-✦- Signa Vitae

ORIGINAL RESEARCH

Transfusion-related outcomes: investigating the interplay between blood transfusions, deep vein thrombosis, arterial thromboembolism, and mortality rates in Saudi Arabia

Haifa M. AlNafea[1], Hayat Y. Alzhrani[1], Farjah H. AlGahtani[2],*, Shatha A. AlOmar[1], Hajera Tabassum[3]

[1]Department of Clinical Laboratory Sciences, College of Applied Medical Sciences, King Saud University, 12371 Riyadh, Saudi Arabia
[2]Department of Medicine, Division of Hematology/Oncology (Oncology Center), College of Medicine, King Saud University Medical City (KSUMC), King Saud University, 12371 Riyadh, Saudi Arabia
[3]Department of Clinical Laboratory Sciences, Chair of Medical and Molecular Genetics Research, College of Applied Medical Sciences, King Saud University, 12371 Riyadh, Saudi Arabia

*Correspondence
falgahtani@ksu.edu.sa
(Farjah H. AlGahtani)

Abstract

Blood transfusions are integral to modern medical practice, playing a crucial role in managing various medical conditions. However, concerns have arisen regarding potential complications associated with transfusions, particularly their impact on haemostasis and thrombotic events. Deep vein thrombosis (DVT) and arterial thromboembolism (ATE), serious complications linked to altered haemostasis, present challenges to patient care, and require a nuanced understanding of their relationship with blood transfusions. This retrospective, population-based, cohort study investigated the association between blood transfusions, venous thromboembolism (VTE), ATE and subsequent mortality in patients undergoing recurrent blood transfusions. A total of 1000 patients who received red blood cells (RBCs), platelets, fresh frozen plasma (FFP), and cryoprecipitate between 2015 and 2022 were analysed. Post-transfusion occurrences of VTE and ATE were assessed using the chi-square test and multivariate logistic regression to identify independent risk factors. Multivariable regression analysis revealed a significant association between platelet transfusion and increased odds of development of ATE. However, no correlation was found between blood transfusions and the development of DVT. Notably, patients aged 55–69 years in the blood transfusion cohort exhibited a higher risk of DVT ($p < 0.05$), particularly those without chronic or cardiovascular diseases. Haematological diseases increased the demand for platelets and FFP, while patients without chronic diseases favoured platelet transfusions. Furthermore, patients with haematological or malignancy diseases, free of chronic diseases, had a higher likelihood of mortality within the blood transfusion cohort. Although the cause-and-effect relationship remains undetermined, these findings underscore the significant association between platelet transfusions and the risk of ATE, emphasising the importance of vigilant blood transfusion management practices. The study's outcomes would facilitate a clear understanding of the potential risks associated with blood transfusion, thereby aiding healthcare providers in making informed decisions, particularly in emergency medicine.

Keywords

Blood transfusion; Venous thromboembolism; Arterial thromboembolism; Platelet transfusion

1. Introduction

Blood transfusion is a widely practiced medical intervention essential for saving and improving countless lives each year [1–3]. Individuals facing critical conditions such as trauma, surgical blood loss, or severe anaemia often require this life-saving treatment, which can involve whole blood or separate blood components such as red blood cells (RBCs), platelets or plasma, each stored at different temperatures, potentially altering blood properties during storage [4–6]. The absence of universally accepted guidelines poses a challenge to blood transfusion practices worldwide, underscoring the necessity for comprehensive strategies in blood surveillance, conservation, and identifying suitable transfusion groups to maximise benefits and minimise risks [7]. Despite being generally safe, blood transfusion may potentially lead to the occurrence of adverse transfusion reactions (TRs) and transfusion-transmitted infections (TTIs) [8]. The risks associated with blood transfusions have expanded beyond infectious concerns to include thrombosis, a leading global cause of mortality [9]. Recent

studies have revealed that blood transfusions are associated with a higher likelihood of experiencing life-threatening events such as pulmonary embolism (PE) and deep vein thrombosis (DVT) [10–16]. This potential association between blood transfusions and thrombotic events is especially noted in high-risk patients undergoing surgery or those with cancer. Arterial thrombosis, which includes events such as cerebral and myocardial infarction, is linked to platelet accumulation triggered by plaque rupture. In contrast, venous thromboembolism (VTE), comprising DVT and PE, results from blood stasis and endothelial dysfunction, leading to the formation of red clots rich in RBCs and fibrin [11].

Hence, the risk of thrombosis should be evaluated in patients requiring blood transfusions, especially in those with underlying medical conditions predisposing them to clotting disorders. A clear understanding of the potential risks associated with blood transfusions, including thromboembolic events, is essential for informed decision-making in emergency medicine. The current investigation aims to examine adverse outcomes associated with thrombosis following blood transfusions, exploring factors influencing thrombosis onset, and identifying specific patient populations particularly vulnerable to these complications.

2. Methods

2.1 Study design and setting

In this retrospective cohort study, we examined the association between transfusions and thrombotic events leading to mortality in patients undergoing repeated blood transfusions. The study population comprised individuals who had received blood transfusions from 2015 to 2022, with data collected from 1000 patients in the King Khalid University Hospital database.

