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Analysis of the Role of Age Factors on Hemoglobin, Leukocyte and Platelet Levels in Breast Cancer Patients Post Chemotherapy 3 Cycles at Dr. Mohammad Hoesin General Hospital, Palembang, Indonesia

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A B S T R A C T

Introduction: Breast cancer is one of the most common cancers in women. Chemotherapy is one of the main modalities in the treatment of breast cancer, but it can cause hematological side effects such as anemia, leukopenia, and thrombocytopenia. Age is one factor that is thought to influence these side effects. **Methods:** This study used an analytical observational design with data collected from medical records of breast cancer patients who had undergone 3 cycles of chemotherapy at Dr. Mohammad Hoesin General Hospital Palembang. Data on hemoglobin, leukocyte, and platelet levels before and after chemotherapy were analyzed using the t-test and ANOVA. **Results:** A significant decrease in hemoglobin levels was observed in patients aged > 60 years after chemotherapy ($p < 0.05$). Leukocyte levels showed fluctuations, especially in patients aged <40 years, while platelet levels fluctuated more in patients aged <40 years and decreased in the age group 40-60 years after chemotherapy. **Conclusion:** Age does not significantly influence the decrease in hemoglobin, leukocyte, and platelet levels in breast cancer patients after chemotherapy.

1. Introduction

Breast cancer is one of the most common cancers in women, with an increasing incidence. In Indonesia, breast cancer is the first cancer in women, with an estimated 65,858 new cases and 30,935 deaths in 2020. Chemotherapy is one of the main modalities in treating breast cancer and has been proven to be effective in increasing patient life expectancy. Chemotherapy works by killing cancer cells that are actively dividing. However, chemotherapy can also damage healthy cells in the body, including blood cells in the bone marrow. The most common hematological side effects that occur in breast cancer patients undergoing chemotherapy are anemia, leukopenia, and thrombocytopenia. Anemia is a condition where there is a lack of red blood cells that carry oxygen throughout the body. Anemia can cause fatigue, shortness of breath, and dizziness. Leukopenia is a condition where there is a lack of white blood cells that fight infection. Leukopenia can increase the risk of infection. Thrombocytopenia is a condition where there is a lack of platelets that help blood clot. Thrombocytopenia can increase the risk of bleeding.[1-3]

Age is one of the factors that is thought to influence hematological side effects in breast cancer patients

undergoing chemotherapy. Older patients may be more susceptible to these side effects due to several factors, including decreased bone marrow function that occurs with age, the presence of comorbidities that can worsen the side effects of chemotherapy, and a decrease in the body's ability to detoxify chemotherapy drugs.[4,5] This study aims to analyze the role of age factors on hemoglobin, leukocyte, and platelet levels in breast cancer patients post chemotherapy 3 cycles at Dr. Mohammad Hoesin General Hospital, Palembang, Indonesia.

2. Methods

This study used an analytical observational design with data collected retrospectively from patient medical records. The study population was breast cancer patients who had undergone 3 cycles of chemotherapy at Dr. Mohammad Hoesin General Hospital Palembang. The research sample was 106 breast cancer patients who met the inclusion and exclusion criteria. The inclusion criteria for this study are breast cancer patients who have undergone 3 cycles of chemotherapy at Dr. Mohammad Hoesin General Hospital Palembang, have complete data on hemoglobin, leukocyte, and platelet levels before and after chemotherapy, and are willing to provide informed consent. Meanwhile, the exclusion criteria are patients with comorbid diseases that can affect hemoglobin, leukocyte, and platelet levels, as well as patients who are pregnant or breastfeeding.

Data was collected from patient medical records using a data collection sheet containing patient demographic data (age, gender) as well as data on hemoglobin, leukocyte, and platelet levels before and after chemotherapy. Data were analyzed using the SPSS version 25 program. The t-test was used to compare hemoglobin, leukocyte, and platelet levels before and after chemotherapy. The ANOVA test was used to analyze the relationship between patient age and hemoglobin, leukocyte, and platelet levels. This research was approved by the Health Research Ethics Committee of Dr. Mohammad Hoesin General Hospital Palembang. Informed consent was obtained from all patients participating in this study.

