# Hematological toxicity assessment in breast cancer patients receiving paclitaxel: Retrospective study and single center experience

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Abstract: Hematological toxicity is a predominant concern encountered during cancer treatment. Regular blood tests and follow-up are crucial for cancer patients. The objective of this study was to evaluate and compare the hematological toxicities seen by breast cancer patients who were administered paclitaxel during treatment cycles. An observational retrospective study was conducted at the Oncology Clinic at Hiwa Hospital in The Kurdistan Region of Iraq between January 2021 and May 2022. Among the 141 breast cancer patients included in the study, 74 patients did not receive granulocyte-colony stimulating factor prior to the baseline, while 67 patients did receive it. A significant statistical difference was observed in the White Blood Cells parameter among cancer patients who did not receive granulocyte-colony stimulating factor before the baseline when comparing the 2<sup>nd</sup> cycle to the 3<sup>rd</sup> cycle of Paclitaxel treatment (P-value = 0.001). Statistically significant differences were seen between the Baseline and 1<sup>st</sup> Cycle, Baseline and 2<sup>nd</sup> Cycle and Baseline and 3<sup>rd</sup> Cycle (P-value = 0.0312, 0.031 and 0.031, respectively) in grade 1 neutropenia among the 67 patients who received granulocyte-colony stimulating factor prior to the baseline. This study determined that anemia is a frequently observed hematological side effect of chemotherapy in breast cancer patients who are undergoing treatment with paclitaxel, followed by grade 1 neutropenia.

Keywords: Hematological toxicity, Hiwa hospital, paclitaxel, breast cancer, cancer patients.

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#### **INTRODUCTION**

Breast cancer, accounting for 36% of all oncology cases, can be defined by the malignant proliferation of epithelial cells in the ducts or lobules of the breast. Breast cancer is also a leading cause of cancer-related deaths among women worldwide. According to Nardin et al. (2020), 1 in 8 women is diagnosed with breast cancer at some point in their lives. In Iraq, where this study was conducted, there has been a steady increase in new breast cancer cases, with the rate rising from 52.00 per 100,000 in 2000 to 91.66 per 100,000 in 2019 (Al-Hashimi, 2021). Reports from the Children's Cancer Research Institute and the World Health Organization show that breast cancer accounts for approximately one-third of all cancer cases in Iraq, making it the most frequently diagnosed type of cancer among Iraqi women (Khalifa, 2022). This trend is particularly concerning in the Kurdistan Region of Iraq (hence KRI), which has been exposed to a range of carcinogenic hazards, including chemical weapons and pollution from the Iraqi-Iran War (Salih, 1995; Othman et al., 2011).

Paclitaxel, a widely used chemotherapeutic treatment in the battle against breast cancer, has demonstrated to be efficient, tolerable, and resistant to anthracycline crossresistance in treating the disease (Alalawy, 2024). However, its use is often associated with adverse effects such as bone marrow toxicity. This occurs because the hematopoietic cells in the bone marrow, responsible for producing and maturing blood cells quickly, are vulnerable to medications that specifically target rapidly dividing cells. These toxicities can be life-threatening as they might hinder the synthesis of: Red blood cells causing anemia, white blood cells causing neutropenia or granulocytopenia and platelets, which leads to thrombocytopenia (Basak *et al.*, 2021). A recent study evaluating the safety and effectiveness of weekly paclitaxel in combination with other chemotherapy treatments found that a significant number of participants experienced severe neutropenia (grade 3-4) in 88% of cases and severe thrombocytopenia (grade 3-4) in 38% of cases (Takahashi *et al.*, 2022).

Given these concerns and the unique environmental and genetic factors present in Iraq, it is crucial to investigate the specific patterns of hematological toxicity associated with paclitaxel treatment in Iraqi breast cancer patients. This study aims to evaluate and compare the hematological toxicities, neutropenia, thrombocytopenia, and anemia in Iraqi patients receiving paclitaxel treatment over their chemotherapy cycles. Whilst paclitaxel's side effects have been studied extensively in a variety of cultures, little is known about how it affects patients from Iraq. Focusing on this under-researched population, this study contributes to existing literature by providing insights that could lead to better management of chemotherapy side effects in Iraqi breast cancer patients.

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Additionally, the findings could help healthcare providers in Iraq and similar regions to tailor chemotherapy treatments more effectively, thereby improving patient outcomes and quality of life during cancer treatment.