2.2 Data collection

Demographics and clinical profiles of blood recipients, including age, sex, medical backgrounds, and occurrences of DVT or ATE following blood transfusions, were extracted from electronic health records within the hospital. A standardised data collection form was utilised to systematically collect these data. The analysis entailed categorising patients based on the type of blood components administered, such as RBCs, platelets, fresh frozen plasma (FFP) or cryoprecipitate. Patients' medical histories were meticulously reviewed to identify pre-existing conditions, including haematological disorders, cancers, cardiovascular ailments and other health concerns.

2.3 Statistical analysis

In the preliminary phase, a descriptive analysis was conducted, presenting categorical variables as frequencies and percentages and numerical variables as means and standard deviations. Subsequently, the second stage of analysis involved employing the Mann-Whitney U test, chi-square test, and multivariate logistic regression analysis using SPSS Statistics (version 25, IBM-International Business Machines Corporation, Armonk, NY, USA). A significance level of $p < 0.05$ was established to

denote statistical significance.

3. Results

3.1 Demographic characteristics

The study included 1720 participants, comprising 372 males (37.2%) and 1348 females (62.8%). Participants were categorised by health status: 669 individuals (66.4%) had no specific health issues, 72 (7.1%) had haematological disorders, 134 (13.3%) had malignant diseases, 52 (5.2%) had cardiovascular diseases, and 80 (7.9%) had other diseases. The ages of participants ranged from 25 to 102 years. Clinical outcomes showed that VTE occurred in 16 patients (1.6%), ATE in 15 patients (1.5%), and death in 25 patients (25.1%) (Table 1).

TABLE 1. Demographics data of the study population.

Characteristic (n = 1000)	n	(%)
	Mean ± SD	
Number of RBC transfusions	18.080 ± 6.49	
Number of platelet transfusion	8.446 ± 1.83	
FFP transfusion	13.837 ± 2.34	
Cryoprecipitates	2.579 ± 0.38	
Deep vein thrombosis (DVT)		
No	984	98.4
Yes	16	1.6
ATE		
No	985	98.5
Yes	15	1.5
Mortality		
Death	251	25.1
Survival	749	74.9
Age (yr)		
25–39	116	11.6
40–54	188	18.8
55–69	348	34.8
70–84	279	27.9
85 and above	69	6.9
Gender		
Male	372	37.2
Female	628	62.8
Diseases (n = 1000) (k = 1007)		
Free of chronic disease	669	66.4
Hematological diseases	72	7.1
Malignancy diseases	134	13.3
Cardiovascular diseases	52	5.2
Other diseases	80	7.9

All values are presented as numbers and percentages for categorical variables, mean and standard deviation for numerical variables.
For multiple responses questions, k: total number of responses, n: total number of cases. RBC: red blood cells; FFP: fresh frozen plasma; ATE: arterial thromboembolism; SD: Standard Deviation.

3.2 Blood transfusion

The mean $\pm$ standard deviation value for RBC transfusions, platelet transfusion, FFP transfusion, and cryoprecipitate transfusions were 18.08 ± 6.49, 8.446 ± 1.83, 13.837 ± 2.34 and 2.579 ± 0.83 respectively.

3.2.1 Relationship of blood products with thrombosis in recurrent blood transfusion recipients

Fig. 1 illustrates the relationship between the number of RBC, platelet, FFP and cryoprecipitate transfusions with DVT and ATE. In our study cohort, patients with DVT who received blood transfusions exhibited a higher demand for RBCs (average: 18.08 units) but a lower demand for cryoprecipitates (average: 2.57 units). Despite the notable contrast in the quantities of RBCs and cryoprecipitates received, no significant association was observed between any blood component and the occurrence of DVT. Conversely, patients with ATE showed a higher demand for RBCs than for other blood components. However, the analysis revealed a significant association between ATE and platelet transfusion ($p < 0.05$), although the demand for platelets was lower than that for RBC and FFP transfusions.

3.2.2 Effect of age and sex on thrombosis in recurrent blood transfusion recipients

Table 2 presents the association between age, sex, and the occurrence of DVT and ATE within our study cohort. Notably,

individuals aged 55–69 years were significantly more likely to experience DVT ($p < 0.05$). When comparing males and females who received blood transfusions, we found no statistically significant association between sex and the incidence of DVT. However, other factors showed statistically significant associations and were identified as important risk factors for DVT.