3. Results

Table 1 shows that of the 106 respondents, 9 people (8.5%) were under 40 years old, 88 people (83%) were between 40-60 years old, and 9 people (8.5%) were 60 years old or more. This age distribution shows that breast cancer can affect women in all age groups, although it is more common in older women. All respondents (100%) were women. This shows that breast cancer is a disease that almost exclusively attacks women. Men can get breast cancer, but the cases are very rare. A total of 72 respondents (67.9%) were married, 24 people (22.6%) were single, and 10 people (9.5%) were widows. Marital status does not appear to have a significant influence on breast cancer risk. A total of 12 respondents (11.3%) had no school or only completed elementary school education, 58 people (54.7%) completed secondary school or high school, 28 people (26.4%) had a diploma or bachelor's degree, and 8 people (7.6%) had a master's or doctoral degree. Higher levels of education appear to be associated with a lower risk of breast cancer, although more research is needed to confirm this association. A total of 42 respondents (39.6%) did not work, 38 people (35.9%) were housewives, 18 people (17.0%) were private employees, and 8 people (7.5%) were civil servants/TNI/Polri. Type of employment does not appear to have a significant influence on breast cancer risk. Table 1 provides an overview of the population studied in this study. Data shows that breast cancer can affect women in all age groups, although it is more common in older women. Marital status, education, and employment do not appear to have a significant influence on breast cancer risk.

Table 1. Characteristics of respondents.

Characteristics	Category	Frequency	Percentage (%)
Age	<40 years	9	8.5%
	40-60 years	88	83%
	>60 years	9	8.5%
Gender	Female	106	100%
Marital status	Married	72	67.9%
	Single	24	22.6%
	Widow	10	9.5%
Education	No school/primary school	12	11.3%
	Junior high school/Senior high school	58	54.7%
	Diploma/Bachelor's degree	28	26.4%
	Master's degree/Doctoral degree	8	7.6%
Occupation	Not working	42	39.6%
	Housewife	38	35.9%
	Private employee	18	17.0%
	Civil servants/TNI/Polri	8	7.5%

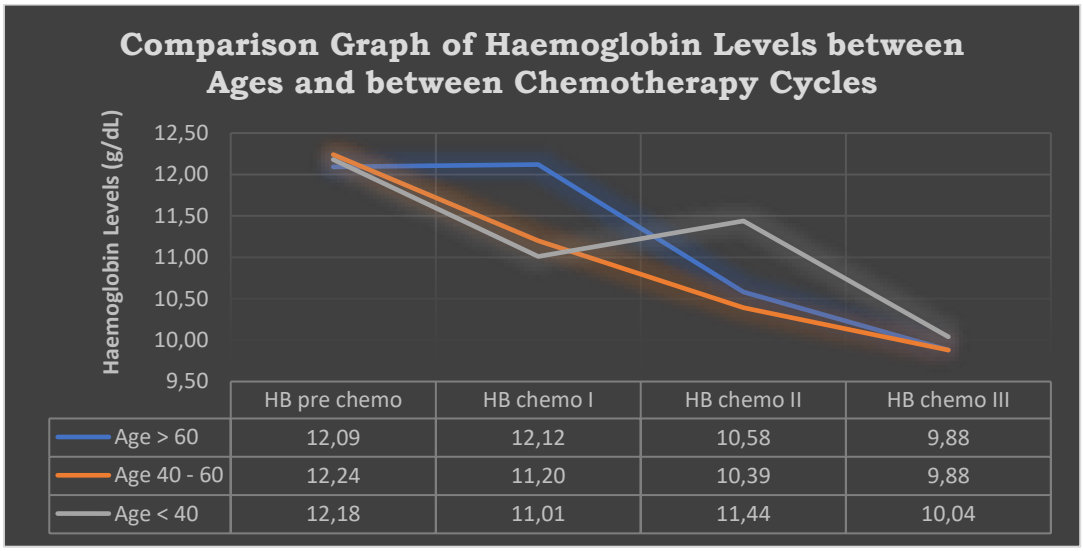
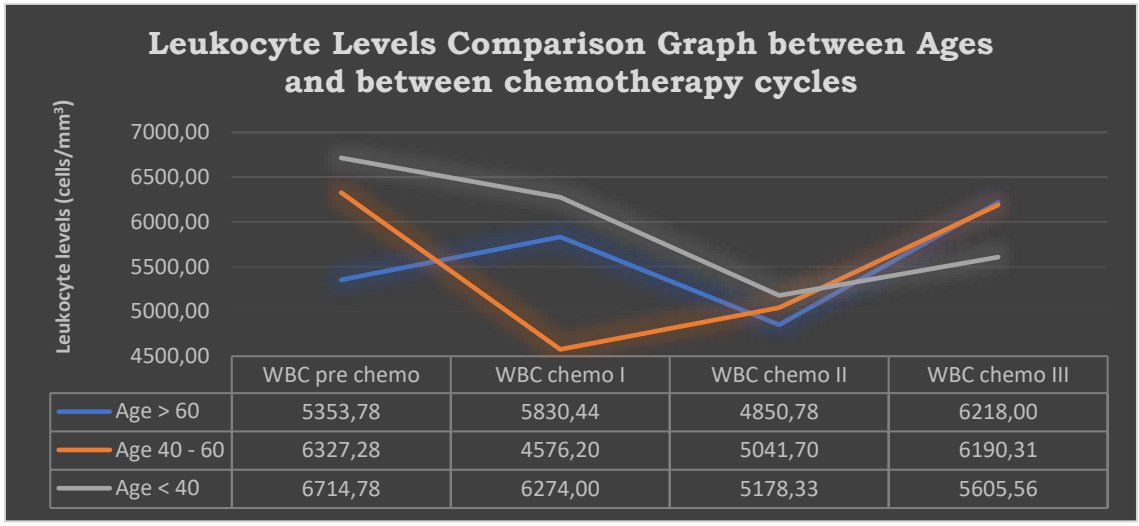