## MATERIALS AND METHODS

#### Study design

This retrospective observational study was carried out at the Oncology Clinic of Hiwa Hospital in the Kurdistan Region of Iraq from January 2021 to May 2022. Inclusion criteria included breast cancer patients aged 18 or older who were undergoing paclitaxel chemotherapy treatment at Hiwa Hospital and had accessible medical records. Patients were excluded if they were younger than 18, not receiving paclitaxel chemotherapy, deceased during treatment, or unable to complete at least four chemotherapy cycles at Hiwa Hospital.

Prior to paclitaxel treatment, all breast cancer patients in this study received AC (Cyclophosphamide and Doxorubicin) therapy. Patients were then divided into two groups based on whether they received granulocytecolony stimulating factor (G-CSF) during their AC therapy. G-CSF is known to impact the blood cell counts of breast cancer patients. The study included two groups: breast cancer patients who were treated with G-CSF for hematological toxicity resulting from prior chemotherapy and breast cancer patients who received chemotherapy but did not receive G-CSF treatment (fig. 1).

Hemogram parameters of breast cancer patients receiving Paclitaxel were assessed at baseline and throughout the 1<sup>st</sup>, 2<sup>nd</sup> and 3<sup>rd</sup> cycles of treatment. Hematological toxicities, including lymphocytopenia, neutropenia, anemia and thrombocytopenia, were assessed using the National Cancer Institute Common Terminology Criteria for Adverse Events, version 5.0.

Fig. 2 shows the sequential stages of chemotherapy. This blood test served as a reference point for hemogram measurements in this study. The pre-cycle blood test involved assessing the outcomes of the preceding cycle. The study was approved by the Hiwa Cancer Hospital in Iraq.

#### STATISTICAL ANALYSIS

The data analysis was conducted using SPSS version 25. Descriptive statistics were used to analyze continuous data (mean ( $\pm$  SD), while categorical data, such as age and hematological toxicity levels were displayed as frequency and percentage. Each patient was assessed for four distinct adverse effects linked to Paclitaxel therapy: Neutropenia, Thrombocytopenia, Lymphocytopenia, and Anemia. The treatment phase consisted of 4 cycles: Baseline, 1<sup>st</sup>, 2<sup>nd</sup> and 3<sup>rd</sup> cycles. To evaluate the variations in hemogram parameters throughout different phases, the

Paired t-test was used to compare the baseline measurements with those taken during the  $1^{st}$ ,  $2^{nd}$  and  $3^{rd}$  cycles, as well as comparisons between the  $1^{st}$ ,  $2^{nd}$  and  $3^{rd}$  cycles. The significant difference between the pairs in tables 4–7 was determined using the Mc Nemar test. A level of significance of 0.05 was accepted with a 95% confidence level.

#### Ethical approval

This study was approved by the Scientific Research Unit of Hiwa Cancer Hospital on April 19, 2022.

# RESULTS

This study included 141 breast cancer patients at Hiwa Hospital from January 2021 to May 2022. 141 patients were analyzed in this study, 74 patients with breast cancer did not get G-CSF prior to the baseline, while 67 patients did receive G-CSF before the baseline (fig. 1). All participants were female, with an average age of  $49.52\pm$  8.83 and an average body surface area of  $1.75\pm0.19$ .

In patients who did not receive G-CSF prior to baseline, a study was conducted to analyze the hemogram parameters during the baseline, 1<sup>st</sup>, 2<sup>nd</sup> and 3<sup>rd</sup> cycles of Paclitaxel treatment. Among the 74 patients included in the study, a statistically significant difference was observed in the White Blood Cells parameter between the 2<sup>nd</sup> and 3<sup>rd</sup> Paclitaxel treatment (P-value=0.001). cycles of Statistically significant differences were observed in the platelet parameter for cancer patients receiving Paclitaxel when comparing baseline to 1st cycle (P-value = 0.013), baseline to  $2^{nd}$  cycle (P-value = 0.007), and baseline and  $3^{rd}$  cycle (P-value = 0.001) (table 1) and (fig. 3).