3.2.3 Relationship of haematological, cardiovascular, and other diseases with thrombosis in recurrent blood transfusion recipients

To explore the association of each disease type with the incidence of DVT and ATE, patients were categorised into five groups based on the type of disease (Fig. 2). Among patients with DVT, those with cardiovascular disease (9 patients (56.3%)) showed a notable correlation with DVT, followed by patients with no chronic diseases (6 patients (37.5%)). Statistically significant differences in the incidence of DVT were observed in both the cardiovascular disease group ($p < 0.01$) and the group without chronic diseases ($p < 0.05$). Conversely, no statistically significant association was found between ATE and medical history among patients with ATE. The findings also indicated a substantial demand for platelets and FFP in patients with haematological diseases (Table 3).
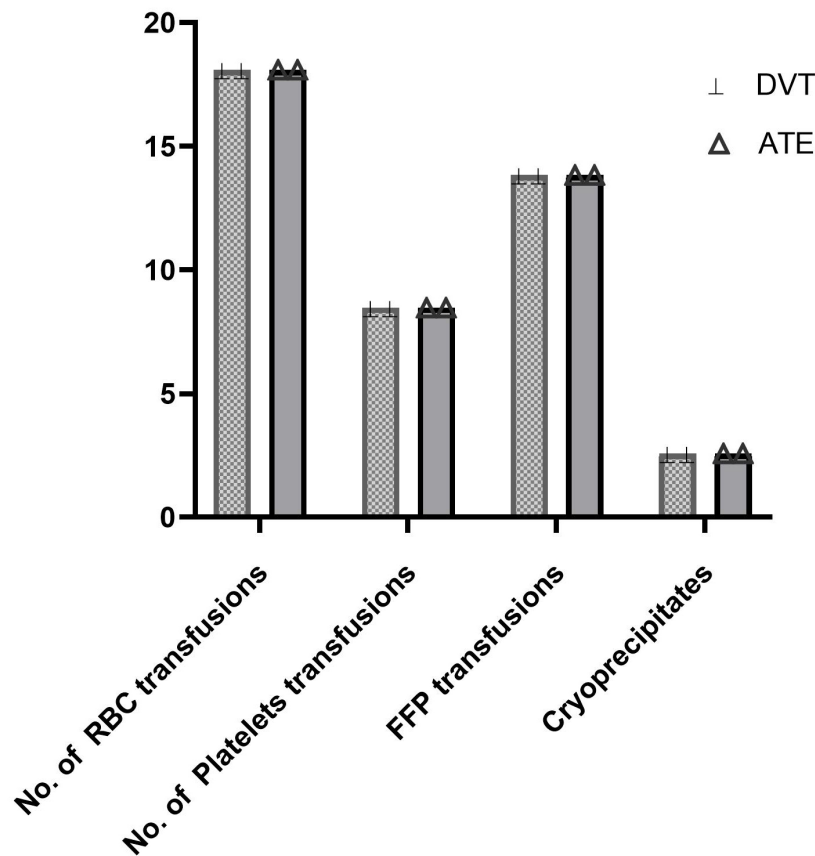

F I G U R E 1. Number of RBC transfusions, number of platelet transfusion, FFP transfusion and cryoprecipitates with DVT and ATE. DVT: deep vein thrombosis; ATE: arterial thromboembolism; RBC: red blood cells; FFP: fresh frozen plasma.

T A B L E 2. Effect of age and sex on DVT and ATE.

Characteristics	DVT		ATE	
	No	Yes	No	Yes
	n (%)	n (%)	n (%)	n (%)
Age (yr)				
From 25 to 39	116 (100.0)	0 (0.0)	115 (99.1)	1 (0.9)
From 40 to 54	185 (98.4)	3 (1.6)	187 (99.5)	1 (0.5)
From 55 to 69	343 (98.6)	5 (1.4)*	339 (97.4)	9 (2.6)
From 70 to 84	276 (98.9)	3 (1.1)	277 (99.3)	2 (0.7)
85 years and above	64 (92.8)	5 (7.2)	67 (97.1)	2 (2.9)
Gender				
Male	368 (98.9)	4 (1.1)	366 (98.4)	6 (1.6)
Female	616 (98.1)	12 (1.9)	619 (98.6)	9 (1.4)

*Statistically significant at p < 0.05. DVT: deep vein thrombosis; ATE: arterial thromboembolism.
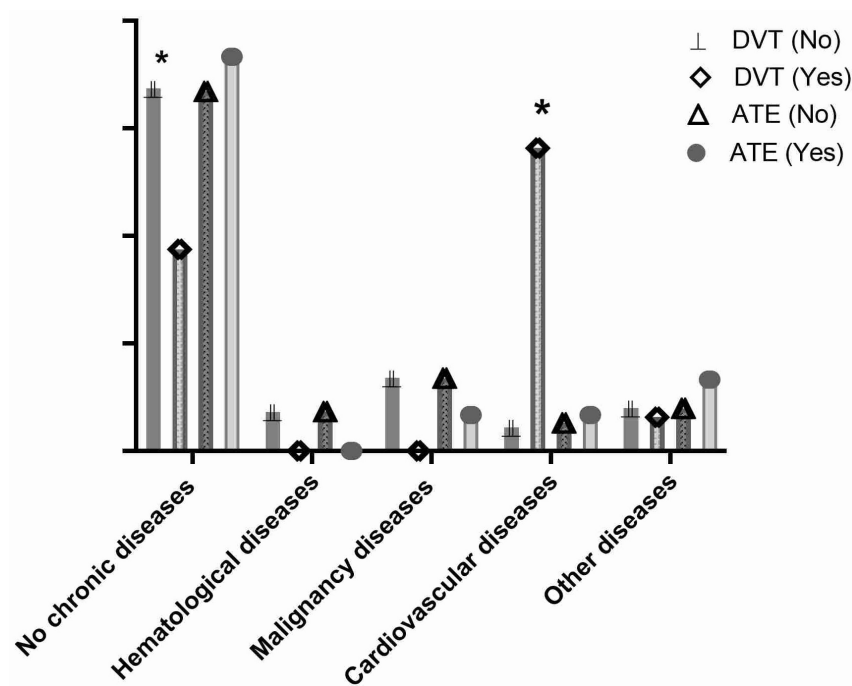

