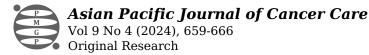


# **Transfusion Practice Patterns in Cancer Patients with Anemia: A Retrospective Study from a Single Oncology Center in** Najran, Saudi Arabia

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Background: Recent studies support the safety of restrictive pretransfusion hemoglobulin thresholds ( $\leq$ 7-8 g/dL) for adult cancer patients on chemotherapy. However, the restrictive transfusion strategies role in decreasing inappropriate red blood cell (RBC) transfusion practice in Saudi Arabia is not yet understood. This study aims to evaluate transfusion practices among oncologic patients at Najran Oncologic Center, Saudi Arabia.

Materials and Methods: A retrospective chart review study between January 1, 2020, and December 31, 2022, involving 59 adult cancer patients presented to King Khaled Hospital in Najran, Saudi Arabia. Clinical variables for prescribing RBC transfusions based on liberal (> 7 g/dL) or restricted (Hb < 7 g/dL) baseline hemoglobin levels and number of transfused RBCs were investigated in univariate analysis.



**Results:** The mean age was  $65.0 \pm 10.2$  years, and most cases were male (n=40, 67.8%). The common primary tumor location was colorectal cancers (n=27, 45.8%), and most cases were in metastatic stages (n=44, 74.6%). The majority of cases (n=36, 61.0%) had severe anemia (Hb < 7 g/dL) at admission. The mean number of RBC units received was  $4.9 \pm 2.4$  RBC. Variables associated with restricted prescribing RBC transfusions were male gender (OR: 3.21; 95% CI: 1.05-10.33, p= 0.044), high ECOG-PS status (OR: 2.95; 95% CI: 1.01-9.03, p=0.048), cardiac disease history (OR: 2.05; 95% CI: 0.69-6.44, p= 0.009), and platinum-based chemotherapy (OR: 233.33; 95% CI: 33.12-5054.45, p <0.001). However, survival status was higher among patients with restrictive strategy (OR: 0.25; 95% CI: 0.08-0.73, p= 0.025). Factors associated with an increased number of transfused RBCs were male gender (OR:1.43; 95% CI: 1.07-1.93, p= 0.012), platinum-based chemotherapy (OR:1.55; 95% CI: 1.18-2.15, p= 0.004), history of bleeding (OR: 1.31, 95% CI: 1.02-1.73, p= 0.032), and history of cardiac disease (OR: 1.31 (1.02-1.73; p= 0.002).

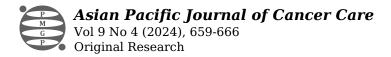
**Conclusion:** The study concluded that factors like male gender, platinum-based chemotherapy, bleeding history, and concurrent cardiac disease were associated with an increased number of RBC transfusions. In addition to that, we found a clear adherence to the clinical practice guidelines among the transfused patients. The study suggests an etiology-based approach to cancer-related anemia and transfusions, enabling clinicians to plan safe, targeted therapy and improve patients' quality of life by synchronizing chemotherapy efficacy.

## Introduction

Anemia treatment is critical in cancer patients because it can lead to impaired physical function, a worse prognosis, and a lower quality of life [1]. The decision to prescribe packed red blood cell (RBC) transfusions in patients with chemotherapy-induced anemia (CIA) is based on clinical factors such as the patient's cancer type and treatment plan, the severity of anemia symptoms, and the presence of comorbidities, which are an essential supportive measure in patient care [2]. Overall, the uses and indications for transfusion therapy have evolved in recent years, with a shift toward a more restrictive transfusion policy [2, 3]. However, healthcare professionals should consider concurrent conditions and medications, particularly for cancer patients receiving chemotherapy, when deciding whether to recommend RBC transfusions. Likewise, the advantageous effects of a blood transfusion have to be weighed toward known risks, which include transfusion-related reactions such as circulatory overload, acute lung injury, allergic reaction, and febrile nonhemolytic transfusion reaction, as well as the transmission of bloodborne pathogens [2, 4]. Other factors include the time constraints in transfusion administration, the inconvenience to patients and healthcare workers, and the associated costs [2].

