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Correlation between Anxiety Level and CD8⁺ Cell Count in Breast Cancer Patients

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ABSTRACT

Cancer is the second leading cause of death in the world, with 9.6 million deaths each year. Many studies have shown that the prevalence of psychological distress among breast cancer patients is high, and they are at higher risk of developing anxiety and major depression. Prolonged stress and anxiety can affect one's immunity. CD8⁺ cells are immune cells that play an important role in destroying cancer cells. This study aims to determine the correlation of anxiety levels with the number of CD8⁺ cells in breast cancer patients. This study used analytic observation with a cross-sectional design in breast cancer patients from March to May 2024. Data were analyzed for normality test using Kolmogorov-Smirnov test and to determine the relationship between the two variables using Pearson test. HARS questionnaire was used to determine the level of anxiety, and BD FACS lyric tool to determine the number of CD8⁺ cells. Of the 30 respondents, the results showed that 30% of respondents did not experience anxiety (n=9) with an average CD8⁺ cell count of 518 cells/ μ L, 53% experienced mild anxiety (n=16) with an average CD8⁺ cell count of 484 cells/ μ L, and 17% experienced moderate anxiety with an average CD8⁺ cell count of 246 cells/ μ L. The results of statistical analysis of Pearson correlation is 0.077. This shows that there is no correlation between anxiety levels and CD8⁺ cell counts in breast cancer patients. The effect of anxiety on the immune system in breast cancer is very complex. So it requires additional research to explain completely.

Keywords: Breast Cancer, Anxiety, CD8⁺ Cells

INTRODUCTION

Cancer is the second leading cause of death in the world, causing 9.6 million deaths each year. An estimated 70% of cancer deaths occur in developing countries, including Indonesia. Based on Globocan data in 2020, new cases of cancer in Indonesia reached 396,914 cases with deaths reaching 234,511 people, and will continue to increase if no cancer prevention efforts are made (Ministry of Health, 2023).

Many studies have shown that most of the effector cells that play a role in anti-tumor mechanisms are CD8⁺ T cells, which are phenotypically and functionally identical to CTLs that play a role in killing virus-infected cells or allogeneic cells. Recent studies have shown that CD8⁺ T cells can inhibit tumor cell growth through

cytotoxic effects, especially for metastasized tumor cells (Siti Boedina, 2011).

Many studies have shown that the prevalence of psychological distress among breast cancer patients is high, and they are at higher risk of developing anxiety and major depression. As known, the diagnosis and treatment of breast cancer cases can be a very stressful issue during and after treatment. It is very important to take early action to overcome these psychosocial problems in breast cancer patients and their partners so as to improve their quality of life (Alagizy et.al., 2020).

Research conducted by Katty Cooper, et al. in the UK in 2023 show that there are relationship between stress, depression or anxiety with cancer

concluded that there is consistent evidence of an association between psychological stress, depression or anxiety with cancer incidence in the population. In addition, there are some evidence of a positive correlation between psychological stress, depression or anxiety and the number of deaths in cancer populations.

Suppression of various aspects of protective immunity caused by chronic stress increases susceptibility to cancer. Research conducted by Michael H. Antoni and Firdaus S. Dhabhar in 2019 found that tumor severity is one of the effects of high anxiety, and can be exacerbated by life stressors, cancer diagnosis, and treatment-related stress. This can contribute to increased metastatic progression of the tumor.

Prolonged stress and anxiety will affect HPA (hypothalamus pituitary adrenal) axis. This results is increasing secretion of Corticotropine Releasing Hormone (CRH) which will further stimulate an increase in Glucocorticoid and Catecholamine. Glucocorticoid and catecholamine receptor interactions are involved in the development of cancer, namely tumorigenesis and angiogenesis. The mechanism of tumorigenesis occurs through genomic instability, DNA damage, reactivation of latent oncogenic infections, increased regulation of oncogenes and malignant transformation in stem cells. While the mechanism of angiogenesis will result in tumor progression characterized by the presence of Tumor Microenvironment (TEM).

In TEM, regulatory T cells and Myeloid Derived Suppressor Cells (MDSC) can suppress the immune response and result in decreased antitumorigenic immune cells (CD8⁺). So that high levels of anxiety can be associated with a decrease in the number of CD8⁺ T cells as immune cells that fight cancer cells. Based on the description above, this study was conducted to determine the correlation of anxiety levels with the number of CD8⁺ cells in breast cancer

patients.

RESEARCH METHOD

The type of research conducted was analytic observational with a cross sectional design. The inclusion criteria for this study were breast cancer patients who were undergoing chemotherapy treatment aged 20-65 years from March to May 2024. The number of samples used was 30 respondents. For the participation of patients in the study, they expressed their consent by filling out an informed consent form. Data were entered into Microsoft excel 2019 and analyzed using SPSS.