F I G U R E 2. Association between disease type and incidence of DVT and ATE. DVT: deep vein thrombosis; ATE: arterial thromboembolism. *: $p < 0.05$.

T A B L E 3. The correlation between blood components and type of diseases.

Blood products	p-value				
	Non chronic disease	Hematological diseases	Malignancy diseases	Cardiovascular diseases	Other diseases
RBCs transfusions	0.075	0.927	0.271	0.536	0.750
Platelet transfusions	0.003*	0.003*	0.110	0.963	0.436
FFP transfusion	0.087	0.004*	0.911	0.550	0.826
Cryoprecipitates transfusions	0.882	0.638	0.964	0.986	0.558

*Statistically significant at p < 0.05. RBC: red blood cells; FFP: fresh frozen plasma.

3.2.4 Mortality and thrombosis in recurrent blood transfusion recipients

The mortality rate among patients who received blood transfusions was 25.1% (251 patients). While four patients (1.6%) succumbed to DVT and four (1.6%) to ATE, these differences lacked statistical significance (Fig. 3; Table 4). Blood transfusion recipients with haematological disorders, malignancies, or without chronic diseases exhibited shorter median survival times than those with other ailments ($p < 0.01$).
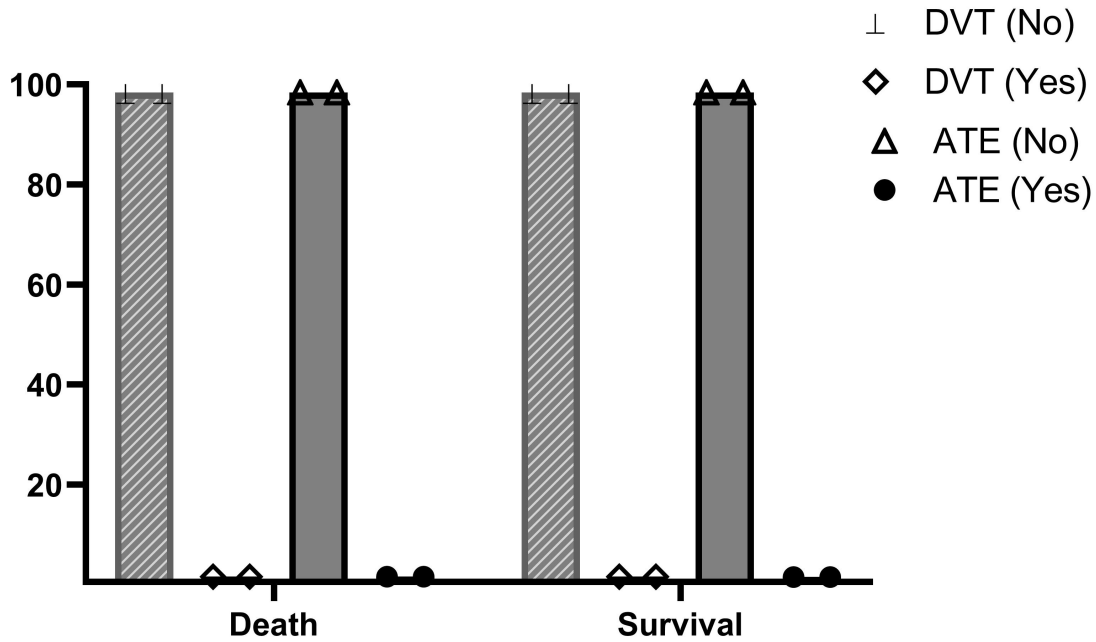
F I G U R E 3. Mortality and thrombosis in recurrent blood transfusion patients. DVT: deep vein thrombosis; ATE: arterial thromboembolism.

T A B L E 4. Correlation between groups of diseases and mortality.

Diseases	Mortality		p-value
	Death n (%)	Survival n (%)	
Free of chronic disease (n = 669)	142 (21.2%)	527 (78.8%)	<0.001*
Hematological diseases (n = 72)	7 (9.7%)	65 (90.3%)	0.002*
Malignancy diseases (n = 134)	67 (50.0%)	67 (50.0%)	<0.001*
Cardiovascular diseases (n = 52)	14 (26.9%)	38 (73.1%)	0.755
Other diseases (n = 80)	25 (31.3%)	55 (68.8%)	0.186

Statistically significant at p < 0.05.