The National Comprehensive Cancer Network (NCCN) recommends limiting the use of transfusions for cancer-related anemia to achieve a hemoglobin (Hb) concentration of  $\geq$  7 g/dL. However, transfusions may still be necessary for patients with anemia symptoms or comorbidities like cardiac disease, chronic pulmonary disease, or cerebrovascular disease [5, 6]. While studies examining treatment with erythropoiesis-stimulating agents (ESAs) have provided a substantial body of data on patients with CIA, there is still a lack of evidence on clinical criteria used to determine whether to transfuse patients with CIA [7, 8]. As a result, a study evaluating the clinical criteria used to order transfusions for patients with CIA can aid practitioners in understanding current practice patterns [2].

The benefits of blood transfusions in advanced cancer patients have been studied but are inconsistent, with a limited duration of response. The Cochrane study found a 31%-70% improvement in fatigue, breathlessness, or well-being, with a 49% improvement in primary target symptoms [9]. Marote et al. discovered that symptomatic benefit was achieved in 36% of transfusion recipients sustained after 15 days, with no benefit observed in 31%. The number of RBC



units did not affect the benefit [10]. The role of restrictive transfusion strategies in decreasing inappropriate RBC transfusion practice in Saudia Arabia is still not understood and not documented in our center. This study aims to evaluate RBC transfusion practices among cancer patients at Najran Oncologic Center, Saudi Arabia.

## **Materials and Methods**

#### Study protocol and exclusion criteria:

A retrospective chart review was conducted on adult cancer chemotherapy patients at King Khaled Hospital in Najran, Saudi Arabia, covering the period from January 1, 2020, to December 31, 2022. The study included adult cancer patients (>18 years) who received RBC transfusion during the study period. Because patients may have received RBC transfusions at different times, we classified each date associated with the transfusion of one or more units as a transfusion episode.

In this study, RBC transfusion was based on the NCCN guidelines for treating anemia in cancer patients. According to the guidelines, patients with no cardiovascular risk factors should get a transfusion if their Hb level is < 7-8 g/dl, and rarely if it is > 9-10 g/ dl. Patients with cardiovascular risk factors, particularly coronary heart disease, should have a higher minimum Hb threshold, around 9 g/d; patients with symptomatic anemia should receive transfusions regardless of Hb criteria [11]. Previous cohort studies reviewing anemia and RBC transfusion in advanced cancer patients have utilized similar criteria [10].

### Data sources and study procedures

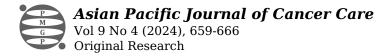
Medical records of patients were evaluated to obtain information on age, gender, cancer type, cancer stage at initial diagnosis, the regimen of chemotherapy received, comorbidities, therapies used to treat or prevent anemia in the previous six months, signs and symptoms of anemia affecting the decision to prescribe RBC transfusions, and the number of transfusion events, Eastern Cooperative Oncology Group performance status (ECOG-PS), pretransfusion report of active bleeding, pretransfusion Hb level, symptomatic benefit in the 15 days following the transfusion episode, adverse events, and survival. A safety endpoint was used to determine the number of adverse events (death vs. survival).

#### Main outcome

The main outcomes were to investigate the clinical variables for prescribing RBC transfusions based on liberal (> 7 g/dL) or restricted (Hb < 7 g/dL) baseline hemoglobin levels. The secondary outcome was factors associated with the increased number of transfused RBCs.

### **Statistical analysis**

Continuous data were presented as mean and standard deviation (SD) if normally distributed and median (interquartile range: IQR) if skewed. Categorical data were presented as numbers (%). Categorical variables were analyzed using the Chi-square test or Fisher's exact test, whereas continuous variables were evaluated using Student's t-test or the Mann-Whitney U test. The odds ratios and 95% confidence intervals were calculated to assess the strength of the associations. Statistical significance was set at p < 0.05. IBM SPSS version 25 software (IBM Corp., Armonk, New York) was used for statistical analyses.



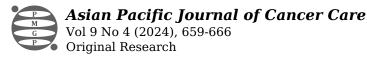
## Ethical approval

In adherence to the Declaration of Helsinki, the ethics committee of King Khaled Hospital obtained ethical approval. All participants provided informed consent, emphasizing voluntary participation, anonymity, and confidentiality.

## **Results**

The mean age was  $65.0 \pm 10.2$  years (Rang: 43.0 - 79.0), and most cases were male (n=40, 67.8%). The common tumor location was colorectal cancers (n=27, 45.8%), followed by hematological cancers (n=11, 18.6%) and genitourinary (n=11, 18.6%). A significant proportion of patients (74.6%) were in locally advanced stages. Most patients (n=22, 37.3%) were in ECOG-PS 4 and received platinum-containing chemotherapy (n=36, 61%), and most received first-line chemotherapy (n=44, 74.6%). Most cases had severe anemia (Hb= 8-6.5 g/dL) at admission (n=34, 57.6%), and life-threatening anemia (Hb < 6.5 g/dL) was seen in 19 (32.2%) while 6 (10.2%) had moderate anemia (Hb= 10-8 g/dL) (Table 1).

