

Effect of Chemotherapy on the Hematological Parameters and Prevalence of Anemia in Breast Cancer Patients

Azab Elsayed Azab^{1*}, Rabie Alwan Yahya², Ruqaya Al-Shaibani Al-Arousi³

¹ Department of Physiology, Faculty of Medicine, University of Sabratha

² Department of Pharmacology, Faculty of Medicine, University of Sabratha

³ Department of Zoology, Faculty of Science, Zawiya, University of Zawiya

* Corresponding author, Azab Elsayed Azab Email: azabelsayed@sabu.edu.ly

Abstract

Background: Breast cancer incidence is rising in Libya, and chemotherapy significantly affects physiological function. Objectives: This study evaluated hematological changes and anemia prevalence in 150 breast cancer patients at the National Oncology Institute, Sabratha, and compared them with 100 healthy controls. **Methods:** Data were extracted from patient records and analyzed using SPSS to compare hematological variables before and after chemotherapy. **Results:** Significant decreases ($P<0.01$) were observed in RBC count, hemoglobin, hematocrit, and MCHC compared with controls, with further declines after chemotherapy. Anemia prevalence rose from 62.67% to 76.67%, with moderate anemia becoming predominant (59.13%) and severe anemia emerging (1.74%). White blood cell and platelet counts significantly decreased after treatment ($P<0.01$). **Conclusion:** Chemotherapy induces significant hematological toxicity. Regular blood monitoring and early anemia management through dose modifications or nutritional support are essential. Long-term follow-up is recommended to assess the impact of these alterations on patient prognosis.

Keywords: Chemotherapy, Hematological parameters, Anemia, Breast cancer. National Oncology Institute in Sabratha, Western Libya

Introduction

Cancer is a group of diseases that cause cells in the body to change and grow uncontrollably, forming a mass called a tumor [1, 2]. Breast cancer originates in breast tissue and occurs due to the interaction between environmental triggers and genetic predisposition [3, 4]. Symptoms of breast cancer may include a lump in the breast, a change in the shape or size of the breast, dimpling of the skin, nipple discharge, and red, flaky skin [4, 5]. Breast cancer is one of the most common cancers among women worldwide, representing a significant health and social challenge [6]. It is the second leading cause of cancer-related deaths among women globally, and its incidence is rising in Libya [7]. With over one million new cases and 370,000 deaths annually worldwide, breast cancer remains a major challenge today. Despite the increasing incidence of breast cancer, the mortality rate associated with this disease is declining in most developed countries [8, 9].

Risk factors for breast cancer include being female, obesity, physical inactivity, alcohol consumption, hormone replacement therapy during menopause, ionizing radiation, early menarche, delayed or no childbearing, and advanced age [4, 10]. Breast cancer has become a major public health problem in both developed and developing countries [2]. In industrialized countries, it is the most common cancer among women. There has been a steady increase in the incidence of breast cancer over the past 40 years. Accordingly, it is the second leading cause of cancer-related deaths among women aged 20–59 years worldwide [11, 12]. Currently,

developing countries account for 50% of new cases and 60% of breast cancer deaths [13].

Despite significant advances in diagnostic and treatment methods, chemotherapy remains a cornerstone of many breast cancer cases, whether as adjuvant therapy after surgery, neoadjuvant therapy, or palliative care in advanced stages [14]. Doxorubicin and cyclophosphamide are among the most important drugs recently used to treat patients with advanced breast cancer [15].

Cancer drugs target and precisely destroy cancer cells, which is the majority of anticancer therapies. However, this treatment also destroys precursor cells for healthy blood cells in the bone marrow [13, 16].

According to a study by Nurgalieva *et al.* [17], proliferating cells, such as cancer cells and normal stem cells, are the primary targets of chemotherapy drugs. The toxic effects of chemotherapy can lead to bone marrow suppression, resulting in changes in hematological parameters [15, 18–20] due to the non-specific targeting of cancer cells [15]. Combined treatment of breast cancer with doxorubicin and cyclophosphamide affects various biological parameters, leading to physiological abnormalities [15].