Figure 1. Comparison of hemoglobin levels between ages and between chemotherapy cycles.

Figure 1 shows the comparison of hemoglobin levels between ages and between chemotherapy cycles in patients undergoing chemotherapy. There was a decrease in Hb levels in all age groups after undergoing chemotherapy. This decline was most significant in the 40-60 year age group. Hb levels pre-chemotherapy and after chemotherapy cycle I was higher in the age group > 60 years compared to other age groups. Hb levels tend to decrease as the chemotherapy cycle increases. Chemotherapy can cause a decrease in Hb levels in breast cancer patients. The most significant decrease in Hb levels was in the 40-60-year age group. Patients aged > 60 years have higher Hb levels than other age groups. Hb levels tend to decrease as the chemotherapy cycle increases. In all age groups, the average hemoglobin level decreased from cycle I to

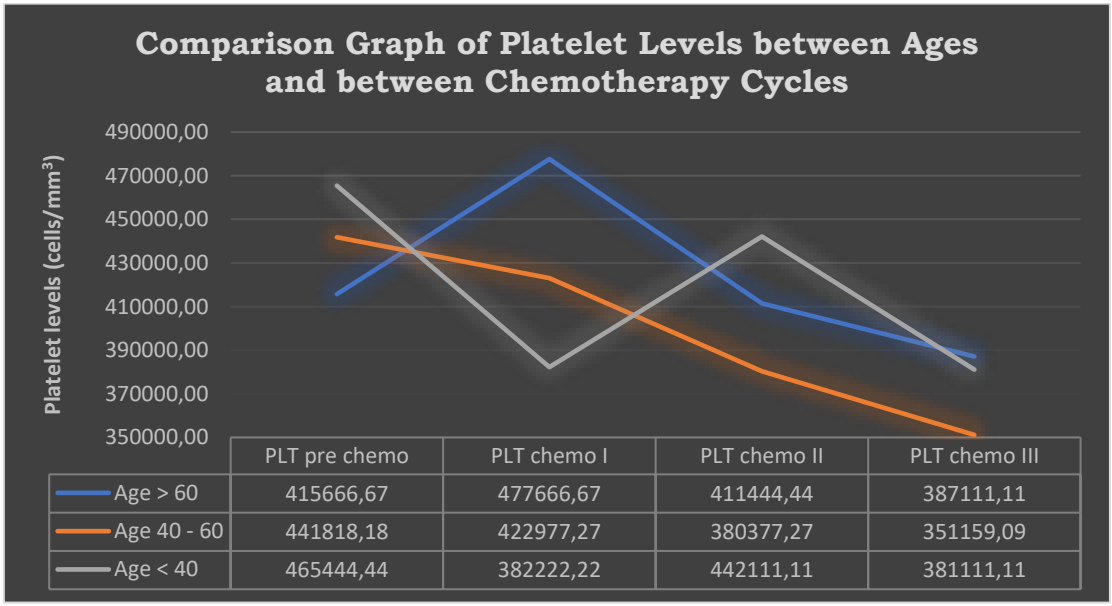
cycle III. The most significant decrease in hemoglobin levels occurred in cycle I to cycle II. The decrease in hemoglobin levels in cycle II to cycle III was relatively smaller than in cycle I to cycle II. Hemoglobin levels generally decrease with increasing age. Chemotherapy can reduce hemoglobin levels. The most significant decrease in hemoglobin levels occurred in cycle I of chemotherapy.