Variables	N (%)	
Age (year), Mean ±SD	65.0 ±10.2	
	(Rang: 43 - 79)	
Gender		
Female	19 (32.2)	
Male	40 (67.8)	
Primary tumor location		
Colorectal	27 (45.8)	
Hematology	11 (18.6)	
Genitourinary	11 (18.6)	
Gynecological	4 (6.8)	
Breast	3 (5.1)	
Head and neck	3 (5.1)	
Cancer stage		
Locally advanced	15 (25.4)	
Metastatic	44 (74.6)	
Type of cancer N (%)		
Colon cancer	7 (11.9)	
Gastric Cancer	7 (11.9)	
Adenocarcinomas of prostate	7 (11.9)	
Hepatocellular carcinoma	4 (6.8)	
Multiple myeloma	4 (6.8)	
Bladder cancer	3 (5.1)	
Uterine cancer	3 (5.1)	
Pancreatic cancer	3 (5.1)	
Breast cancer	3 (5.1)	
Lymphoma	3 (5.1)	
Bone cancer	2 (3.4)	
Neuroendocrine tumors	2 (3.4)	
Soft tissue sarcoma	2 (3.4)	
Cholangiocarcinoma	2 (3.4)	
Rectal cancer	2 (3.4)	
Pretransfusion hemoglobin	6.8 ±1.0 (Rang: 3.5 - 8.4)	
Severity of anemia		
Severe (Hb= 8-6.5 g/dL)	34 (57.6)	



Life-threatening (Hb < $6.5 \text{ g/dL}$ )	19 (32.2)
Moderate (Hb= 10-8 g/dL)	6 (10.2)

Table 1. Patients and Disease Characteristics (N=59).

Abbreviations; Hb, hemoglobin

Comorbidities include a history of cardiovascular disease in 12 (20.3%) cases and anemia in 16 (27.1%) cases. History of colonoscopy and upper endoscopy were presented in 13 (22.4%) and 24 (41.4%) cases, respectively. A history of intravenous iron intake was seen in 9 (15.3%) and a history of ESA use in 27 (45.8%) cases. The main indication for RBC transfusions was hemoglobin< 7 g/dL in 33 (55.9%) cases, followed by anemia symptoms (tachycardia, tachypnea, postural hypotension) in 18 (30.5%) cases. The main symptoms were fatigue/asthenia in 29 (49.2%), followed by palpitations in 13 (22.0%) cases, dizziness in 9 (15.3%) cases, and shortness of breath in 7 (11.9%) cases. The mean pretransfusion hemoglobin was  $6.8 \pm 1.0$  g/dL (Rang: 3.5 - 8.4 g/dL). The mean number of RBC units received was  $4.9 \pm 2.4$  RBC (range: 1.0 - 13.0 RBC) with a median of 5 RBC, a minimum of 1 RBC, and a maximum of 13 RBC (Table 2).

Variables	N (%)
ECOG-PS	
1	18 (30.5)
2	6 (10.2)
3	13 (22.0)
4	22 (37.3)
Indication for RBC transfusions	
Hemoglobin< 7 g/dL to maintain hemoglobin 7-9 g/dL	33 (55.9)
Hgb <10 g/dL (with cardiopulmonary disease)	8 (13.6)
Symptomatic (tachycardia, tachypnea, postural hypotension)	18 (30.5)
Main symptom	
Fatigue/asthenia	29 (49.2)
Palpitations	13 (22.0)
Dizziness	9 (15.3)
Shortness of breath	7 (11.9)
Other	1 (1.7)
Relevant Background	
History of cardiovascular disease	12 (20.3)
History of IV iron intake	9 (15.3)
History of anemia	16 (27.1)
History of Erythropoiesis-Stimulating Agents use	27 (45.8)
History of colonoscopy	13 (22.4)
History of upper endoscopy	24 (41.4)
Treatment received	
Number of RBC units received, Mean ±SD	4.9 ±2.4 (range: 1.0 - 13.0)
Number of RBC units received, median (min-max)	5 (1 -13)

Table 2.Collected Data of ECOG-PS, Indication for RBC Transfusions, Symptoms, Comorbidities, and TreatmentReceived by Transfusion Episode.