4. Discussion

The main finding of the study was a significant correlation identified between platelet transfusions and an increased risk of ATE. No significant correlation was found between blood transfusions and DVT. Patients aged 55–69 years in the blood transfusion cohort showed a higher risk of DVT ($p < 0.05$), especially those without chronic or cardiovascular diseases. Haematological diseases increased the demand for platelets and FFP. Patients without chronic diseases preferred platelet transfusions. Patients with haematological or malignancy diseases, but without chronic conditions, had a higher mortality risk within the blood transfusion cohort.

There is a in high demand for platelet transfusions among haematology patients, which poses logistical challenges due to storage requirements and short shelf-life. Platelets play a dual role in host defence and thrombotic risk. Vigilant monitoring and tailored interventions are essential to maximise benefits and minimise adverse events associated with platelet transfusion. In our study, no significant correlation was identified between RBC and cryoprecipitate transfusions and the risk of DVT and ATE. Interestingly, a significant correlation

was found between platelet transfusions and ATE. However, platelet transfusions did not correlate with DVT. These findings are consistent with those reported previously. Schmidt *et al*. [17], 2018 suggested an association between platelet transfusion and increased rates of both DVT and ATE. Similarly, Goel *et al*. [18], 2015 found that platelet transfusions were linked to higher odds of arterial thrombosis. Conversely, some studies have reported no occurrence of thrombotic events following platelet transfusion in any patients [19, 20]. Aligning with the current study's findings, Marušič *et al*. [21], 2017 found no correlation between RBC and FFP transfusions and the risk of DVT.

Arterial and venous thrombosis are two biologically distinct processes with distinct risk factors. Circulating von Willebrand factor levels tend to increase gradually over time, particularly after the age of 40, potentially due to the overproduction of reactive oxygen species, which disrupts the balance between thrombosis and haemorrhage [22, 23]. Emerging pathophysiological changes include disturbances in the levels of procoagulant and natural anticoagulant factors, along with thrombopathy, creating a hypercoagulable state and haemostatic difficulties, thereby increasing the risk of venous and

arterial thrombosis [24, 25]. In the current study, we aimed to validate these findings and identify additional predictors of arterial versus venous thrombosis. Our results indicate that patients aged 55–69 years exhibited a significantly higher risk of DVT than those in any other age group. These findings are consistent with previous studies that have explored the relationship between age and the risk of thrombosis [26, 27]. Studies have reported that perioperative allogeneic blood transfusion is associated with an increased risk of developing VTE in women but not in men [28, 29]. However, in a recent study, the risk of DVT was found to be higher in men than in women [30]. Interestingly, our study showed a different result, indicating no association between sex and the risk of VTE. discrepancies in the association between DVT and sex following transfusion are not explicitly clear and warrant further investigations.

In our analysis, we made efforts to incorporate as many potential confounding factors as possible to elucidate the correlation. We categorised diseases into five groups to investigate their effects on the incidence of DVT and ATE. Cardiovascular diseases emerged as a significant factor in thrombosis, with our results indicating an association between cardiovascular disease and the development of DVT ($p < 0.001$), aligning with the findings of Ando et al. [31] (2020), which suggested that a history of heart disease could be a risk factor for DVT ($p < 0.05$). Similarly, Wang et al. [32] 2022 reported a strong association between CVD risk factors and the risk of DVT. Dicks et al. [33] 2024 reported that increasing age, presence of central venous lines, oestrogens, and a wide variety of inherited and acquired haematological conditions increase the risk of VTE and DVT. Gregson et al. [34], (2019) found that older age increases the risk of CVD and VTE. Besides cardiovascular diseases, haematological diseases characterised by complement-mediated RBC lysis are linked to an increased risk of thromboembolic complications. This association has also been observed in haemolytic anaemias such as sickle cell disease (SCD), paroxysmal nocturnal haemoglobinuria, and thalassaemia [35]. Notably, a single-institution study reported that patients with SCD had an elevated incidence of DVT, with a prevalence of 25% in adults with SCD [36]. Similarly, in patients with transfusion-dependent thalassaemia, 6.2% experienced thromboembolic events [37]. The release of haemoglobin and haeme stimulates endothelial activation and tissue factor expression, while free circulating haemoglobin consumes nitric oxide (NO). Reduced NO levels, a major regulator of endothelial integrity and functionality, as well as a smooth muscle tone regulator, promote platelet activation and vasoconstriction [38].

Moreover, in the present study's population, different disease groups exhibited similar consumptive blood transfusion patterns. Statistically, we observed that platelets and FFP were more consumptive in patients with haematological diseases than in those with other diseases. This elevated consumption may play a significant role in the development of thrombosis, as suggested by published studies. FFP and platelet transfusions have been associated with increased thrombin generation and platelet counts, indicating a prothrombotic effect [39]. Consistently, Zeng et al. [29], 2019 reported a substantial increase in the incidence of DVT among cardiac surgery patients receiving multiple blood products, especially when accompanied by FFP (25%–40%), highlighting the significant role of FFP in thrombosis. Besides CVD, cancer represents a strong risk factor for the development of cancer-associated thrombosis (CAT). Khorana et al. [40], 2008 and Anderson, 2009 reported that cancer is a risk factor for DVT [41]. In a recent publication by Pastori et al. [42], 2023, patients with cancer had an increased risk of CAT, with a 4–6.5-times higher likelihood of VTE, compared with those without cancer. Nevertheless, we found no significant correlation between cancer and the risk of DVT.