Hemogram parameters were analyzed in 67 breast cancer patients who received Paclitaxel during different treatment cycles. Prior to the baseline, all patients had received G-CSF (granulocyte-colony stimulating factor). The results showed statistically significant differences in the platelet parameter when comparing the baseline to the  $1^{st}$  cycle (P-value =0.0001), the baseline to the  $2^{nd}$  cycle (P-value=0.001) and the  $2^{nd}$  cycle to the  $3^{rd}$  cycle (P-value=0.037). Additionally, statistically significant differences were observed in the lymphocyte parameter among cancer patients who received Paclitaxel. These differences were evident when comparing the baseline measurements to the  $1^{st}$  cycle (P-value = 0.002), the  $2^{nd}$ cycle (P-value =0.020) and the  $3^{rd}$  cycle (P-value = 0.024) (table 2) and (fig. 4).

Among the 74 patients who did not receive G-CSF (granulocyte-colony stimulating factor) before the baseline, no cases of all-grade thrombocytopenia were observed at baseline or throughout the 1<sup>st</sup> 2<sup>nd</sup> and 3<sup>rd</sup> cycles. At baseline, there were 4 cases (5.4%) of grade 1 neutropenia and 2 cases (2.7%) of grade 2 neutropenia.

	(N)	$Mean \pm SD$	(Baseline vs 1 <sup>st</sup> Cycle)	(Baseline vs 2 <sup>nd</sup> Cycle)	(Baseline vs 3 <sup>rd</sup> Cycle)	(2nd cycle vs 3 <sup>rd</sup> Cycle)	
WBC (Baseline)	74	6.04±5.76			* /		
WBC (First cycle)	74	5.45±1.79	0.384	0.897	0.0(2	0.001	
WBC (Second cycle)	74	5.95±3	0.384		0.063	0.001	
WBC (Third cycle)	74	4.73±1.69					
LYMPH (Baseline)	74	$1.52{\pm}0.7$					
LYMPH (First cycle)	74	1.57±0.62	0.514	0.386	0.804	0.389	
LYMPH (Second cycle)	74	$1.58 \pm 0.63$	0.314	0.380	0.894	0.389	
LYMPH (Third cycle)	74	$1.53 \pm 0.65$					
GRAN (Baseline)	74	3.47±2.55					
GRAN (First cycle)	74	3.35±1.46	0.731	0.239	0.865	0.759	
GRAN (Second cycle)	74	3.91±2.43	0.731	0.239	0.865	0.739	
GRAN (Third cycle)	74	$3.63 \pm 7.52$					
RBC (Baseline)	74	$4.26 \pm 0.58$					
RBC (First cycle)	74	$4.21 \pm .61$	0.283	0.240	0.298	0.906	
RBC (Second cycle)	74	4.21±0.47	0.285	0.249		0.896	
RBC (Third cycle)	74	$4.22 \pm 0.41$					
HGB (Baseline)	74	$11.46{\pm}1.41$					
HGB (First cycle)	74	11.21±1.35	0.044	0.376	0.065	0.002	
HGB (Second cycle)	74	$11.35 \pm 1.09$	0.044	0.370	0.065	0.093	
HGB (Third cycle)	74	$11.23 \pm .96$					
PLT (Baseline)	74	328.32±93.02					
PLT (First cycle)	74	$294.32 \pm 78.32$	0.012	0.007	0.001	0 (15	
PLT (Second cycle)	74	$294.95{\pm}64.07$	0.013	0.007		0.615	
PLT (Third cycle)	74	291.47±69.16					

Table 1: Hemogram parameters in cancer patients (who did not receive filgrastim before baseline) during baseline,  $1^{st}$  cycle,  $2^{nd}$  and  $3^{rd}$  cycle.

**Table 2**: Hemogram parameters in cancer patients (who received Filgrastim before baseline) during baseline,  $1^{st}$  cycle,  $2^{nd}$  and  $3^{rd}$  cycle.