Abbreviations, ECOG-PS, Eastern Cooperative Oncology Group performance status; RBC, red blood cell; SD, standard deviation, Hb, hemoglobin.

Regarding RBC transfusion episode assessment, 40 (67.8%) showed symptomatic benefits from RBC transfusion. Transfusion reaction was presented in 2 (3.4%) cases. Death occurred in 30

(50.8%) cases with a median survival time of 14.5 days (6 - 30 days) (Table 3).

Variables	N (%)
Symptomatic benefit	
Yes	40 (67.8)
No	19 (32.2)
Adverse events	
Alive	29 (49.2)
Dead	30 (50.8)
Transfusion reaction	2 (3.4)
Time to death (day)	
Mean ±SD	$16.8 \pm 10.7$
Median (min-max)	14.5 (6 - 30)

 Table 3. Transfusion Episodes Assessment by Symptomatic Benefit, Adverse Events, and Mortality.

Factors associated with restrictive strategy (Hb  $\leq$  7 g/ dL) for RBC transfusion:Variables associated with the restrictive strategy for prescribing RBC transfusions were male gender (OR: 3.21; 95% CI: 1.05-10.33, p= 0.044), high ECOG-PS status (OR: 2.95; 95% CI: 1.01-9.03, p=0.048), cardiac disease history (OR: 2.05; 95% CI: 0.69-6.44, p= 0.009), and platinum-based chemotherapy (OR: 233.33; 95% CI: 33.12-5054.45, p <0.001) that were statistically significant (Table 4).

Variables	Subgroup	Hb > 7 g/dL (N=23)	$Hb \le 7 \text{ g/dL}$ (N=36)	OR (95%CI)	p-value
Age (years)	Median (IQR)	67.0 (60.0 to 77.0)	62.5 (60.0 to 75.5)	1.00 (0.94-1.05)	0.862
Age (years)	<65 years	11 (35.5)	20 (64.5)	RF	0.562
	≥65 years	12 (42.9)	16 (57.1)	0.73 (0.25-2.10)	
Gender	Female	11 (57.9)	8 (42.1)	RF	0.044
	Male	12 (30.0)	28 (70.0)	3.21 (1.05-10.33)	
Symptoms	Dizziness	4 (44.4)	5 (55.6)	RF	
	Fatigue	12 (41.4)	17 (58.6)	1.13 (0.24-5.18)	0.871
	Palpitations	4 (30.8)	9 (69.2)	1.80 (0.30-11.12)	0.514
	Breathlessness	3 (37.5)	5 (62.5)	1.33 (0.19-10.07)	0.772
ECOG-PS	Low	13 (54.2)	11 (45.8)	RF	0.048
	High	10 (28.6)	25 (71.4)	2.95 (1.01-9.03)	
Cancer location	Head and neck	1 (33.3)	2 (66.7)	RF	
	Colorectal	12 (44.4)	15 (55.6)	0.63 (0.03-7.31)	0.714
	Hematological	3 (27.3)	8 (72.7)	1.33 (0.05-20.21)	0.837
	Breast	1 (33.3)	2 (66.7)	1.00 (0.02-40.40)	1
	Genitourinary	4 (36.4)	7 (63.6)	0.88 (0.03-12.39)	0.923
	Gynecological	2 (50.0)	2 (50.0)	0.50 (0.01-10.86)	0.661
Cancer stage	Nonmetastatic	7 (46.7)	8 (53.3)	RF	0.481
	Metastatic	16 (36.4)	28 (63.6)	1.53 (0.46-5.07)	
History of iron intake	No	20 (42.6)	27 (57.4)	RF	0.273
	Yes	3 (25.0)	9 (75.0)	2.22 (0.58-10.98)	
History of bleeding	No	18 (43.9)	23 (56.1)	RF	0.247
	Yes	5 (27.8)	13 (72.2)	2.03 (0.64-7.31)	
History of cardiac disease	No	23 (100.0)	27 (75.0)	Reference group	0.009
	Yes	0 (0.0)	9 (25.0)	2.05 (0.69-6.44)	
History of anemia	No	20 (46.5)	23 (53.5)	RF	0.062
	yes	3 (18.8)	13 (81.2)	3.77 (1.03-18.17)	
ESA use	No	15 (46.9)	17 (53.1)	RF	0.179