	WBC pre chemo	WBC chemo I	WBC chemo II	WBC chemo III
Age > 60	5353,78	5830,44	4850,78	6218,00
Age 40 - 60	6327,28	4576,20	5041,70	6190,31
Age < 40	6714,78	6274,00	5178,33	5605,56

Figure 2. Comparison of leukocyte levels between ages and between chemotherapy cycles.

Figure 2 shows fluctuations in leukocyte levels in all age groups after undergoing chemotherapy. These fluctuations are most significant in the 40-60 year age group. Leukocyte levels pre-chemotherapy and after chemotherapy cycles I and III were higher in the age group > 60 years compared to other age groups. Leukocyte levels tend to fall in cycle II and then rise again in cycle III. Chemotherapy can cause fluctuations in leukocyte levels in breast cancer patients. Fluctuations in leukocyte levels were most significant in the 40-60 year age group. Patients aged > 60 years had higher leukocyte levels than other age groups in cycles I and III. Leukocyte levels tend to fall in cycle II and then rise again in cycle III.



	PLT pre chemo	PLT chemo I	PLT chemo II	PLT chemo III
Age > 60	415666,67	477666,67	411444,44	387111,11
Age 40 - 60	441818,18	422977,27	380377,27	351159,09
Age < 40	465444,44	382222,22	442111,11	381111,11

Figure 3. Comparison of platelet levels between ages and between chemotherapy cycles.

Figure 3 shows a decrease in platelet levels in all age groups after undergoing chemotherapy. This decline was most significant in the 40-60 year age group. Platelet levels pre-chemotherapy and after chemotherapy cycles, I and II were higher in the age group > 60 years compared to other age groups. Platelet levels tend to decrease as chemotherapy cycles increase. Chemotherapy can cause a decrease in platelet levels in breast cancer patients. The most significant decrease in platelet levels was in the 40-60-year age group. Patients aged > 60 years had higher platelet levels than other age groups in cycles I and II. Platelet levels tend to decrease as chemotherapy cycles increase.

Table 2. Statistical analysis of age groups with hemoglobin, leukocyte, and platelet levels.

Parameter	**Pre chemotherapy**	**Post chemotherapy I**	**Post chemotherapy II**	**Post chemotherapy III**
Hemoglobin	p = 0,972	p = 0,142	p = 0,162	p = 0,964
Leukocytes	p = 0,872	p = 0,426	p = 0,987	p = 0,866
Platelets	p = 0,751	p = 0,337	p = 0,227	p = 0,731

Table 2 shows the results of the analysis of the relationship between age group and hemoglobin, leukocyte, and platelet levels in breast cancer patients, both before and after chemotherapy. There was no significant relationship between the age group and pre-chemotherapy hemoglobin levels (p = 0.972). There was no significant relationship between age group and post-chemotherapy hemoglobin levels I (p = 0.142), II (p = 0.162), and III (p = 0.964). There was no significant relationship between the age group and pre-chemotherapy leukocyte levels (p = 0.872). There was no significant relationship between age group and post-chemotherapy leukocyte levels I (p = 0.426), II (p = 0.987), and III (p = 0.866). There was no significant relationship between the age group and pre-chemotherapy platelet levels (p = 0.751). There was no significant relationship between age group and post-chemotherapy platelet levels I (p = 0.337), II (p = 0.227), and III (p = 0.731). Based on the results of the analysis, there was no significant relationship between age group and hemoglobin, leukocyte, and platelet levels in breast cancer patients, either before or after chemotherapy.

4. Discussion

Hematopoiesis is the process of forming blood cells in the bone marrow. This process begins with hematopoietic stem cells, which then differentiate into various types of blood cells, including red blood cells (erythrocytes), white blood cells (leukocytes), and platelets. Age can influence hematopoiesis in several ways. First, the bone marrow becomes less active as we age. This causes a decrease in the production of all types of blood cells. Second, hematopoietic stem cells in the elderly are more susceptible to damage due to oxidative stress and radiation. This damage can cause a decrease in blood cell production. Several studies have shown that age is a risk factor for anemia in breast cancer patients undergoing chemotherapy. A study found that breast cancer patients aged 65 years or older had twice the risk of developing anemia compared to younger patients. Another study found that breast cancer patients aged 70 years or older had three times the risk of developing anemia compared to younger patients.[6-8]