Chemotherapy can cause bone marrow suppression, leading to anemia, leukopenia, and thrombocytopenia [21]. Anemia is a common complication that negatively impacts patients' quality of life and their ability to tolerate prescribed chemotherapy doses, and may require intervention such as blood transfusions or the use of

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erythropoiesis stimulators [22]. Given the prevalence of breast cancer and the increasing use of chemotherapy in its treatment, understanding the effects of this treatment on hematological variables has become crucial. Therefore, this study aims to evaluate these effects and the prevalence of anemia in breast cancer patients receiving chemotherapy, with the goal of improving care and developing strategies to mitigate these side effects.

Objectives

Due to the scarcity of studies demonstrating the effect of chemotherapy on hematological variables in breast cancer patients in the Western Region, and the limited number of currently published studies on the effects of chemotherapy on these variables in breast cancer patients at the National Cancer Institute in Sabratha, this study aims to evaluate the changes occurring in hematological variables and the prevalence of anemia in breast cancer patients undergoing chemotherapy at the National Cancer Institute in Sabratha.

Materials and Methods

Study Design

This study was conducted on 150 breast cancer patients undergoing chemotherapy at the National Cancer Institute in Sabratha, and 100 healthy women without any chronic diseases were included as a control group. The ages of the participants ranged from 25 to 80 years. Ethical approval was obtained from the National Cancer Institute in Sabratha to conduct the study.

2.4. Collection of Hematological Analyses

The analyses recorded in the medical records of the female patients participating in the study who were undergoing chemotherapy were collected. These analyses included hematological variables (red blood cell count, Hb, HCT, MCV, MCH, MCHC, white blood cell count, differential white blood cell count, and platelet count).

Statistical Analysis

Statistical analysis of the data was performed using the Statistical Package for the Social Sciences (SPSS) (version 25) through one-way analysis of variance (ANOVA). Results are expressed as mean ± standard error. The probability level (P<0.05, P<0.01) was considered significant in all statistical tests.

Results

1.Effect of Chemotherapy on Hematological Variables

2.Effect of Chemotherapy on Red Blood Cells and Their Indices

Statistical analysis of the results in Table (1) shows a significant decrease (P<0.01) in the red blood cell count (x10⁶ cells/μl) in breast cancer patients before (3.90±0.04) and after chemotherapy (3.10 ±0.03) compared to the control group (4.42 ±0.05). There is also a significant decrease (P<0.01) in the red blood cell count (x10⁶ cells/μl) after treatment (3.10 ±0.03) compared to before chemotherapy (3.90±0.04) Table (1) shows a significant decrease (P<0.01) in hemoglobin concentration (g/dl) in women with breast cancer before (12.12±0.06) and after chemotherapy (10.3±0.07) compared to the control group (13.71±0.09). There was also a significant decrease (P<0.01) in hemoglobin concentration (g/dL) after treatment (10.3±0.07 g/dL) compared to before chemotherapy (12.12 ±0.06 g/dL). Table (1) shows a significant decrease (P<0.01) in hematocrit percentage (%) in breast cancer patients before (34.14 ±0.14 g/dL) and after chemotherapy (30.04 ±0.19 g/dL) compared to the control group (37.19 ±0.16 g/dL). There was also a significant decrease (P<0.01) in hematocrit percentage (%) after treatment (30.04 ±0.19 g/dL) compared to before chemotherapy (34.14 ±0.14 g/dL).

The results indicate a significant decrease (P<0.01) in mean red blood cell volume (μ3) in breast cancer patients before (82.02 ±0.08 g/dL) and after chemotherapy (79.4 ±0.14 g/dL). Compared to the control group (85.12 ±0.12). There was also a significant decrease (P<0.01) in the mean red blood cell volume (μ3) after treatment (79.4 ± 0.14) compared to before chemotherapy (82.02± 0.08) (Table 1).

Conversely, there was a significant increase (P<0.01) in mean erythrocyte hemoglobin (pg) concentration in breast cancer patients after chemotherapy (33.23 ± 0.13) compared to the control group (31.10 ± 0.11). There was also a significant increase (P<0.05) in mean erythrocyte hemoglobin (pg) concentration after treatment (33.23 ± 0.13) compared to before chemotherapy (31.08 ± 0.14) (Table 1). Meanwhile, mean erythrocyte hemoglobin concentration (g/dL) decreased significantly (P<0.05) in breast cancer patients before (35.42 ± 0.16) and (P<0.01) after chemotherapy (34.1 ± 0.13) compared to the control group (36.9 ± 0.13). There was also a significant decrease (P<0.05) in the mean concentration of hemoglobin in red blood cells (g/dl) after treatment (34.1±0.13) compared to before chemotherapy (35.42±0.16) (Table 1).

