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Relationship between Cholesterol Levels and Ca 15-3 Tumor Markers in Patients with *Carcinoma Mammae*

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Abstract
Breast cancer is the most common malignancy among women worldwide and remains a major cause of cancer-related mortality in Indonesia. Various risk factors, including hormonal, genetic, lifestyle, and metabolic factors, such as elevated cholesterol levels, have been associated with the development and progression of breast cancer. Cholesterol plays a crucial role in cell membrane formation and hormone synthesis, and recent studies have suggested its potential role in tumor growth and metastasis, particularly through the modulation of estrogen receptors and inflammatory pathways. CA 15-3 is a tumor marker widely used for monitoring breast cancer progression and recurrence. However, the correlation between cholesterol levels and CA 15-3 remains underexplored. The research objective is to determine the correlation between total cholesterol levels and the breast cancer tumor marker CA 15-3 in patients diagnosed with breast carcinoma at the Regional General Hospital of West Nusa Tenggara Province (RSUDP NTB). A cross-sectional analytic observational study was conducted using secondary data from the medical records of 33 breast carcinoma patients collected between January to November 2024. Cholesterol and CA 15-3 levels were analyzed using standard laboratory procedures. Data distribution was tested using the Kolmogorov-Smirnov test, and Pearson correlation analysis was applied to evaluate the relationship between cholesterol levels and CA 15-3. Showed that the mean cholesterol level was 214.24 mg/dL, and the mean CA 15-3 level was 41.55 U/mL, both exceeding normal reference values. Pearson correlation analysis demonstrated a very strong and statistically significant positive correlation between total cholesterol and CA 15-3 levels ($r = 0.940$, $p < 0.001$), indicating that higher cholesterol levels are associated with increased CA 15-3 concentrations. The study found a significant correlation between cholesterol levels and CA 15-3 in breast carcinoma patients, suggesting that cholesterol may influence tumor activity. Routine monitoring of cholesterol levels may be valuable in the clinical management of breast cancer, especially in assessing disease progression.

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INTRODUCTION

Cancer is a general term for malignant tumors or any uncontrolled growth of tissue or cells. Cancer cells grow rapidly and usually attack and damage other healthy cells. Cancer cells can spread through the bloodstream (hematogenous metastasis) and lymphatic system (lymphogenous metastasis) or lymph nodes. Cancer can spread to other organs. One of the most common types of cancer affecting women worldwide is breast cancer. Breast cancer is one of the most common types of cancer experienced by women worldwide. According to data from the World Health Organization (WHO), breast cancer accounts for approximately 24.5% of all cancer cases in women. Breast cancer in Indonesia is one of the most commonly diagnosed types of cancer, with a relatively high mortality rate. (Saputro & Pradana, 2022)

Breast cancer in Indonesia is a serious health issue, with 66,271 new cases reported. This figure places Indonesia as the eighth country with the highest number of breast cancer cases globally. The disease is also the leading cause of cancer-related deaths in Indonesia, with 22,598 deaths recorded. This places Indonesia fourth globally in terms of the highest number of deaths due to breast cancer (WCRF, 2023).

According to data from the West Nusa Tenggara Provincial Health Office in 2021, the number of women of childbearing age who underwent breast cancer screening reached 36,084, including: 601 in West Lombok, 309 in Central Lombok, 3,492 in East Lombok, 1,346 in Sumbawa, Dompu with 276 people, Bima with 1,576 people, West Sumbawa with 2,595 people, North Lombok with 24,053 people, and Bima City with 1,040 people. (Putri et al., 2024). The causes of breast cancer are multifactorial, involving various genetic, hormonal, lifestyle, dietary patterns high in lipids, and environmental factors. Some studies have shown a link between metabolic conditions, such as high cholesterol levels, and an increased risk of breast cancer (Saputro and Pradana, 2020).

The increasing prevalence of obesity also contributes to high cholesterol levels and the risk of breast cancer. Excess cholesterol not only plays a role in stimulating the growth of cancer cells, but can also affect the tumor microenvironment, increase inflammation, and facilitate the spread of cancer to other organs (metastasis) (Setiawati, 2021). Cholesterol levels have been identified as one of the factors influencing cancer. Cholesterol plays a role in the development of several types of cancer, including breast cancer. Cholesterol is an important lipid component for the body, particularly in the formation of cell membranes, steroid hormones, and vitamin D. Cholesterol levels can influence the development of breast cancer through several biological mechanisms, such as the role of cholesterol in cancer cell membranes. (Sugeng et al., 2023)

Cholesterol is a primary component of cell membranes that influences membrane fluidity and function. In cancer cells, high cholesterol levels can increase cell proliferation. Cholesterol is required to build new cell membranes during cell division, so cancer cells with high division activity require higher cholesterol levels and activate receptors on the cell membrane. Excess cholesterol can modulate signals at receptors such as estrogen receptors (ER), which play a crucial role in breast cancer. (Hidayat et al., 2023)