	(N)	$Mean \pm SD$	Baseline vs 1. Cycle	Baseline vs 2. Cycle	Baseline vs 3. Cycle	2. cycle vs 3. Cycle
WBC (Baseline)	67	6.35±4.27	-			-
WBC (First cycle)	67	6.10±5.33	0.758	0.010	0.202	0.156
WBC (Second cycle)	67	$4.89 \pm 1.68$	0.738	0.010	0.202	0.150
WBC (Third cycle)	67	$5.44 \pm 3.49$				
LYMPH (Baseline)	67	$1.34{\pm}0.5$				
LYMPH (First cycle)	67	$1.58 \pm .64$	0.002	0.020	0.024	0.967
LYMPH (Second cycle)	67	$1.49{\pm}0.46$	0.002	0.020	0.024	0.867
LYMPH (Third cycle)	67	$1.50\pm0.52$				
GRAN (Baseline)	67	4.51±3.86				
GRAN (First cycle)	67	$4.04 \pm 4.69$	0.504	0.002	0.107	0.125
GRAN (Second cycle)	67	3.02±1.29	0.524	0.003	0.127	0.135
GRAN (Third cycle)	67	$3.55 \pm 3.03$				
RBC (Baseline)	67	4.21±1.1				
RBC (First cycle)	67	$4.06 \pm 0.51$	0.217	0 222	0.557	0.107
RBC (Second cycle)	67	$4.1 \pm 0.44$	0.217	0.333	0.557	0.197
RBC (Third cycle)	67	4.15±0.45				
HGB (Baseline)	67	$11.26 \pm .1.1$				
HGB (First cycle)	67	11.14±0.95	0.211	0 (01	0.020	0.207
HGB (Second cycle)	67	$11.20\pm0.89$	0.211	0.601	0.920	0.397
HGB (Third cycle)	67	$11.27 \pm .99$				
PLT (Baseline)	67	$254.82 \pm 66.88$				
PLT (First cycle)	67	306.99±84.53	0.0001	0.001	0.145	0.027
PLT (Second cycle)	67	$280.58 \pm 66.82$	0.0001	0.001	0.145	0.037
PLT (Third cycle)	67	266.63±62.89				

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Fig. 2: Cycles process

Table 3: Comparison of Hematological Toxicity between Baseline, 2<sup>nd</sup> and 3<sup>rd</sup> Cycle of Paclitaxel (N: 74)

Cancer Medications	Hematological Toxicity	Grade	Baseline N (%)	1. Cycle N (%)	Baseline vs 1. Cycle	2. Cycle N (%)	Baseline vs 2. Cycle
		G1	1(1.35%)	-	-	-	-
	I ymae ha ayrtae ania	G2	-	-	-	-	-
	Lymphocytopenia	G3	-	-	-	-	-
		G4	-	-	-	-	-
		G1	4(5.4%)	-	-	-	-
	Neutropenia	G2	2(2.7%)	-	-	-	-
	Neuropenia	G3	-	-	-	-	-
Paclitaxel		G4	-	-	-	-	-
Facilitaxei		G1	32(43.2%)	36(48.6%)	0.125	36(48.6%)	0.125
	Anemia	G2	4(5.4%)	4(5.4%)	-	2(2.7%)	0.5
	Allellilla	G3	-	2(2.7%)	-	-	-
		G4	-	-	-	-	-
		G1	-	-	-	-	-
	Thromboostononio	G2	-	-	-	-	-
	Thrombocytopenia	G3	-	-	-	-	-
		G4	-	-	-	-	-

Cancer Medications	Hematological Toxicity	Grade	Baseline N (%)	3. Cycle N (%)	Baseline vs 3. Cycle	2. cycle vs 3. Cycle
		G1	1(1.35%)	-	-	-
	T	G2	-	-	-	-
	Lymphocytopenia	G3	-	-	-	-
		G4	-	-	-	-
	Neutropenia	G1	4(5.4%)	1(1.35%)	0.25	-
		G2	2(2.7%)	-	-	-
		G3	-	-	-	-
Paclitaxel		G4	-	-	-	-
Pacifiaxei		G1	32(43.2%)	37(50%)	0.0625	0.5
	Anemia	G2	4(5.4%)	2(2.7%)	0.5	-
	Anemia	G3	-	-	-	-
		G4	-	-	-	-
		G1	-	-	-	-
	Throwbeersterenie	G2	-	-	-	-
	Thrombocytopenia	G3	-	-	-	-
		G4	-	-	-	-

Table 4: Comparison of Hematological Toxicity between Baseline, 2<sup>nd</sup> and 3<sup>rd</sup> Cycle of Paclitaxel (N: 74)

Table 5: Comparison	of Hematological Toxicit	y between Baseline,	1 <sup>st</sup> and 2 <sup>nd</sup> Cyc	le of Paclitaxel (N: 67)