Hematopoietic stem cells are very important cells in the human circulatory system. Apart from their numbers decreasing with age, hematopoietic stem cells in the elderly also face other challenges. As we age, hematopoietic stem cells not only decrease in number, but their quality also decreases. They become less efficient at producing new blood cells, so the overall production of red and white blood cells and platelets decreases. Exposure to harmful substances from the environment, such as pollutants and cigarette smoke, can damage the DNA of hematopoietic

stem cells in the elderly more easily than at a young age. The ability of hematopoietic stem cells to respond to stress, such as infection or bleeding, is also reduced in the elderly. This has an impact on the slow regeneration of blood cells to compensate for this condition. The combination of these factors causes the elderly's bone marrow to be less able to produce blood cells in the quantities the body needs, thereby increasing the risk of anemia and other blood disorders.[9,10]

The bone marrow microenvironment is a complex environment consisting of various cells, proteins, and molecules that interact with each other to support the growth and development of blood cells. This microenvironment is analogous to fertile "soil" for blood cell "seeds" (hematopoietic stem cells) to grow and develop into mature blood cells. An optimal bone marrow microenvironment has several characteristics. Bone marrow needs an adequate blood supply to provide oxygen and nutrients for developing blood cells. The extracellular matrix is a network of proteins that supports blood cells and provides signals that are important for their growth and development. Stromal cells are the cells that form the bone marrow microenvironment. These cells produce various proteins and molecules that are important for the growth and development of blood cells. The immune system must be able to protect the bone marrow from infection but must not attack the developing blood cells. The bone marrow microenvironment becomes less optimal with age. Bone marrow vascularization decreases with age. This causes a decrease in the supply of oxygen and nutrients to the developing blood cells. The extracellular matrix becomes stiffer and less supportive with age. This can interfere with the growth and development of blood cells. Stromal cells become less active and produce fewer proteins and molecules that are important for the growth and development of blood cells. The immune system becomes weaker and more susceptible to infection. This can increase the risk of bone marrow damage. Decreased function of the bone marrow microenvironment with increasing age can cause various problems in the hematopoietic system. Decreased red blood cell production can cause anemia, while decreased white blood cell production can increase the risk of infection. Blood cells produced by aging bone marrow may not function properly. This can increase the risk of complications, such as bleeding and infection. An optimal bone marrow microenvironment is essential for the growth and development of blood cells. This microenvironment becomes less optimal with age, which can cause various problems in the hematopoietic system.[11-13]

Leukocytes are white blood cells that play an important role in the immune system. Fluctuations in leukocyte levels can occur in all age groups, including breast cancer patients. Leukocyte levels in the body are regulated by various factors. Bone marrow constantly produces new leukocytes. Leukocytes are released from the bone marrow into the bloodstream when needed to fight infection or disease. Leukocytes circulate throughout the body and accumulate in places where they are needed. Old or damaged leukocytes are destroyed by the spleen and liver. Several studies have shown that fluctuations in leukocyte levels occur in all age groups, including breast cancer patients. A study found that leukocyte levels in breast cancer patients can fluctuate significantly from day to day. A study found that leukocyte levels in breast cancer patients can fluctuate depending on the stage of the cancer and the type of treatment received.[14,15]

Chemotherapy is one of the main treatments for cancer. Chemotherapy works by killing cancer cells that multiply rapidly. However, chemotherapy can also damage healthy cells in the body, including cells in the bone marrow. Bone marrow is the soft tissue found in bone cavities. This tissue is responsible for producing all types of blood cells, including white blood cells (leukocytes). Leukocytes play an important role in the immune system in fighting infection. Chemotherapy can damage cells in the bone marrow, including cells that produce leukocytes. This can cause neutropenia, which is a condition where leukocyte levels fall below normal. Neutropenia increases the risk of infection in cancer patients. Breast cancer patients are more

susceptible to infection due to several factors. Chemotherapy can damage white blood cells, including cells that play a role in fighting infection. This can cause neutropenia, which is a condition where leukocyte levels fall below normal. Corticosteroids are drugs that are often used to reduce inflammation and the side effects of chemotherapy. Corticosteroids can suppress the immune system and increase the risk of infection. Breast cancer surgery can damage tissue and make the body more susceptible to infection. An intravenous (IV) catheter is a tube inserted into a vein to administer medicine or fluids. IV catheters can harbor bacteria and increase the risk of infection. Neutropenic fever infection is a serious infection that can occur in patients with neutropenia. This infection can occur in various parts of the body, such as the lungs, skin, and digestive tract. Urinary tract infections are infections that often occur in breast cancer patients who use IV catheters. Skin and soft tissue infections can occur in breast cancer patients undergoing surgery.[16,17]