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	Yes	8 (29.6)	19 (70.4)	2.10 (0.72-6.38)	
History of colonoscopy	No	18 (40.0)	27 (60.0)	RF	0.92
	Yes	5 (38.5)	8 (61.5)	1.07 (0.30-4.02)	
History of upper GI endoscopy	No	13 (38.2)	21 (61.8)	RF	0.793
	Yes	10 (41.7)	14 (58.3)	0.87 (0.30-2.54)	
Chemotherapy type	Platinum-based	20 (95.2)	1 (4.8)	RF	<0.001
	Non - platinum- based	3 (7.9)	35 (92.1)	233.33 (33.12-5054.45)	
Post-transfusion reaction	No	22 (38.6)	35 (61.4)	RF	0.747
	Yes	1 (50.0)	1 (50.0)	0.63 (0.02-16.44)	
Transfusion numbers	Median (IQR)	3.0 (2.5 to 5.0)	6.0 (4.0 to 7.0)	1.55 (1.18-2.15)	0.004
Status	Alive	16 (69.6)	13 (36.1)	RF	0.025
	Dead	7 (30.4)	23 (63.9)	0.25 (0.08-0.73)	

Table 4. Factors Associated with Primary Clinical Considerations for Prescribing Red Blood Cell TransfusionStratified by Hemoglobin Baseline.

Abbreviations, GI, gastrointestinal; OR, odds ratio; CI, confidence interval; Hb, Hemoglobin; ESA, erythropoiesis-stimulating agents; ECOG-PS, Eastern Cooperative Oncology Group performance status; IQR interquartile range; RF, Reference group

However, survival status was higher among patients with restrictive strategy [16 (69.6%) vs. 13 (36.1%)] (OR: 0.25; 95% CI: 0.08-0.73, p= 0.025).Factors associated with increased number of transfused RBCs:The increased number of transfused RBC was associated with male gender (OR: 1.43; 95% CI: 1.07-1.93, p= 0.012), Platinum-based chemotherapy (OR:1.55;95%CI: 1.18-2.15, p= 0.004), history of bleeding (OR: 1.31, 95% CI: 1.02-1.73, p= 0.032), and history of cardiac disease (OR: 1.31 (1.02-1.73; p= 0.002) that were statistically significant (Table 5).

Variables	Subgroups	Number of transfused RBC(mean± S.D.)	OR (95%)	p-value
Age	<65 years	4.8 ±2.3	Reference group	0.71
	≥65 years	5.1±2.5	1.04 (0.84-1.31)	
Gender	Female	3.8 ±1.9	Reference group	0.012
	Male	$5.5 \pm 2.4$	1.43(1.07-1.93)	
Cancer location	Other locations	5.3±2.8	Reference group	0.361
	Colorectal	4.7±1.9	1.11 (0.89-1.40)	
ECOG-PS	Low	4.3 ±2.3	Reference group	0.104
	High	5.4 ±2.4	1.23 (0.97-1.59)	
Cancer stage	Nonmetastatic	4.1 (2.3)		0.126
	Metastatic	5.2 (2.4)	1.25 (0.96-1.70)	
Chemotherapy type	Non -platinum-based	3.8 (1.8)	Reference group	0.004
	Platinum-based	5.7 (2.4)	1.55 (1.18-2.15)	
Survival	Alive	4.4 ±2.8	Reference group	0.117
	Died	5.4 ±1.8	1.21 (0.96-1.55)	
Palliative care	No	4.7 ±2.5	Reference group	0.305
	Yes	5.3 ±2.1	1.12 (0.90-1.42)	
History of ESA use	No	4.6 ±2.4	Reference group	0.256
	Yes	5.3 ±2.4	1.14 (0.91-1.44)	
History of iron intake	No	4.9 ±2.3	Reference group	0.944
	Yes	5.0 ±2.7	1.01 (0.73-1.35)	
History of bleeding	No	4.5 ±2.4	Reference group	0.032



	Yes	$5.9 \pm 2.1$	1.31 (1.02-1.73)	
History of cardiac disease	No	4.5 ±2.4	Reference group	0.002
	Yes	5.9 ±2.1	1.31 (1.02-1.73)	

 Table 5. Factors Associated with Increased Transfused RBCs in Univariate Analysis.

Abbreviations, RBC, red blood cell; OR, odds ratio; CI, confidence interval; ESA, erythropoiesisstimulating agents; ECOG-PS, Eastern Cooperative Oncology Group performance status; SD, standard deviation.