Cancer Medications	Hematological Toxicity	Grade	Baseline N (%)	1. Cycle N (%)	Baseline vs 1. Cycle	2. Cycle N (%)	Baseline vs 2. Cycle
		G1	1(1.35%)	1(1.35%)	-	-	-
	I ymae hoortoe onio	G2	-	-	-	-	-
	Lymphocytopenia	G3	-	-	-	-	-
		G4	-	-	-	-	-
	Neutropenia	G1	10(14.9%)	4(5.9%)	0.031	4(5.9%)	0.031
		G2	-	-	-	-	-
		G3	-	-	-	-	-
Paclitaxel		G4	-	-	-	-	-
Pacifiaxei		G1	35(52.2%)	40(59.7%)	0.062	38(56.7%)	0.25
	۰ ·	G2	2(2.9%)	1(1.35%)	0.5	-	-
	Anemia	G3	-	-	-	-	-
		G4	-	-	-	-	-
		G1	-	-	-	-	-
	Thus with a sector sector	G2	-	-	-	-	-
	Thrombocytopenia	G3	-	-	-	-	-
		G4	-	-	-	-	-

Table 6: Comparison	of hematological toxicit	y between baseline,	2 <sup>nd</sup> and 3 <sup>rd</sup> Cy	ycle of Paclitaxel (	N: 67)

Cancer Medications	Hematological Toxicity	Grade	Baseline N (%)	3. Cycle N (%)	Baseline vs 3. Cycle	2. cycle vs 3. Cycle
		G1	1(1.35%)	-	-	-
	T 1 / '	G2	-	-	-	-
	Lymphocytopenia	G3	-	-	-	-
		G4	-	-	-	-
		G1	10(14.9%)	4(5.9%)	0.031	-
	Neutropenia	G2	-	-	-	-
		G3	-	-	-	-
Paclitaxel		G4	-	-	-	-
Pacifiaxei	Anemia	G1	35(52.2%)	33(49.2%)	0.5	0.0625
		G2	2(2.9%)	2(2.9%)	-	-
		G3	-	-	-	-
		G4	-	-	-	-
		G1	-	-	-	-
	Thrombooutononia	G2	-	-	-	-
	Thrombocytopenia	G3	-	-	-	-
		G4	-	-	-	-



Fig. 3: Hemogram parameters in cancer patients (who did not receive filgrastim before baseline) during baseline, 1<sup>st</sup> cycle, 2<sup>nd</sup> and 3<sup>rd</sup> cycle.

Grade 1 anemia was prevalent in 32 (43.2%), 36 (48.6%), 36 (48.6%), and 37 (50%) of patients at baseline and in the 1<sup>st</sup>, 2<sup>nd</sup> and 3<sup>rd</sup> cycles, respectively. No statistically significant differences were observed in terms of grade 1 anemia between the Baseline and 1<sup>st</sup> Cycle, Baseline and 2<sup>nd</sup> Cycle and Baseline and 3<sup>rd</sup> Cycle (tables 3 and 4).

Among the 67 patients who received G-CSF prior to the initial assessment, no instances of thrombocytopenia were observed at any grade throughout the baseline, 1<sup>st</sup>, 2<sup>nd</sup>, and 3<sup>rd</sup> cycles. At baseline, there was one case (1.35%) of grade 1 lymphocytopenia and one case (1.35%) of grade 2 lymphocytopenia. In the first cycle, there was also one case (1.35%) of grade 1 lymphocytopenia and one case

(1.35%) of grade 2 lymphocytopenia. The prevalence of grade 1 anemia was 35 (52.2%), 40 (59.7%), 38 (56.7%), and 33 (49.2%) at baseline, the 1<sup>st</sup>, 2<sup>nd</sup> and 3<sup>rd</sup> cycles, respectively. There were no statistically significant differences seen in grade 1 anemia between the Baseline and 1st Cycle (P-value = 0.062), Baseline and 2<sup>nd</sup> Cycle (P-value = 0.25) and Baseline and 3<sup>rd</sup> Cycle (P-value = 0.5). The incidence of grade 1 neutropenia was 10 (14.9%), 4 (5.9%), 4 (5.9%) and 4 (5.9%) at baseline, the 1<sup>st</sup>, 2<sup>nd</sup> and 3<sup>rd</sup> cycles, respectively. Statistically significant differences were observed between the Baseline and 1<sup>st</sup> Cycle, Baseline and 2<sup>nd</sup> Cycle and Baseline and 3<sup>rd</sup> Cycle (P-value = 0.0312, 0.031 and 0.031 correspondingly) in grade 1 neutropenia (tables 5 and 6).