Table 1. Effect of chemotherapy on RBCs count and its indices

Groups Parameters	Control	Before Chemotherapy	After Chemotherapy
	Mean ± SE	Mean ± SE	Mean ± SE
RBCs Count (x10 ⁶ cell/μl)	4.42 ± 0.05	3.90 ± 0.04**	3.10 ± 0.03***
Hb (g/dl)	13.71 ± 0.09	12.12 ± 0.06**	10.3 ± 0.07***
Hct (%)	37.19± 0.16	34.14± 0.14**	30.04± 0.19***
MCV (μ ³)	85.12 ± 0.12	82.02± 0.08**	79.4 ± 0.14***

MCH (Pg)	31.10± 0.11	31.08± 0.14	33.23 ± 0.13***
MCHC (g/dl)	36.9± 0.13	35.42± 0.16*	34.1± 0.13**

*: Significant at $P < 0.05$ compared with the control; **: Significant at $P < 0.01$ compared with the control; #: Significant at $P < 0.05$ compared with before Chemotherapy; ###: Significant at $P < 0.01$ compared before Chemotherapy.

2.4. Effect of Chemotherapy on White Blood Cell Count and Differential Count

The results show a significant increase ($P < 0.01$) in white blood cell count ($\times 10^3$ cells/ μ l) in breast cancer patients before chemotherapy (8.83 ± 0.19) and a significant decrease ($P < 0.01$) after chemotherapy (4.65 ± 0.09)

compared to the control group (6.03 ± 0.15). Conversely, there was a significant decrease ($P < 0.01$) in white blood cell count ($\times 10^3$ cells/ μ l) after chemotherapy (4.65 ± 0.09) compared to before chemotherapy (8.83 ± 0.19) (Table 2).

Table 2. Effect of chemotherapy on WBCs count, Neutrophils %, Lymphocytes%, Mixed%, and Platelets Count

Groups Parameters	Control	Before Chemotherapy	After Chemotherapy
	Mean ± SE	Mean ± SE	Mean ± SE
WBCs Count ($\times 10^3/\mu$ l)	6.03± 0.15	8.83 ± 0.19**	4.65± 0.09***
Neutrophils %	54.09± 0.14	60.01 ± 0.53**	50.11± 0.04***
Lymphocytes %	36.01± 0.91	34.00± 0.24**	32.4± 0.14***
Mixed%	9.01 ± 0.12	6.01± 0.13	18.4± 0.13***

**: Significant at $P < 0.01$ compared with the control; ###: Significant at $P < 0.01$ compared before Chemotherapy.

The results indicate a significant increase ($P < 0.01$) in the percentage of neutrophils in breast cancer patients before chemotherapy (60.01 ± 0.53) and a significant decrease ($P < 0.01$) after chemotherapy (50.11 ± 0.04) compared to the control group (54.09 ± 0.14). A significant decrease ($P < 0.01$) in the percentage of neutrophils after chemotherapy (50.11 ± 0.04) was also observed compared to the pre-chemotherapy level (60.01 ± 0.53) Table 2. Table 1 shows a significant decrease ($P < 0.01$) in the percentage of lymphocytes in breast cancer patients before (34.00 ± 0.24) and after chemotherapy (32.4 ± 0.14) compared to the control group (36.01 ± 0.91). There was also a significant decrease ($P < 0.01$) in the percentage of lymphocytes after treatment (32.4 ± 0.14) compared to before chemotherapy (34.00 ± 0.24).

The data in Table 2 indicate a significant increase ($P < 0.01$) in the percentage of mixed cells in breast cancer patients after chemotherapy (18.4 ± 0.33) compared to the control group (9.01 ± 0.12) and after chemotherapy (6.01 ± 0.13).

5. Effect of Chemotherapy on Platelet Count

As shown in Table 3, we observe a significant decrease ($P < 0.01$) in the platelet count ($\times 10^3$ cells/ μ l) in breast cancer patients before (270 ± 5.08) and after chemotherapy (241.4 ± 3.04) compared to the control group (286 ± 6.07). There was also a significant decrease ($P < 0.01$) in the number of platelets ($\times 10^3$ cell/ μ l) after treatment (241.4 ± 3.04) compared to before chemotherapy (270 ± 5.08).