Increasing evidence suggests a higher risk of death associated with blood transfusions, with potential mechanisms including excessive volume load, adult acute respiratory distress syndrome and TRs. Additional hazards may involve an increased risk of infection or thrombosis and platelet-monocyte aggregation [18, 43]. During platelet transfusions, the anticoagulation and fibrinolytic systems are inhibited. In conditions where coagulation activation is already heightened, platelet transfusion may further exacerbate thrombosis, leading to microvascular occlusion of tissues and organs, ultimately causing organ damage [44].

Our observations revealed that patients with haematological and malignancy diseases or those with no chronic diseases had higher mortality rates. In patients with a malignancy, the effects of chemotherapy can necessitate RBC and platelet transfusions due to anaemia, significantly impacting patients' quality of life and mortality [45]. Consistent with this, Cho et al. [46], 2021 explored the impact of blood transfusions on the survival outcomes of patients with cancer, revealing that the receipt of blood components shortened overall patient survival. In haematological disorders, transfusion becomes a reasonable option for treating bleeding or providing procedural prophylaxis [47]. For example, the incidence of VTE was higher in patients with SCD than in matched controls and was associated with increased mortality [48]. Similarly, in beta-thalassemia patients, atrial fibrillation is a major cause of mortality, potentially linked to various complications such as iron overload, resulting in elevated iron-mediated oxidative stress [49]. Despite these potential risks, post-transfusion adverse effects are rare due to established blood banking protocols. Efforts are focused on preventing such adverse events from occurring, prioritising patient safety.

5. Limitations of the study

Despite the significant findings, this study has few limitations that must be acknowledged. While multivariate logistic regression was used to adjust for known confounders, there may be other unmeasured variables that influenced the outcomes, such as genetic predispositions, variations in transfusion practices, or undiagnosed comorbidities. Detailed information on the timing of transfusion-related complications, the specific indications for each transfusion, and the exact volume of blood products administered was not available. This lack of granularity limits the ability to perform more detailed subgroup analyses. Further research is needed to thoroughly understand confounding factors' impact on outcomes, potentially refining transfusion guidelines for enhanced patient safety and fewer

adverse events. Larger sample sizes and meticulously matched study designs are recommended for future investigations, with attention to storage duration as a key variable.

6. Conclusions

Blood transfusions have a noteworthy correlation with the onset of fresh or progressive thrombosis and elevated mortality rates. Our investigation specifically underscores an association between platelet transfusions and an augmented susceptibility to ATE. Additionally, the influence of age and underlying medical conditions substantially impacts the likelihood of DVT. These findings emphasise the necessity to modify blood transfusion protocols for alleviating complications and improving patient well-being.

AVAILABILITY OF DATA AND MATERIALS

The data that support the findings of this study are available from the corresponding author upon reasonable request.

AUTHOR CONTRIBUTIONS

FHA and HMA—designed the research study. FHA and HYA—performed the research. HYA and SAA—analyzed the data. HMA, HYA, SAA and HT—wrote the manuscript. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethical approval was obtained from the Ethics Committee of King Saud University (approval number: E-23-7566). Due to the retrospective nature of the study, subjects' consent to participate was not required. However, patient consent during sampling and clinical investigation was obtained by the hospital staff.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

[1] Watson P, Watson D, Dhesi A, New HV, Davidson A, Armstrong R, *et al*. Improving blood-prescribing decisions: evaluating the efficacy of a blood guidelines app. Transfusion Medicine. 2020; 30: 485–491.

[2] McGann PT, Weyand AC. Lessons learned from the COVID-19 pandemic blood supply crisis. Journal of Hospital Medicine. 2022; 17: 574–576.

[3] Maintained by Ministry of Health. Health days 2023—blood donation day. 2023. Available at: https://www.moh.gov.sa/en/HealthAwareness/healthDay/2023/Pages/HealthDay-2023-06-14-001.aspx (Accessed: 06 June 2023).

[4] Feyisa T, Tesfaye Kiya G, Maleko WA. Assessment of recipients' characteristics, transfusion appropriateness, and utilization pattern of blood and blood products in Jimma Medical Center, Jimma, Ethiopia. PLOS ONE. 2021; 16: e0250623.

[5] Geneen LJ, Brunskill SJ, Doree C, Estcourt LJ, Green L. The difference in potential harms between whole blood and component blood transfusion in major bleeding: a rapid systematic review and meta-analysis of RCTs. Transfusion Medicine Reviews. 2022; 36: 7–15.

[6] Ebrahimi S, Bagchi P. A computational study of red blood cell deformability effect on hemodynamic alteration in capillary vessel networks. Scientific Reports. 2022; 12: 4304.