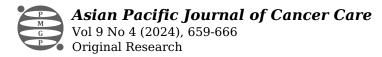
## Discussion

Survival status was higher among patients with restrictive strategies in blood transfusion, based on that, the NCCN guidelines and most of the respected international guidelines are recommending the restrictive transfusion strategy. In a previous report from KSA, Badheeb et al. noted a high prevalence of anemia (50.5%) in patients receiving active cancer treatment [16]. This fact encouraged us to conduct this study to assess the adherence of the treating physicians in Najran Cancer Center to the guidelines upon ordering blood transfusion. Anemia is a prevalent problem in cancer patients, particularly before therapy. It is also a common side effect of chemotherapy, with 58% of patients seeing a decrease in Hb by week nine from < 10 g/dL to < 9 g/dL [12]. The pathophysiology of anemia in cancer patients may be attributed to inflammation, reducing RBC formation, while chemotherapy decreases bone marrow production, and renal disease [13]. A survey in Japan revealed an average Hb level of 9.5 g/dL before therapy [15]. Western Denmark's median Hb level of 8.1 g/dL before therapy, and 52.1% of cases had Hb less than eight g/dL [2]. The European Cancer Anemia Study discovered that the average Hb level in cancer patients before iron supplementation, transfusion, or ESA use was 9.7 g/dL [13].

In this study, factors such as male gender, high ECOG-PS status, cardiac disease history, and platinum-based chemotherapy were associated with low Hb at admission and subsequently more blood transfusion, this can be explained by the higher percentage of male cancers in this cohort (male (n=40, 67.8%), the exclusion of the palliative patients without active anticancer therapy from the study, the need to keep the hemoglobin above 10 g/dL among cardiac patients, and finally the well-known myelosuppressive effect of platinum chemotherapy [14, 15].

In this study, survival status was higher among patients with restrictive strategy (OR: 0.25; 95% CI: 0.08-0.73, p=0.025). Similarly, a recent systematic review found that restrictive transfusion strategies with reduced RBC unit transfusions are as safe as liberal ones, with similar 30-day mortality rates [16]. Link et al. found that constant adherence to guideline recommendations improves anemia therapy outcomes significantly with no difference in survival [18].

The main indication for RBC transfusions in this study was hemoglobin < 7 g/dL in 33 (55.9%) patients, followed by predominant symptoms in 18 (30.5%) patients with fatigue/asthenia being the predominant symptom in 29 (49.2%) patients. Our result aligns with the correlation recognized in the existing literature, such as Granfortuna et al.'s report, which stated that anemic symptoms were the most common reason for transfusions in 72.1% of the patients [2]. While absolute Hb value was merely a secondary concern, it was indicated as a reason for transfusion in 25.2% of cases. However, the mean symptoms were identical to our previous findings, in which fatigue was the most common symptom in 69.2% of patients [2]. Anemia symptoms played a substantial role in the choice to transfuse cancer patients, although fatigue was not a key indication for transfusion outside of the cancer scenario. Cancer-related fatigue, physical and psychological symptoms of cancer, treatment effects, repeated chemotherapy cycles, and recuperation intervals all have an impact on cancer management decisions [2]. Although most of our patients had no underlying



comorbidities, the majority of them had advanced malignancy. In this study, comorbidities include a history of cardiovascular disease in 12 (20.3%) and anemia in 16 (27.1%) cases. Our findings were almost identical to those of Granfortuna et al., who reported comorbidities in 27.9% of patients [2]. However, clinicians must identify the treatable causes of anemia before chemotherapy and begin iron supplementation even before patients are genuinely deficient.

Anemia in cancer patients on chemotherapy is a complex illness impacted by several aspects, including chemotherapeutic drug, malignancy stage, hemoglobin levels, intervention timing, nutritional status, renal function, age, gender, ECOG performance score, and bleeding history, making it challenging to create universal care standards [17]. However, the debate on factors contributing to anemia in cancer patients is ongoing, with limited clear criteria, leading to inconsistent prognostic factors. In this study, the mean number of RBC units received was  $4.9 \pm 2.4$  RBC (range: 1.0 - 13.0 RBC) with a median of 5 RBC, a minimum of one RBC, and a maximum of 13 RBC. Furthermore, the increased number of transfused RBCs was associated with male gender, platinum-based chemotherapy, history of bleeding, and history of cardiac disease. In the Skillings et al. trial, the predictors for increased RBC transfusion were platinum and anthracycline treatment, baseline hemoglobin, and illness stage [18]. In another study, Hensley et al. found that prechemotherapy hemoglobin <10 g/dL and those receiving carboplatin-paclitaxel were predictors for increased risk of requiring RBC transfusion [19]. To gain a better understanding of the true impact of a restricted RBC transfusion strategy on clinical outcomes, a well-conceived and implemented study is needed.