Stress is the body's natural response to challenging or dangerous situations. When the body experiences stress, the sympathetic nervous system is activated, which triggers the release of various hormones, including stress hormones such as adrenaline and cortisol. This stress hormone can increase the release of leukocytes from the bone marrow into the bloodstream through several mechanisms. Bone marrow stores reserves of leukocytes that can be released into the bloodstream when needed. Stress hormones can mobilize these leukocyte reserves by increasing the production and release of granulocyte colony-stimulating factors (G-CSF) and macrophages (M-CSF). Stress hormones can increase leukocyte adhesion to endothelial cells in blood vessels. This allows leukocytes to exit the bloodstream and migrate to stressed tissues. Stress hormones can increase leukocyte production in the bone marrow by stimulating the proliferation and differentiation of hematopoietic progenitor cells. The release of leukocytes from the bone marrow into the bloodstream is an important part of the body's immune response. Leukocytes mobilized to stressed tissue can help fight infection and clean damaged tissue. Chronic stress can cause a sustained increase in leukocyte levels. Elevated leukocyte levels can increase the risk of atherosclerosis and thrombosis. Elevated leukocyte levels can increase insulin resistance and the risk of type 2 diabetes. Elevated leukocyte levels can increase the risk of certain cancers, such as breast cancer and colorectal cancer. Stress can increase the release of leukocytes from the bone marrow into the bloodstream. The release of leukocytes is an important part of the body's immune response. However, chronic stress can cause a sustained increase in leukocyte levels, which can increase the risk of various diseases.[15-17]

Platelets are blood cells that play an important role in blood clotting. Decreased platelet levels (thrombocytopenia) can occur in breast cancer patients undergoing chemotherapy. Platelet levels in the body are regulated by various factors. Bone marrow constantly produces new platelets. Old or damaged platelets are destroyed by the spleen and liver. Platelets are consumed when blood clots occur. Several studies have shown that the reduction in platelet levels is more significant in the 40-60-year age group than in other age groups in breast cancer patients undergoing chemotherapy. A study found that breast cancer patients aged 40-60 years had twice the risk of experiencing thrombocytopenia compared to younger or older patients. Another study found that breast cancer patients aged 40-60 years had three times the risk of experiencing thrombocytopenia compared to younger or older patients.[16-18]

Chemotherapy drugs work by killing the developing cancer cells. However, these drugs can also damage healthy cells, including cells in the bone marrow. Bone marrow damage can cause a decrease in the production of red blood cells, white blood cells, and platelets. Some types of chemotherapy drugs are more toxic to the bone marrow than others. This more toxic type of chemotherapy drug is more often used in patients aged 40-60 years. Patients aged 40-60 years more often suffer from more aggressive cancers that

require stronger treatment. Patients aged 40-60 years generally have fewer comorbidities than older patients, so they can tolerate stronger treatment. Patients aged 40-60 years generally have better recovery abilities than older patients, so they can recover from the side effects of chemotherapy more quickly. Patients receiving these more toxic types of chemotherapy drugs should be closely monitored for side effects, such as anemia, leukopenia, and thrombocytopenia. Types of chemotherapy drugs that are more toxic to the bone marrow are more often used in patients aged 40-60 years. Patients receiving this type of chemotherapy drug should be closely monitored for side effects and receive optimal supportive care.[17-19]

Patients aged 40-60 years more often receive higher chemotherapy doses than younger or older patients due to several factors. Patients aged 40-60 years generally have better physical capacity than older patients. This allows them to tolerate a higher level of chemotherapy side effects. Patients aged 40-60 years generally have faster drug metabolism than older patients. This allows them to clear chemotherapy drugs from their bodies more quickly, allowing higher doses to be administered. Patients aged 40-60 years generally have a lower risk of comorbidities than older patients. This allows them to receive higher doses of chemotherapy without increasing the risk of complications. In general, cancer in patients aged 40-60 years is more aggressive than in older patients. This requires higher chemotherapy doses to achieve optimal treatment results. Patients aged 40-60 years may have more treatment options than older patients. This allows them to choose a more intensive chemotherapy regimen with higher doses.[18-20]

5. Conclusion

Age has no effect on the decrease in hemoglobin, leukocyte, and platelet levels in breast cancer patients after chemotherapy. However, chemotherapy has a significant effect on hemoglobin, leukocyte, and platelet levels.

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