Table 5. Effect of chemotherapy on platelet count

Groups Parameters	Control	Before Chemotherapy	After Chemotherapy
	Mean ± SE	Mean ± SE	Mean ± SE
Platelets Count ($\times 10^3$)	286± 6.07	270± 5.08**	241.4± 3.04***

**: Significant at $P < 0.01$ compared with the control; ###: Significant at $P < 0.01$ compared before Chemotherapy.

9.5. Prevalence of Anemia Among Breast Cancer Patients Undergoing Chemotherapy

Table 4 shows an increased prevalence of anemia after chemotherapy, reaching 76.67%, compared to 62.67% before treatment.

Table 4. The prevalence of anemia before and after chemotherapy

Groups	Before Chemotherapy		After Chemotherapy	
	Frequency	Percent (%)	Frequency	Percent (%)

Anemic Patients	94	62.67	115	76.67
Non-anemic Patients	56	37.33	35	23.33

Table 5 shows the severity of anemia among breast cancer patients undergoing chemotherapy. Before treatment, the prevalence was mild anemia (63.8%) and

moderate anemia (36.2%). After treatment, the prevalence was mild anemia (39.13%), moderate anemia (59.13%), and severe anemia (1.74%).

Table 5. Distribution of anemic patients before and after chemotherapy according to the degrees of anemia

Degrees of anemia	Before Chemotherapy		After Chemotherapy	
	Frequency	Percent (%)	Frequency	Percent (%)
Mild anemia	60	63.8	45	39.13
Moderate anemia	34	36.2	68	59.13
Severe anemia	0	0	2	1.74

From the statistical analysis of the results, we note that the percentage of normal hypochromic anemia was 95.5% before chemotherapy and became 67% after chemotherapy, while the percentage of microcytic

hypochromic anemia increased from 4.3% before chemotherapy to 31.3% after chemotherapy, and the percentage of macrocytic hypochromic anemia was 1.7% after chemotherapy Table 6.

Table 6. Distribution of anemic patients before and after chemotherapy according to the type of anemia

Types of anemia	Before Chemotherapy		After Chemotherapy	
	Frequency	Percent (%)	Frequency	Percent (%)
Normocytic hypochromic [MCV(80-98)]	90	95.7	77	67
Microcytic hypochromic (MCV<80)	4	4.3	36	31.3
Macrocytic Hypochromic Anemia (MCV>98)	0	0	2	1.7

Discussion

Chemotherapy is an important treatment method used in the management of breast cancer patients. Blood biochemical variables show the chemicals secreted or produced during metabolic processes in the body, and these substances provide vital information about the functions of various organs. Numerous studies have demonstrated that chemotherapy has both short-term and long-term effects on organ function [23-25]. Chemotherapy remains the preferred treatment for hundreds of thousands of patients diagnosed with cancer annually [26]. This study was conducted on a sample of breast cancer patients undergoing chemotherapy at the National Cancer Institute in Sabratha. Data for the study participants were collected from the records of patients undergoing chemotherapy, including hematological analysis to assess the effect of chemotherapy on hematological parameters and the prevalence of anemia. Hematological parameters have diagnostic value in breast cancer patients [27], making them a crucial test for breast cancer patients before initiating any treatment [28]. The results of this study show a significant decrease ($P<0.01$) in red blood cell count, hemoglobin concentration, hematocrit percentage, mean corpuscular volume, and mean corpuscular hemoglobin

concentration in breast cancer patients before and after chemotherapy compared to the control group. This decrease in red blood cell count, hemoglobin concentration, MCV, and MCH was significantly increased after treatment compared to before chemotherapy. Furthermore, a significant increase ($P<0.01$) in mean corpuscular hemoglobin concentration was observed in breast cancer patients after chemotherapy compared to the control group. This significant increase ($P<0.05$) in mean red blood cell hemoglobin concentration was observed after treatment compared to before chemotherapy. These findings are consistent with previous studies [29-31], which demonstrated a decrease in red blood cell count in cancer patients treated with chemotherapy compared to the control group. Similarly, the study by Akinbami *et al.* [32] showed that mean corpuscular volume, mean corpuscular hemoglobin, and mean corpuscular hemoglobin concentration were lower in breast cancer patients than in the control group. Ufelle *et al.* [33] also reported a significant decrease in hematocrit levels in breast cancer patients compared to the control group. Storph *et al.* [4] observed a decrease in hemoglobin levels after the second cycle of chemotherapy.