Elevated cholesterol levels in the blood, particularly low-density lipoprotein (LDL), can trigger various health issues, including cancer. Recent research indicates that cholesterol, such as 27-hydroxy cholesterol (27-HC), can act as an estrogen receptor agonist that stimulates breast cancer cell growth. This suggests that excess cholesterol can promote breast cancer cell proliferation, particularly in estrogen receptor-positive cancers (Smith et al., 2022). The findings of Kumie et al. (2020) indicate that cholesterol factors also play a role in the occurrence of cancer in women. Changes in serum lipid concentrations in breast cancer patients lead to increased production of tumor necrosis factor-alpha (TNF-α) and inhibition of adipose lipoprotein lipase activity by insulin. These changes disrupt the catabolism of very-low-density lipoprotein cholesterol.

Cholesterol is transported by low-density lipoprotein cholesterol (LDL-c) and high-density lipoprotein cholesterol (HDL-c). Abnormal serum levels of LDL-c and HDL-c are associated with breast cancer and are considered prognostic markers for breast tumors. Elevated total cholesterol (TC) and triglyceride (TG) levels stimulate cell proliferation and induce fibrosarcoma or may cause a decrease in sex hormone-binding globulin levels, which may increase the risk of breast cancer (Calhoun and Anderson, 2018). The test used for diagnosing breast cancer is CA 15-3 (Kumie et al., 2020).

CA 15-3 is a tumor marker specific to breast cancer, particularly for monitoring advanced disease and detecting recurrence. CA 15-3 has higher sensitivity for detecting breast cancer,

especially in advanced stages. CA 15-3 is often used to monitor therapy, detect early metastasis development, and is therefore more relevant for breast cancer patients. CA 15-3 produces identical cell nuclei and is overexpressed in breast cancer, making it a suitable tumor marker. This study is expected to serve as a scientific foundation for developing more comprehensive breast cancer prevention strategies, particularly through cholesterol level control.

METHOD

This study used an analytical observational study with a cross-sectional approach. Secondary data were obtained from the medical records of 33 breast cancer patients at RSUDP NTB during the period from January to November 2024. The data collected included total cholesterol levels (mg/dL) and CA 15-3 levels (U/mL). Normality tests were performed using Kolmogorov-Smirnov, and the relationship between variables was analyzed using Pearson's correlation test.

RESULTS AND DISCUSSION

Research Result

The results are shown in Table 1, relationship between Cholesterol Levels and Carcinoma Mammae (CA 15-3) Tumor Markers. A total of 33 patient data were collected from January to November 2024. The descriptive data results are shown in Table 1.

Table 1 Descriptive Data Results

		Statistics		
		Age	**CA 15.3 (U/mL)**	**Cholesterol Total (mg/dL)**
N	Valid	33	33	33
	Missing	0	0	0
Mean		50.06	41.552	214.24
Median		50.00	38.000	206.00
Minimum		38	22.6	158
Maximum		62	68.7	299

The results of the descriptive analysis of total cholesterol levels and CA 15-3 levels in 33 patients with breast cancer are shown in Table 1. From Table 1, the average age of the patients was 50 years, with the youngest being 38 years old and the oldest being 62 years old. CA 15-3 levels with an average level of 41.55 µ/ml, the highest level being 68.7 µ/ml, and the lowest level being 22.6 µ/ml, and total cholesterol levels with an average of 214.24 mg/dl, the lowest total cholesterol level being 158 mg/dl, and the highest being 299 mg/dl.

From the descriptive data in Table 1, the average total cholesterol level of patients exceeded the normal range, with a high threshold of 200–239 mg/dl and a normal range of <200 mg/dl. Meanwhile, the average CA 15-3 level exceeded the normal range, with a normal range of ≤30 mg/dl.

Before conducting the relationship analysis, a Kolmogorov-Smirnov test was performed to determine whether the data obtained was normally distributed. Table 2 shows the results of the Kolmogorov-Smirnov test. After performing the normality test, it was found that the data was normally distributed because the Asymp. Sig. (2-tailed) results of both variables were >0.05.

After that, the data will be tested with a Pearson correlation test to determine whether the total cholesterol level variable affects CA 15-3 and to determine the strength and direction of the relationship, whether it will be positive or negative. A positive relationship means that the

higher the total cholesterol level, the higher the CA 15-3 level, while a negative relationship means that an increase in total cholesterol will decrease the CA 15-3 level.

Table 2 Kolmogorov-Smirnov Test Results

One-Sample Kolmogorov-Smirnov Test

		CA 15.3 (U/mL)	Cholesterol Total (mg/dL)
N		33	33
Normal Parameters[a,b]	Mean	41.552	214.24
	Std. Deviation	13.5601	36.952
Most Extreme Differences	Absolute	.127	.103
	Positive	.127	.103
	Negative	-.081	-.064
Test Statistic		.127	.103
Asymp. Sig. (2-tailed)		.193[c]	.200[c,d]

a. Test distribution is Normal.