[7] Vincent J, Jaschinski U, Wittebole X, Lefrant J, Jakob SM, Almekhlafi GA, *et al*. Worldwide audit of blood transfusion practice in critically ill patients. Critical Care. 2018; 22: 102.

[8] Thurn L, Wikman A, Westgren M, Lindqvist PG. Incidence and risk factors of transfusion reactions in postpartum blood transfusions. Blood Advances. 2019; 3: 2298–2306.

[9] Marik PE. Transfusion of blood and blood products. Evidence-Based Critical Care. 2015; 325: 585–619.

[10] Goel R, Patel EU, Cushing MM, Frank SM, Ness PM, Takemoto CM, *et al*. Association of perioperative red blood cell transfusions with venous thromboembolism in a North American registry. JAMA Surgery. 2018; 153: 826.

[11] Byrnes JR, Wolberg AS. Red blood cells in thrombosis. Blood. 2017; 130: 1795–1799.

[12] Bilgin YM. Clinical effects and possible mechanisms of transfusion-related immunomodulation. IntechOpen: London. 2022.

[13] Alsughayyir J, Almalki Y, Alburayk I, Alalshaik M, Aljoni I, Kandel M, *et al*. Prevalence of transfusion-transmitted infections in Saudi Arabia blood donors. Saudi Medical Journal. 2022; 43: 1363–1372.

[14] Smethurst P, Cardigan R. Current challenges in platelet transfusion. Platelets. 2022; 33: 5–13.

[15] Chen B, Xia R. Pro-inflammatory effects after platelet transfusion: a review. Vox Sanguinis. 2020; 115: 349–357.

[16] Rizk JG, Gupta A, Sardar P, Henry BM, Lewin JC, Lippi G, *et al*. Clinical characteristics and pharmacological management of COVID-19 vaccine-induced immune thrombotic thrombocytopenia with cerebral venous sinus thrombosis. JAMA Cardiology. 2021; 6: 1451.

[17] Schmidt AE, Henrichs KF, Kirkley SA, Refaai MA, Blumberg N. Prophylactic preprocedure platelet transfusion is associated with increased risk of thrombosis and mortality. American Journal of Clinical Pathology. 2018; 149: 87–94.

[18] Goel R, Ness PM, Takemoto CM, Krishnamurti L, King KE, Tobian AAR. Platelet transfusions in platelet consumptive disorders are associated with arterial thrombosis and in-hospital mortality. Blood. 2015; 125: 1470–1476.

[19] Baschin M, Selleng S, Zeden J-P, Westphal A, Kohlmann T, Schroeder HW, *et al*. Platelet transfusion to reverse antiplatelet therapy before decompressive surgery in patients with intracranial haemorrhage. Vox Sanguinis. 2017; 112: 535–541.

[20] Refaai MA, Chuang C, Menegus M, Blumberg N, Francis CW. Outcomes after platelet transfusion in patients with heparin-induced thrombocytopenia. Journal of Thrombosis and Haemostasis. 2010; 8: 1419–1421.

[21] Marušič AP, Locatelli I, Mrhar A, Caprnda M, Gaspar L, Adamek M, *et al*. Influence of prescribed blood products on the incidence of deep vein thrombosis and pulmonary embolism in surgical patients. Clinical and Applied Thrombosis/Hemostasis. 2017; 23: 938–942.

[22] Alavi P, Rathod AM, Jahroudi N. Age-associated increase in thrombogenicity and its correlation with von willebrand factor. Journal of Clinical Medicine. 2021; 10: 4190.

[23] Gwozdzinski K, Pieniazek A, Gwozdzinski L. Reactive oxygen species

and their involvement in red blood cell damage in chronic kidney disease. Oxidative Medicine and Cellular Longevity. 2021; 2021: 6639199.

[24] Tzoran I, Hoffman R, Monreal M. Hemostasis and thrombosis in the oldest old. Seminars in Thrombosis and Hemostasis. 2018; 44: 624–631.

[25] Tschan SL, Bolliger D. Coagulation and aging: implications for the anesthesiologist. Current Anesthesiology Reports. 2021; 11: 387–395.

[26] Wang P, Kandemir U, Zhang B, Wang B, Li J, Zhuang Y, et al. Incidence and risk factors of deep vein thrombosis in patients with pelvic and acetabular fractures. Clinical and Applied Thrombosis/Hemostasis. 2019; 25: 107602961984506.

[27] Raskob GE, Wendelboe AM, Campbell J, Ford L, Ding K, Bratzler DW, et al. Cancer-associated venous thromboembolism: incidence and features in a racially diverse population. Clinical and Applied Thrombosis/Hemostasis. 2022; 20: 2366–2378.

[28] Trinchero A, Scheres LJJ, Prochaska JH, Ambaglio C, Wild PS, Middeldorp S, et al. Sex-specific differences in the distal versus proximal presenting location of acute deep vein thrombosis. Thrombosis Research. 2018; 172: 74–79.