Fig. 4: Hemogram parameters in cancer patients (who received Filgrastim before baseline) during baseline, 1<sup>st</sup> cycle, 2<sup>nd</sup> and 3<sup>rd</sup> cycle.

### DISCUSSION

Chemotherapy is known to cause frequent hematological toxicity, which is a common adverse effect. Physicians and oncology pharmacists should regularly evaluate the hemograms of breast cancer patients before each chemotherapy cycle. For breast cancer patients, it is most advisable to consider supportive care or delaying treatment if deemed essential. Therefore, it is imperative to limit adverse effects in order to enhance the efficacy of treatment and improve the quality of life for those diagnosed with breast cancer.

Previous studies have also shown that hematological adverse effects significantly impact oncologists' decisions

to discontinue cancer treatment for patients resulting in decreased rates of efficacy and mortality (Daniel and Crawford, 2006). The findings of this study showed that breast cancer patients undergoing four rounds of paclitaxel chemotherapy had hematological toxicity mainly in the form of anemia followed by neutropenia. In a different study Feliu *et al.*, (2020) explored the broad spectrum of hematologic toxicities associated with chemotherapy, focusing on anemia, neutropenia and thrombocytopenia. The study, in agreement with Daniel and Crawford (2006), highlighted that these toxicities not only compromise the efficacy of cancer treatments but also significantly affect patients' quality of life. The authors go on to suggest that anemia can lead to fatigue and reduced physical functioning, while neutropenia increases the risk of infections and may necessitate dose adjustments or delays in therapy (Feliu *et al.*, 2020). They emphasize that early detection and management of these toxicities are crucial and therefore advocate for the use of supportive treatments such as erythropoiesis-stimulating agents and granulocyte colony-stimulating factors (G-CSF) to mitigate these adverse effects and improve patient outcomes (Feliu *et al.*, 2020). Additionally, the study emphasizes the importance of regular monitoring of blood counts and adjusting treatment plans accordingly to balance the benefits and risks of chemotherapy, ultimately aiming to maintain the effectiveness of the treatment while enhancing patient well-being (Feliu *et al.*, 2020).

During the study, the incidence of grade 1 neutropenia was observed across multiple cycles, with occurrences noted during both the baseline and subsequent cycles of therapy. By contrast, Multinational phase 3 research was done to assess the effectiveness of Pegfilgrastim in lowering the occurrence of febrile neutropenia caused by docetaxel in breast cancer patients. A total of 928 patients were randomly allocated to 88 sites across Europe and North America. The study revealed that within the starting placebo group, 67% of all instances of febrile neutropenia occurred during the first treatment cycle. The risk of febrile neutropenia is highest during the first two cycles of chemotherapy, regardless of the type of tumor or chemotherapy treatment (Vogel *et al.*, 2005).

Consistent with the findings of Ludwig H *et al.* (2004), who reported anemia in 62% of 3,278 breast cancer patients, our study found that between 47.52% and 53.90% of patients suffered anemia over the four cycles of paclitaxel treatment. In a different study, Havrilesky *et al.* (2012) examined the possible economic consequences of a Paclitaxel drug shortage in ovarian cancer patients who were recently diagnosed. The study discovered that anemia was regularly seen, with no notable variation between chemotherapy cycles (Havrilesky *et al.*, 2012). Our study aligns with these findings, as we also found no statistically significant variation in the prevalence of anemia during treatment cycles. These findings indicate that anemia can manifest at any stage of the therapy cycle.

According to Pizzo and Poplack (2015), effective monitoring and management of hematopoietic toxicities are vital for cancer patients receiving chemotherapy. The adverse effects associated with this treatment can significantly impact patient treatment and quality of life. Therefore, Pizzo and Poplack (2015) stress that mitigating these toxicities requires effective management techniques such as the use of erythropoiesis-stimulating medicines and granulocyte colony-stimulating factors (G-CSF). Such proactive strategies, according to Pizzo and Poplack (2015), can improve the overall treatment efficacy and reduce the occurrence of serious sequelae. Additionally, similar tactics might enhance patient outcomes and enable improved adherence to the prescribed treatment regimen in adult oncology, including breast cancer patients undergoing paclitaxel chemotherapy. In our study, the use of G-CSF for breast cancer patients who had anemia and neutropenia was started or continued as per the cancer treatment plan or the recommendation of the physician. This had an impact on our conclusions. Therefore, the use of G-CSF resulted in a decrease in the occurrence of neutropenia and anemia among breast cancer patients (see table 3-6). Moreover, the consumption of drugs, herbal supplements, and meals by cancer patients before, during, and following treatment can have an impact on blood values. Hence, it is imperative to consider these indicators while assessing hematological toxicity (Alsanad *et al.*, 2016).