Table 3 Results of Pearson Correlation Test

Correlations

		CA 15.3 (U/mL)	Kolesterol Total (mg/dL)
CA 15.3 (U/mL)	Pearson Correlation	1	.940**
	Sig. (2-tailed)		.000
	N	33	33
Kolesterol Total (mg/dL)	Pearson Correlation	.940**	1
	Sig. (2-tailed)	.000	
	N	33	33

If < 0.05, then correlated
If > 0.05, then there is no correlation.

Table 3 shows the results of the Pearson statistical test to determine the relationship between total cholesterol levels and CA 15-3 levels. Table 3 shows a Sig. (2-tailed) value of 0.00<0.05, therefore, the results indicate that there is a relationship between total cholesterol levels and CA 15.3 levels.

DISCUSSION

In this study, the sample used was female patients with positive Ca. Mamae. According to Suparman et al., 2014, women have high levels of oestrogen and progesterone hormones, which are thought to contribute to the formation of tumour tissue. Although men are also at risk of developing breast cancer, most people affected by breast cancer are women because oestrogen and progesterone hormones are more dominant in women.

According to the study by Mirsyad et al. (2018), the average age of patients in this study was 50 years old. At the average age of women, most who are at risk of developing cancer are over 40 years old, so increasing age is one of the factors that can cause cancer. In this study, most patients with CA 15-3 levels above the normal range were those over 40 years of age.

Cholesterol is an important structural component of cell membranes that helps maintain both structural integrity and plasma membrane function. Cholesterol is also involved in cellular signalling pathways that aid in lipid formation in the plasma membrane, transporting high-concentration protein receptors to lower concentrations. This cellular signalling is closely

associated with malignant cell transformation, playing a role in the cytoskeleton, cell migration, and angiogenesis. Additionally, within cells, cholesterol functions as a precursor for the biosynthesis of steroid hormones, including the sex hormones progesterone and estrogen, which are important risk factors in the development of breast cancer (Jung et al., 2020).

High cholesterol levels, particularly low-density lipoprotein (LDL), are known to contribute to the development of breast cancer. This finding aligns with previous research showing that cholesterol can facilitate the growth and proliferation of cancer cells. Cholesterol is a primary component of cell membranes and influences membrane fluidity and function. Cancer cells with high division activity require more cholesterol to build new cell membranes during division (Sugeng et al., 2023).

In this study, most patients had cholesterol levels higher than the normal range (<200 mg/dL). High cholesterol levels are a risk factor identified in association with breast cancer. This study suggests that excess cholesterol may contribute to cancer cell growth, particularly through mechanisms involving estrogen receptors. CA 15-3 has higher sensitivity in advanced stages of breast cancer. This test is often used to detect recurrence and monitor treatment response, making it an important tool in the clinical management of breast cancer patients (Kurebayashi et al., 2004).

CA 15-3 is a tumour marker commonly used to monitor the progression of breast cancer. Normal CA 15-3 levels are typically ≤30 mg/dl, while study results indicate an average CA 15-3 level of 41.55 µ/ml in patients, suggesting a higher risk of cancer. These findings support the hypothesis that high cholesterol levels are associated with elevated CA 15-3 levels. The study results indicate that CA 15-3 levels in patients with high cholesterol levels also increase. This suggests that excess cholesterol may contribute to increased tumour activity.

The results of this study highlight the importance of monitoring cholesterol levels in the management of breast cancer patients. By monitoring cholesterol levels, healthcare professionals can detect the potential for more aggressive tumour growth earlier.

This study successfully demonstrated a significant association between cholesterol levels and the CA 15.3 tumour marker in patients with breast cancer. These results highlight the importance of monitoring cholesterol levels in the management of breast cancer and suggest the need for further research to explore the underlying mechanisms of this association. By understanding this association, it is hoped that more effective and comprehensive strategies for the prevention and treatment of breast cancer can be developed.

CONCLUSION

Based on the research results, it was concluded that the number of female breast cancer patients in 2024 at RSUDP NTB was 4,958 samples. The samples used in this study were 33 samples. The average cholesterol level of patients suspected of having breast cancer was 214.24 mg/dl. Meanwhile, the average Ca 15-3 level was 41.552 U/ml. The results of this study indicate a significant correlation between cholesterol levels and Ca 15-3 levels.

RECOMMENDATIONS

1. For Students

   The results of this study are expected to add to knowledge in the fields of clinical chemistry, serology, and cytology, particularly regarding cholesterol levels, CA 15-3 levels, and cytological findings in patients suspected of having breast cancer.

2. For Future Researchers

   Further research is needed on the relationship between electrolyte levels and breast cancer tumour markers.

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