### **Study limitations**

This study has been limited by its retrospective methodology and small sample size, which assessed the electronic medical records of cancer patients who attended the King Khaled Hospital in Najran, Saudi Arabia. Moreover, because this is a single-center study, it cannot exclude possible selection biases according to our transfusion practices. A retrospective document review for patients' ultimate diagnosis may be unrelated to their principal complaint, which needed to be more comprehensive and sensitive to anemia-related tools. Further prospective studies are required to help guide the pragmatic and productive use of RBC transfusions utilizing a prospective registry of consecutive cases used in their pharmacovigilance series.

In conclusion, the study concluded that factors like male gender, platinum-based chemotherapy, bleeding history, and concurrent cardiac disease were associated with an increased number of RBC transfusions. In addition to that, we found a clear adherence to the clinical practice guidelines among the transfused patients. The study suggests an etiology-based approach to cancer-related anemia and transfusions, enabling clinicians to plan safe, targeted therapy and improve patients' quality of life by synchronizing chemotherapy efficacy.

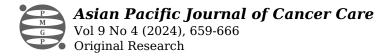
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none.

Study approval



The study was reviewed and approved by the King Khalid Hospital research ethics committee.

#### Availability of data

Data is available from the authors upon written request.

#### Conflict of Interest

The authors declare that they have no competing interests.

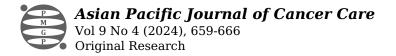
#### Authors' contributions

Ahmed Badheeb, Bandar Alotaibi, Abdelaziz Aman, and Islam Seada: conducted data collection and interpretation, and drafting of the manuscript. Abdullah Abubakar, Samer Alkarak, Mohammed Alramahi, and Mohammed Bazuqamah: were responsible for data analysis and interpretation, and revision of the manuscript. Ali Garbo, Mahran Mohammed, Ammar Idris, Nadeem Nagi, Faisal Ahmed, Mohamed Badheeb, and Hamoud Obied: did conception of work, data interpretation, and critical revision of the manuscript. All authors have read and approved the final manuscript.

## **References**

## **References**

- Natalucci V, Virgili E, Calcagnoli F, Valli G, Agostini D, Zeppa SD, Barbieri E, Emili R. Cancer Related Anemia: An Integrated Multitarget Approach and Lifestyle Interventions. *Nutrients*. 2021; 13(2)DOI
- 2. Granfortuna J, Shoffner K, DePasquale SE, Badre S, Bohac C, De Oliveira Brandao C. Transfusion practice patterns in patients with anemia receiving myelosuppressive chemotherapy for nonmyeloid cancer: results from a prospective observational study. *Supportive Care in Cancer.* 2018; 26(6)DOI
- 3. Montoro M, Cucala M, Lanas Á, Villanueva C, Hervás AJ, Alcedo J, Gisbert JP, Aisa AP, Bujanda L, Calvet X, Mearin F, Murcia Ó, Canelles P, García López S, Martín de Argila C, Planella M, Quintana M, Jericó C, García Erce JA. Indications and hemoglobin thresholds for red blood cell transfusion and iron replacement in adults with gastrointestinal bleeding: An algorithm proposed by gastroenterologists and patient blood management experts. *Frontiers in Medicine*. 2022; 9DOI
- 4. Watkins T, Surowiecka MK, McCullough J. Transfusion indications for patients with cancer. *Cancer Control: Journal of the Moffitt Cancer Center.* 2015; 22(1)DOI
- Franchini M, Marano G, Mengoli C, Pupella S, Vaglio S, Muñoz M, Liumbruno GM. Red blood cell transfusion policy: a critical literature review. *Blood Transfusion = Trasfusione Del Sangue*. 2017; 15(4)<u>DOI</u>
- 6. Shah N, Andrews J, Goodnough LT. Transfusions for anemia in adult and pediatric patients with malignancies. *Blood Reviews*. 2015; 29(5)DOI
- 7. Bormanis J, Quirt I, Chang J, Kouroukis CT, MacDonald D, Melosky B, Verma S, Couture F. Erythropoiesis-stimulating agents (ESAs): do they still have a role in chemotherapy-induced anemia (CIA)?. *Critical Reviews in Oncology/Hematology*. 2013; 87(2)DOI
- 8. Li X, Yan Z, Kong D, Zou W, Wang J, Sun D, Jiang Y, Zheng C. Erythropoiesis-stimulating agents in the management of cancer patients with anemia: a meta-analysis. *Chinese Journal of Cancer Research = Chung-Kuo Yen Cheng Yen Chiu.* 2014; 26(3)DOI
- 9. Preston NJ, Hurlow A, Brine J, Bennett MI. Blood transfusions for anaemia in patients with