During the study period encompassing the four cycles of paclitaxel chemotherapy, no patient experienced mortality. Consequently, there were no deaths reported among the patients under observation. As previously mentioned, our study reports statistically significant differences in hematologic toxicities among breast cancer patients undergoing paclitaxel chemotherapy. While these differences are statistically significant, it is crucial to also consider their clinical significance to fully understand their impact on patient outcomes and treatment decisions. For instance, while grade 1 neutropenia might be less severe than higher grades, its presence can still influence patient management decisions, such as the need for supportive care interventions like granulocyte colonystimulating factors (G-CSF). These interventions can affect the overall treatment plan, potentially influencing of chemotherapy cycles, dosage the frequency adjustments, and patient quality of life (Schelenz et al., 2012). Based on these observations, future studies should aim to integrate these results into the broader context of clinical practice to better understand how these disparities affect patient outcomes. This may involve determining how patient symptoms, treatment tolerance, and overall therapy efficacy are impacted by changes in hematologic markers. Understanding the practical implications of these results is crucial for improving treatment procedures and making informed decisions that balance effectiveness with patient safety and well-being (Testart-Paillet et al., 2007).

# Study Limitations

This study is limited by restrictions on patient data, small sample size, single-center design, and the absence of a control group. Firstly, while this study included major medical data, access to patients' medical histories, including chronic conditions like hypertension, diabetes mellitus, etc., was restricted and hence not part of the analysis. These conditions could have influenced the metabolism of the chemotherapy agent, leading to an increase in hematological toxicities associated with chemotherapy. Relevant social history factors such as smoking, alcohol consumption, and any medication or food allergies were also not accessible. Secondly, the small sample size compared to the total number of breast cancer patients limits the generalizability of the results. A larger sample size could offer a more comprehensive understanding of the broader implications. However, the information gathered for this study provides valuable insights into paclitaxel's effects on blood parameters.

Thirdly, the single-center design limits the applicability of these findings to a broader population. Therefore, a multicentric study with a larger sample size would enhance the robustness and applicability of the results, allowing for a more comprehensive evaluation of hematologic toxicities and the effectiveness of management strategies across diverse patient populations. Future research should focus on expanding the sample size and including multiple centers to validate these findings and optimize treatment protocols for breast cancer patients.

A last and notable limitation of this study is the absence of a control group not receiving chemotherapy or G-CSF. This made it challenging to isolate and assess the specific effects of paclitaxel and G-CSF from other potential variables influencing hematologic outcomes. Without a control group, it is difficult to differentiate the impacts of the chemotherapy regimen and supportive care from those of other factors that might affect hematologic parameters. To address this limitation, it is recommended for future research to incorporate control groups, allowing for a more rigorous evaluation of the specific effects of paclitaxel and G-CSF, separate from other variables. Such studies could provide more robust data on the efficacy of treatments and help refine management strategies for hematologic toxicities in breast cancer patients.

# CONCLUSION

This study identified anemia as a prevalent hematological toxicity associated with paclitaxel chemotherapy in breast cancer patients, occurring at various stages of treatment. Regular complete blood count (CBC) monitoring is for early detection and management. essential Additionally, grade 1 neutropenia was commonly observed, particularly during initial treatment cycles. Although considered less severe, even mild neutropenia can elevate infection risk, potentially complicating patient health and treatment. Proactive management strategies, including regular neutrophil count monitoring and supportive measures like granulocyte colony-stimulating factors (G-CSF), are recommended to prevent progression. Future research should involve larger, more diverse populations across multiple medical centers to thoroughly assess paclitaxel's efficacy and explore optimal management strategies for mild neutropenia, aiming to improve patient outcomes and maintain chemotherapy effectiveness while minimizing risks.

