	42	23,9
≥45 Years	134	76,1
BMI		
Underweight	14	8,0
Normoweight	79	44,9
Overweight	61	34,7
Obesity	22	12,5
Contraception		
No birth control	50	28,4
Spiral	6	3,4
Pill	46	26,1
Inject	64	36,4
Implant	10	5,7
Lactation		
Yes	161	91,5
No	15	8,5
Clinical stage		
I	1	0,6
IIA	23	13,1
IIB	7	4,0
IIIA	36	20,5
IIIB	4	2,3
IV	105	59,7
Molecular subtype		
Luminal A	14	8,0
Luminal B	87	49,4
HER2+	51	29,0
TNBC	24	13,6
Serum CA 15-3 levels		
Normal (<30 U/mL)	116	65,9
High (≥30 U/mL)	60	34,1
Pleural effusion		
No	131	74,4
Yes	45	25,6

Table 2. Relationship between breast cancer subtypes and pleural effusion at Dr. M. Djamil General Hospital, Padang, Indonesia.

Subtype	Pleural effusion						P-value
	No		Yes		Total		
	f	%	f	%	f	%	
Luminal A	14	100	0	0	14	100	0,105
Luminal B	62	71,3	25	28,7	87	100	
HER-2+	39	76,5	12	23,5	51	100	
TNBC	16	66,7	8	33,3	24	100	

Table 3. Relationship between serum CA 15-3 levels and the incidence of pleural effusion at Dr. M. Djamil General Hospital, Padang.

Serum CA 15-3 levels	Pleural effusion						P-value
	No		Yes		Total		
	f	%	f	%	f	%	0,0001
Normal (<30 U/mL)	98	84,5	18	15,5	116	100	
High (≥30 U/mL)	33	55,0	27	45,0	60	100	

Table 3 shows that the incidence of pleural effusion is higher in the grade group CA 15-3 serum high, namely 45%, compared to levels CA 15-3 serum normal, equal to 15.5%. Statistical test results obtained p-value=0,0001, meaning that there is a

significant relationship between levels CA 15-3 serum with the incidence of pleural effusion in breast cancer patients Dr. M. Djamil General Hospital, Padang, Indonesia.

Table 4. Relationship between serum CA 15-3 levels with pleural effusion based on breast cancer subtype Dr. M. Djamil General Hospital, Padang, Indonesia.

Subtype	Serum CA 15-3 levels	Pleural effusion						P-value
		No		Yes		Total		
		f	%	f	%	f	%	
Luminal A	Normal	12	100	0	0	12	100	-
	High	2	100	0	0	2	100	
Luminal B	Normal	51	85,0	9	15,0	60	100	0,0001
	High	11	40,7	16	59,3	27	100	
HER-2+	Normal	27	84,4	6	15,6	32	100	0,101
	High	12	63,2	7	36,8	19	100	
TNBC	Normal	8	66,7	4	33,3	12	100	1,000
	High	8	66,7	4	33,3	12	100	

Table 4 shows that on the subtype luminal A, there was no incidence of pleural effusion. By subtype luminal B, the incidence of pleural effusion was more in the grade group CA 15-3 serum high (59.3%) compared to the serum CA 15-3 levels normally (15%). By subtype HER-2+, the incidence of pleural effusion was more in the grade group CA 15-3 serum high (36.8%) compared to the serum CA 15-3 levels normal (15.6%). Then based on the triple-negative subtype, the incidence of pleural effusion on the level CA 15-3 serum normal and high are the same (33.3%). The statistical test results showed that there was a

significant relationship between levels of CA 15-3 serum with the incidence of pleural effusion in breast cancer patients (p-value=0,0001). While there is no significant relationship between levels of CA 15-3 serum with the incidence of pleural effusion in breast cancer patients by subtype luminal A, HER-2, and TNBC (p-value>0,05).

4. Discussion

The relationship between breast cancer subtypes and the incidence of pleural effusion has been the subject of research and observation by medical

experts. Different subtypes of breast cancer may have differences in the likelihood of developing pleural effusions and may affect patient prognosis and management. B Several studies have identified an association between breast cancer subtypes and the incidence of pleural effusion. A study showed that a subtype of breast cancer known as triple-negative breast cancer (TNBC) has a higher risk of developing pleural effusion compared to other breast cancer subtypes. Triple-negative breast cancer is characterized by the absence of expression of the three main hormonal receptors (estrogen, progesterone, and HER2) and often has aggressive characteristics. In addition, studies have also observed that the incidence of pleural effusion is more common in patients with breast cancer whose metastases have spread to other organs, including the lungs. Metastasis is the process by which cancer cells spread from their original location to other parts of the body. If breast cancer has metastasized to the lungs, the risk of developing a pleural effusion increases.¹⁰⁻¹⁴

Several studies have shown a relationship between high serum CA 15-3 levels and the incidence of pleural effusion in breast cancer patients. Pleural effusion is a buildup of fluid in the pleural space that surrounds the lungs and can be an indication of the spread of breast cancer to the lungs or other organs. An elevated serum CA 15-3 levels may indicate the presence of a larger tumor or metastatic spread of breast cancer. Studies have shown that patients with breast cancer who develop pleural effusion tend to have higher serum CA 15-3 levels compared to patients without pleural effusion. Serum CA 15-3 levels may also be affected by other factors not associated with pleural effusion. Several non-cancerous conditions, such as liver disease, respiratory disease, and autoimmune diseases, can also cause elevated serum CA 15-3 levels. Therefore, the results of serum CA 15-3 tests need to be evaluated in a comprehensive clinical context and compared with other clinical findings.¹⁵⁻¹⁷

Breast cancer with positive hormone receptor expression (estrogen or progesterone) has

characteristics that are different from other subtypes. Several studies have shown that in patients with hormone receptor-positive breast cancer, high serum CA 15-3 levels may be associated with an increased risk of pleural effusion. Studies show that patients with hormone receptor-positive breast cancer who have high serum CA 15-3 levels may indicate lung metastases that can lead to pleural effusion. HER2-positive breast cancer is a subtype of breast cancer that has high expression of the HER2 gene. Several studies have shown that in patients with her2-positive breast cancer, a high serum CA 15-3 levels may be associated with a higher risk of pleural effusion. Triple-negative breast cancer is a subtype of breast cancer that does not express hormone receptors (estrogen and progesterone) and does not express HER2. Several studies have identified an association between high serum CA 15-3 levels and the incidence of pleural effusion in patients with triple-negative breast cancer.¹⁸⁻²⁰

5. Conclusion

There is a significant relationship between serum levels of CA 15-3 serum with the incidence of pleural effusion in breast cancer patients at Dr. M. Djamil General Hospital, Padang, Indonesia. There is no statistically significant relationship between breast cancer subtypes and the incidence of pleural effusion in patients with breast cancer at Dr. M. Djamil General Hospital, Padang, Indonesia.

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