Then data were described in percentage (%) for categorical distribution data. The normality test used Kologrov smirnov test and Pearson test to analyze the correlation of anxiety level with CD8⁺ cell count in breast cancer patients. The research protocol was approved by the Ethics Committee of the Surabaya Ministry of Health Polytechnic (Certificate of approval no.EA/2206/KEPK-Poltekkes_Sby/V/2024) prior to the implementation of the study.

RESULT AND DISCUSSION

Of the 30 respondents, it was found that 30% of respondents did not experience anxiety (n=9) with an average CD8⁺ cell count of 518 cells/μL, 53% experienced mild anxiety (n=16) with an average CD8⁺ cell count of 484 cells/μL, and 17% experienced moderate anxiety with an average CD8⁺ cell count of 246 cells/μL. Significance value of pearson correlation statistical is 0.077. This shows that there is no correlation between anxiety levels and CD8⁺ cell counts in breast cancer patients.

Table 1. General description of research subjects

Anxiety Level	CD8 ⁺ Cell Count	Frequency (n)	Percentage (%)	Average
No Anxiety	Normal : 190 – 1140 cells/μ	9	30%	518 cells/μL

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Mild Anxiety	Normal : 190 – 1140 cells/μL	16	53%	484 cells/μL
	L			
Moderate Anxiety	Low : <190 sel/μL	2	7%	
	Normal : 190 – 1140 cells/μL	3	10%	246 cells/μL
Total		30	100%	454 cells/μL
Min		71 cells/μL		
Max		944 cells/μL		

The correlation test results concluded that there was no significant correlation between anxiety level and CD8⁺ cell count. This can happen because the number of CD8⁺ cells in breast cancer patients is influenced by several factors, including immunosuppression due to several chemotherapy drugs and variability in the chemotherapy cycle. So that the number of CD8⁺ cells in breast cancer patients with the same level of anxiety is very fluctuating.

Chemotherapy is a therapy used to kill cancer cells, but on the other hand chemotherapy can damage healthy cells, including immune cells. One of the significant impacts of chemotherapy is immunosuppression, which is a decrease in the immune system's ability to fight infection and disease. In addition, chemotherapy can damage precursor cells in the bone marrow that are responsible for producing different types of blood cells, including T lymphocytes. As a result, the production and differentiation of new CD8⁺ cells may be reduced, leading to a decrease in the number of CD8⁺ cells in circulation. This is in line with research conducted by Oishi Mukherjee, et al in 2023 that some chemotherapy drugs such as Cyclophosphamide can affect the immune system directly. Cyclophosphamide is an

alkylating agent that damages the DNA of dividing cells, including immune cells such as CD8⁺ cells. So chemotherapy with Cyclophosphamide in the first cycle will result in a 50% decrease in the number of CD8⁺ cells in the periphery, and the number of CD8⁺ cells does not recover after three cycles of chemotherapy. However, Cyclophosphamide has a positive effect in the TME (Tumor Microenvironment) environment, namely Cyclophosphamide inhibits regulatory T cells. Regulatory T cells are immune cells that play an important role in maintaining the balance and function of the immune system. So the inhibition of regulatory T cells results in CD8⁺ cells being more active and effective against cancer cells in TME.

Variability in chemotherapy cycles can also affect the number of CD8⁺ cells in breast cancer patients. More advanced cycles are likely to have a greater cumulative effect on immunosuppression. In addition, individual response to chemotherapy, as well as the health status of other medical conditions such as nutritional status and infections may affect CD8⁺ cell counts.

Descriptive data analysis showed different results from statistical analysis using Statistical Package for the Social Sciences (SPSS). In the table of general description of the results of the study, it was found that the average number of CD8⁺ in respondents who did not experience anxiety was higher than those who experienced mild and moderate anxiety. As the anxiety level increases, the average CD8⁺ count decreases. This indicates a negative impact of anxiety on the body's immune response.

In the general description table of the research results there is a min value of 71 cells/μL. These results are very much different from the results of other respondents in the same chemotherapy cycle group. These results came from respondents who experienced moderate anxiety. This is in line with psychoneurology that prolonged stress and anxiety can cause worsening of cancer so it

can reduce the number of CD8⁺ cells. The results of this study can be used as a reference for preventive measures to prevent a decrease in the number of CD8⁺ cells in breast cancer patients undergoing chemotherapy. One of the actions is to provide social support to breast cancer patients to remain enthusiastic about undergoing treatment. Social support is important to prevent increased anxiety from becoming more severe. With comprehensive treatment, breast cancer patients have the opportunity to recover faster. In this study, researchers did not study the nutritional status, infection, chemotherapy drugs and variability of chemotherapy cycles in respondents. So the low CD8⁺ cell count in some patients cannot be explained and more research is needed to explain more fully.

CONCLUSION AND RECOMMENDATION

There is no correlation between anxiety level and CD8⁺ cell count in breast cancer patients. The number of CD8⁺ cells in the body is influenced by many factors. More research is needed to analyze subgroups based on variables such as type of chemotherapy drugs, duration of treatment, and other medical conditions to understand how each of these factors affects the relationship between anxiety and CD8⁺ cell count.

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