This may explain the reduced lifespan of red blood cells during chemotherapy and radiotherapy for cancer treatment [29]. Mean hemoglobin levels vary considerably among cancer patients and are slightly lower in cancer patients treated with chemotherapy compared to the control group [29,31, 34]. The decrease in hemoglobin levels may be due to a decrease in partial pressure of oxygen (pO₂) in the tumor [29].

The results of the current study show an increased prevalence of anemia after chemotherapy, reaching 76.67%, compared to 62.67% before chemotherapy. The severity of anemia before chemotherapy was 63.8% mild and 36.2% moderate; after treatment, it was 39.13% mild, 59.13% moderate, and 1.74% severe. The prevalence of normocytic hypochromic anemia was 95.5% before chemotherapy and decreased to 67% after. The prevalence of microcytic hypochromic anemia increased from 4.3% before chemotherapy to 31.3% after, while the prevalence of macrocytic hypochromic anemia decreased to 1.7% after chemotherapy.

The underlying mechanisms responsible for this type of anemia are unclear, and these hematological parameters may have decreased due to breast cancer metastases. Bone marrow involvement may be associated with inhibition of red blood cell production. Infection in fungal malignancies may be associated with hemolysis [32] and elevated levels of pro-inflammatory cytokines, such as IL-1, IL-6, TNF- α , and INF- δ , which cause iron retention in the liver, gastrointestinal tract, and reticuloendothelial system, thereby inhibiting erythroid precursor production [12]. These cytokines may inhibit endogenous erythropoietin (EPO) production, impair iron utilization, and reduce erythroid precursor proliferation [15, 32, 35]. Blood loss due to cancer treatment can also exacerbate anemia. Low hemoglobin levels can lead to immunosuppression in cancer patients. Erythropoietin may be recommended for patients during cancer treatment, particularly in the case of chemotherapy, to maintain cell counts. Red blood cell count and hemoglobin levels [29].

Khan *et al.* [28] indicated that hematological parameters, particularly lymphocytes and neutrophils, are important tools for diagnosing and monitoring breast cancer.

The results of this study show a significant decrease ($P<0.01$) in red blood cell count, hemoglobin concentration, hematocrit percentage, mean red blood cell volume, and mean red blood cell hemoglobin concentration in breast cancer patients before and after chemotherapy compared to the control group. This decrease in red blood cell count, hemoglobin concentration, mean red blood cell volume, and mean red blood cell hemoglobin concentration increased significantly after treatment compared to before chemotherapy. A significant increase ($P<0.01$) in mean red blood cell hemoglobin concentration (pg) was also observed in breast cancer patients after chemotherapy compared to the control group. This significant increase ($P<0.05$) in mean red blood cell hemoglobin

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The results of the current study show an increased prevalence of anemia after chemotherapy, reaching 76.67%, compared to 62.67% before chemotherapy. The severity of anemia before chemotherapy was 63.8% mild and 36.2% moderate; after treatment, it was 39.13% mild, 59.13% moderate, and 1.74% severe. The prevalence of normocytic hypochromic anemia was 95.5% before chemotherapy and decreased to 67% after. The prevalence of microcytic hypochromic anemia increased from 4.3% before chemotherapy to 31.3% after, while the prevalence of macrocytic hypochromic anemia decreased to 1.7% after chemotherapy.

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Khan *et al.* [28] indicated that hematological parameters, particularly lymphocytes and neutrophils, are important tools for diagnosing and monitoring breast cancer.