advanced cancer. The Cochrane Database of Systematic Reviews. 2012; 2012(2)DOI

- 10. Marote S, Marinho J, Silva MC, Ferraz Gonçalves J. Transfusion practices in patients with advanced cancer: a retrospective study in a palliative care service. *Porto Biomedical Journal*. 2022; 7(6)DOI
- Escobar Álvarez Y., Las Peñas Bataller R., Perez Altozano J., Ros Martínez S., Sabino Álvarez A., Blasco Cordellat A., Brozos Vázquez E., Corral Jaime J., García Escobar I., Beato Zambrano C.. SEOM clinical guidelines for anaemia treatment in cancer patients (2020). Clinical & Translational Oncology: Official Publication of the Federation of Spanish Oncology Societies and of the National Cancer Institute of Mexico. 2021; 23(5)DOI
- 12. Pirker R, Pirolli M, Quigley J, Hulnick S, Legg J, Collins H, Vansteenkiste J. Hemoglobin decline in cancer patients receiving chemotherapy without an erythropoiesis-stimulating agent. Supportive Care in Cancer: Official Journal of the Multinational Association of Supportive Care in Cancer. 2013; 21(4)DOI
- Ludwig H, Van Belle S, Barrett-Lee P, Birgegård G, Bokemeyer C, Gascón P, Kosmidis P, Krzakowski M, Nortier J, Olmi P, Schneider M, Schrijvers D. The European Cancer Anaemia Survey (ECAS): a large, multinational, prospective survey defining the prevalence, incidence, and treatment of anaemia in cancer patients. *European Journal of Cancer* (Oxford, England: 1990). 2004; 40(15)DOI
- 14. Hess LM, Smith D, Cui ZL, Montejano L, Liepa A,, Schelman W, Bowman L. The relationship between Eastern Cooperative Oncology Group performance status and healthcare resource utilization among patients with advanced or metastatic colorectal, lung or gastric cancer. *Journal of Drug Assessment.* 10(1)DOI
- 15. Schwartz RN. Anemia in patients with cancer: incidence, causes, impact, management, and use of treatment guidelines and protocols. *American journal of health-system pharmacy: AJHP: official journal of the American Society of Health-System Pharmacists.* 2007; 64(3 Suppl 2)DOI
- 16. Estcourt LJ, Malouf R, Trivella M, Fergusson DA, Hopewell S, Murphy MF. Restrictive versus liberal red blood cell transfusion strategies for people with haematological malignancies treated with intensive chemotherapy or radiotherapy, or both, with or without haematopoietic stem cell support. *The Cochrane Database of Systematic Reviews*. 2017; 1(1)DOI
- Bryer E, Henry D. Chemotherapy-induced anemia: etiology, pathophysiology, and implications for contemporary practice. *International Journal of Clinical Transfusion Medicine*. 2018 2018/11/16; Volume 6(null):21-31.https://www.tandfonline.com/doi/abs/10.2147/IJCTM.S187569.
- 18. Skillings J. R., Rogers-Melamed I., Nabholtz J. M., Sawka C., Gwadry-Sridhar F., Moquin J. P., Rubinger M., et al. An epidemiological review of red cell transfusions in cancer chemotherapy. *Cancer prevention & control: CPC = Prevention & controle en cancerologie: PCC*. 1999; 3(3)
- Hensley M. L., Lebeau D., Leon L. F., Venkatraman E., Waltzman R., Sabbatini P., Almadrones L., Chi D., Spriggs D.. Identification of risk factors for requiring transfusion during front-line chemotherapy for ovarian cancer. *Gynecologic Oncology*. 2001; 81(3)<u>DOI</u>