# REFERENCES

- Alalawy AI (2024). Key genes and molecular mechanisms related to paclitaxel resistance. *Cancer Cell Int.*, **24**(1): 244.
- Al-Hashimi MMY (2021). Trends in breast cancer incidence in Iraq during the period 2000-2019. APJCP, 22(12): 3889-3896.
- Alsanad SM, Howard RL and Williamson EM (2016). An assessment of the impact of herb-drug combinations used by cancer patients. *BMC Complement. Altern. Med.*, **16**(1): 393.
- Basak D, Arrighi S, Darwiche Y and Deb S (2021). Comparison of anticancer drug toxicities: Paradigm shift in adverse effect profile. *Life*, **12**(1): 48.
- Daniel D and Crawford J (2006). Myelotoxicity from chemotherapy. *Seminars in Oncology*, **33**(1): 74-85.
- Feliu J, Heredia-Soto V, Gironés R, Jimenez-Munarriz B, Saldana J, Guillén-Ponce C and Molina-Garrido MJ (2020). Management of the toxicity of chemotherapy and targeted therapies in elderly cancer patients. *Clin. Transl. Oncol.*, **22**: 457-467.
- Havrilesky LJ, Garfield CF, Barnett JC and Cohn DE (2012). Economic impact of paclitaxel shortage in patients with newly diagnosed ovarian cancer. *Gynecol. Oncol.*, **125**(3): 631-634.
- Khalifa MF (2022). Epidemiology of breast cancer in Baghdad City 2018. J. Pharm. Negat. Results, **2022**: 1452-1456.
- Ludwig H, Van Belle S, Barrett-Lee P, Birgegård G, Bokemeyer C, Gascón P, Schrijvers D (2004). The European Cancer Anaemia Survey (ECAS): A large multinational prospective survey defining the prevalence, incidence and treatment of anaemia in cancer patients. *Eur. J. Cancer*, **40**(15): 2293-2306.
- Nardin S, Mora E, Varughese FM, D'Avanzo F, Vachanaram AR, Rossi V and Gennari A (2020). Breast cancer survivorship, quality of life and late toxicities. *Front. Oncol.*, **10**: 864.
- Othman RT, Abdulljabar R, Saeed A, Sadiq S, Kittani HM, Mohammed SA and Hussein NR (2011). Cancer incidence rates in the Kurdistan Region/Iraq from. *Asian Pac. J. Cancer Prev.*, **12**(5): 1261-64.
- Pizzo PA and Poplack DG (2015). Principles and Practice of Pediatric Oncology. Lippincott Williams & Wilkins.
- Salih K (1995). Anfal: The Kurdish genocide in Iraq. *Dig. Middle East Stud.*, **4**(2): 24-39.
- Schelenz S, Giles D and Abdallah S (2012). Epidemiology, management and economic impact of febrile neutropenia in oncology patients receiving routine care at a regional UK cancer centre. *Ann. Oncol.*, **23**(7): 1889-1893.
- Takahashi S, Takei Y, Tamura K, Taneichi A, Takahashi Y, Yoshiba T and Fujiwara H (2022). Response to and toxicity of weekly paclitaxel and carboplatin in patients with stage IIIC-IV ovarian cancer and poor general condition. *Mol. Clin. Oncol.*, **16**(1): 1-7.

- Testart-Paillet D, Girard P, You B, Freyer G, Pobel C and Tranchand B (2007). Contribution of modelling chemotherapy-induced hematological toxicity for clinical practice. *Crit. Rev. Oncol. Hematol.*, **63**(1): 1-11.
- US Department of Health and Human Services (2023). National Cancer Institute. Common Terminology Criteria for Adverse Events (CTCAE) version 5.0.
- Vogel CL, Wojtukiewicz MZ, Carroll RR, Tjulandin SA, Barajas-Figueroa LJ, Wiens BL and Schwartzberg LS (2005). First and subsequent cycle use of pegfilgrastim prevents febrile neutropenia in patients with breast cancer: A multicenter, double-blind, placebo-controlled phase III study. *J. Clin. Oncol.*, **23**(6): 1178-1184.
- World Health Organization (WHO) International Agency for Research on Cancer (IARC) (2013). Latest world cancer statistics: Global cancer burden rises to 14.1 million new cases in 2012. IARC Press Release N 223.