[29] Zeng Q, Tan S, Bao Q, Jiang S. Intra-operative blood transfusion significantly increases the risk of post-operative pulmonary embolism. Journal of Thoracic Disease. 2019; 11: 5566–5571.

[30] Wilcox T, Smilowitz NR, Seda B, Xia Y, Hochman J, Berger JS. Sex differences in thrombosis and mortality in patients hospitalized for COVID-19. The American Journal of Cardiology. 2022; 170: 112–117.

[31] Ando Y, Hayashi T, Sugimoto R, Nishibe S, Ito K, Kawada K, et al. Risk factors for cancer-associated thrombosis in patients undergoing treatment with immune checkpoint inhibitors. Investigational New Drugs. 2020; 38: 1200–1206.

[32] Wang H, Rosendaal FR, Cushman M, van Hylckama Vlieg A. Association between cardiovascular risk factors and venous thromboembolism in the elderly. Research and Practice in Thrombosis and Haemostasis. 2022; 6: e12671.

[33] Dicks AB, Moussallem E, Stanbro M, Walls J, Gandhi S, Gray BH. A comprehensive review of risk factors and thrombophilia evaluation in venous thromboembolism. Journal of Clinical Medicine. 2024; 13: 362.

[34] Gregson J, Kaptoge S, Bolton T, Pennells L, Willeit P, Burgess S, et al. Cardiovascular risk factors associated with venous thromboembolism. JAMA Cardiology. 2019; 4: 163–173.

[35] Delvasto-Nuñez L, Jongerius I, Zeerleder S. It takes two to thrombosis: hemolysis and complement. Blood Reviews. 2021; 50: 100834.

[36] Ogunsile FJ, Naik R, Lanzkron S. Overcoming challenges of venous thromboembolism in sickle cell disease treatment. Expert Review of Hematology. 2019; 12: 173–182.

[37] Osataphan N, Dumnil S, Tantiworawit A, Punnachet T, Hantrakun N, Piriyakhuntorn P, et al. The long-term efficacy in blood transfusions, hematologic parameter changes, and complications after splenectomy in patients with transfusion-dependent thalassemia. Transfusion and Apheresis Science. 2023; 62: 103620.

[38] Vasilopoulou M, Stafylidis C, Politou M. The thrombotic spectrum of B-thalassemia. Thrombosis Update. 2022; 7: 100102.

[39] von Meijenfeldt FA, van den Boom BP, Adelmeijer J, Roberts LN, Lisman T, Bernal W. Prophylactic fresh frozen plasma and platelet transfusion have a prothrombotic effect in patients with liver disease. Journal of Thrombosis and Haemostasis. 2021; 19: 664–676.

[40] Khorana AA, Francis CW, Blumberg N, Culakova E, Refaai MA, Lyman GH. Blood transfusions, thrombosis, and mortality in hospitalized patients with cancer. Archives of Internal Medicine. 2008; 168: 2377.

[41] Anderson FA Jr, Spencer FA. Risk factors for venous thromboembolism. Circulation. 2003; 107: I9–16.

[42] Pastori D, Cormaci VM, Marucci S, Franchino G, Del Sole F, Capozza A, et al. A comprehensive review of risk factors for venous thromboembolism: from epidemiology to pathophysiology. International Journal of Molecular Sciences. 2023; 24: 3169.

[43] He S, Fan C, Ma J, Tang C, Chen Y. Platelet transfusion in patients with sepsis and thrombocytopenia: a propensity score-matched analysis using a large ICU database. Frontiers in Medicine. 2022; 9: 830177.

[44] Zhou W, Fan C, He S, Chen Y, Xie C. Impact of platelet transfusion thresholds on outcomes of patients with sepsis: analysis of the MIMIC-IV database. Shock. 2022; 57: 486–493.

[45] Merolle L, Marraccini C, Di Bartolomeo E, Montella MT, Pertinhez TA, Baricchi R, et al. Postoperative patient blood management: transfusion appropriateness in cancer patients. Blood Transfusion. 2020; 18: 359–365.

[46] Cho S, Park J, Lee M, Lee D, Choi H, Gim G, et al. Blood transfusions may adversely affect survival outcomes of patients with lung cancer: a systematic review and meta-analysis. Translational Lung Cancer Research. 2021; 10: 1700–1710.

[47] Salazar E, Tormey CA. Transfusion in benign haematological disease. In Murphy MF, Roberts DJ, Yazer MH, Dunbar NM (eds.) Practical transfusion medicine (pp. 399–408). 6th edn. Wiley: New Jersey. 2022.

[48] Brunson A, Lei A, Rosenberg AS, White RH, Keegan T, Wun T. Increased incidence of VTE in sickle cell disease patients: risk factors, recurrence and impact on mortality. British Journal of Haematology. 2017; 178: 319–326.

[49] Bahrani S, Teimouri-jervekani Z, Sadeghi M. Thrombotic events and anticoagulants in beta-thalassemia patients with focus on anticoagulants for atrial fibrillation: a brief review. Current Problems in Cardiology. 2022; 47: 100912.