Statistical analysis of the results of the current study shows a significant increase ($P<0.01$) in white blood cell count and neutrophil percentage in breast cancer patients before chemotherapy and a significant decrease ($P<0.01$) after chemotherapy compared to the control group. A significant decrease ($P<0.01$) in white blood cell count and neutrophil percentage was also found after chemotherapy compared to before. A significant decrease ($P<0.01$) in lymphocyte percentage was found in breast cancer patients before and after chemotherapy compared to the control group. This decrease was significantly increased ($P<0.01$) in lymphocyte percentage after treatment compared to before chemotherapy. These results are consistent with those of Akinbami *et al.*[32] A study (2013) showed that the mean white blood cell count and neutrophil percentage in breast cancer patients were higher than in the control group. Infection in fungal malignancies may be associated with an increased white blood cell count [32]. Neutrophilia was an independent predictor of breast cancer risk [36]. Certain chemokines secreted by tumor cells, such as angiotensin II or granulocyte colony-stimulating factor, stimulate the bone marrow to produce more neutrophils [37]. Etim *et al.* [38] and Shilpa *et al.* [39] reached similar findings, reporting a significant decrease in the mean percentage of neutrophils.

It is known that the chemotherapy drugs cyclophosphamide, adriamycin, and 5-fluorouracil (CAF) have a negative effect on hematological variables, causing neutropenia [40]. Storph *et al.* [4] observed a decrease in white blood cell counts during chemotherapy cycles.

Henderson *et al.* [40] noted an increased incidence of anemia with each dose of doxorubicin in breast cancer patients undergoing chemotherapy. The white blood cell count observed during the third cycle of chemotherapy confirms the findings of previous studies [40-42].

Chemotherapy weakens innate and adaptive immune responses by affecting hematopoietic homeostasis through lymphatic depletion [43, 44]. Hematopoietic DNA replication [45-46]. The gradual depletion of hematopoietic stem cells in the bone marrow inhibits cell growth, leading to immune cell death and a decrease in white blood cells [45,46].

Platelet count is an indicator of systemic inflammation resulting from tumor growth [47].

The results of the current study indicate a significant decrease ($P<0.01$) in platelet count in breast cancer patients before and after chemotherapy compared to the control group. This significant decrease ($P<0.01$) in platelet count increased after treatment compared to before chemotherapy. It is known that chemotherapy drugs such as cyclophosphamide, Adriamycin, and 5-fluorouracil (CAF) have a negative effect on hematological variables, causing a decrease in platelet count [40].

Conclusion

This study concludes that the results showed a significant decrease ($P<0.01$) in the red blood cell count, hemoglobin concentration, hematocrit percentage, and mean corpuscular hemoglobin concentration (MCHC) compared to the control group, and this decrease increased significantly after chemotherapy. Significant increases ($P<0.05$) were recorded in the mean corpuscular hemoglobin concentration (MCHC) after treatment compared to before. The prevalence of anemia increased from 62.67% before treatment to 76.67% after treatment. Moderate anemia increased to become the predominant type after treatment (59.13%), with the emergence of severe anemia (1.74%). The incidence of hypochromic anemia decreased. Normocytic hypochromic anemia and microcytic hypochromic anemia increased significantly after treatment. There was a significant increase ($P<0.01$) in the number of white blood cells and neutrophils before treatment compared to the control group, but this decreased significantly after treatment. A significant decrease ($P<0.01$) was recorded in the percentage of lymphocytes before and after treatment, and this decrease increased significantly after treatment. A significant decrease ($P<0.01$) was found in the number of platelets before and after treatment, and this decrease increased significantly after treatment. Regular blood monitoring and early anemia correction should be given top priority in chemotherapy programs in order to manage toxicity by dose modifications and pharmacological or nutritional assistance. To determine environmental risk factors and assess the effect of hematological alterations on patient prognosis, long-term follow-up and comparison studies are also crucial.

Study Limitations

The study was conducted at a single center (the National Oncology Institute in Sabratha). Therefore, the findings may not be fully representative of the entire Libyan population or patients treated at different facilities with varying protocols. Future studies should adopt a multicenter approach, involving oncology institutes across different regions of Libya (e.g., Tripoli, Benghazi, and Sebha). This would provide a more comprehensive national profile of hematological toxicity. Additionally, longitudinal tracking—monitoring patients for 6 to 12 months post-treatment—is essential to determine the recovery rate of bone marrow function. Future investigations should categorize patients based on their specific treatment protocols. This would allow clinicians to identify which specific drug combinations pose the highest risk for severe anemia and neutropenia.

Conflicts of interest: The authors declare that they have no Conflicts of interest related to this study

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