Research Paper: The Survey of Adverse Transfusion Reactions in Burn Patients for Five Years from 2015 to 2020 at Imam Musa Kazim Hospital, Isfahan Province, Iran

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ABSTRACT

While blood transfusions are critical therapeutic interventions for burn patients, they pose a risk of adverse transfusion reactions (ATRs). The present study aimed to evaluate the clinical manifestations and underlying causes of ATRs in burn patients over five years at Imam Musa Kazim Hospital in Isfahan, Iran.This cross-sectional study analyzed the medical records of patients hospitalized from 2015 to 2020. The study focused on transfusion details, including the reasons for transfusion and the types and frequencies of ATRs. Data analysis was performed using SPSS (version 21). A total of 2,086 packed red blood cells were transfused during the study period, with 100 (4.79%) cases resulting in ATRs. Of these, 73% were allergic reactions, followed by transfusion-related acute lung injury (TRALI) (9%), febrile non-hemolytic transfusion reaction (FNHTR) (7%), and hemolytic reactions (4%). Most transfusions (51%) occurred in patients with burns covering 30-60% of their total body surface area (TBSA). Surgery (57%) and anemia (43%) were the leading reasons for transfusion. Most ATRs were mild, with allergic reactions showing the highest severity. The incidence of ATRs in burn patients highlights the need for careful monitoring of transfusion practices. Increased awareness and training of medical staff regarding ATR prevention can reduce unnecessary transfusions and improve patient outcomes in burn care.

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1. Introduction

Blood transfusion is generally suggested as the last resort to rescue patients who suffer from a deficiency in specific or total components of blood (e.g., anemia, thrombocytopenia, and bleeding). The solution should be based on strong indication, which involves extensive evaluation of the patient's condition, such as hemoglobin, platelet blood type, and history of allergic reactions. Blood and its components are vital for many patients, and blood transfusions benefit most of them [1]. Generally, some patients may be exposed to risk factors during the injection of allogeneic blood or blood components [2]. Incompatible transfusion or harmful reactions can be infectious or non-infectious [3]. There are two types of adverse transfusion reactions (ATRs): The first one emerges within 24 h (acute transfusion reaction), and the second reaction turns out in a few days or several days after transfusion (Delayed) [1]. The intensity of transfusion reactions ranges from mild to severe or even life-threatening. Some clinical appearances of transfusion reaction include fever, chills, shortness of breath, multiple organ failure, changing the skin (urticarial, rash, flushing, and edema), jaundice, hemoglobinuria, nausea, vomiting, bleeding, oliguria, anuria, and others [1]. Aside from the underlying diseases, if a transfusion reaction starts, treating the disease entirely before more severe consequences are developed is obligatory. Therefore, transfusion reaction potentially delays patients' management related to underlying diseases, increases medical costs, and lengthens patients' hospitalization. According to international accreditation standards, each hospital must report, monitor, and assess transfusion reactions regularly to reduce the incidence of transfusion reactions [3]. Acute reactions include allergic transfusion reaction, acute hemolytic transfusion reaction, febrile non-hemolytic transfusion reactions (FNHTRs), transfusion-related acute lung injury (TRALI), and transfusion-associated circulatory overload (TACO). The designation of the type of reaction occurring includes researching and combining both the clinical evaluation of the patient and laboratory confirmation, as well as testing [4]. An allergic reaction to a blood transfusion is a common side effect of red blood cell transfusions. It is obligatory to analyze many factors associated with allergic transfusion reaction development, such as donor-product and recipient–related factors. Therefore, it is not easy to investigate all of these factors in a single study. Furthermore, the clinical information details of patients include data obtained from individuals who did not develop allergic transfusion reactions for comparison. Consequently, investigating the factors associated with allergic transfusion reactions in recipients is complex, and there is insufficient evidence to support it. Improved blood management systems contribute to better blood and blood component quality and reduce the potential risks of the transfusion method [5]. Many patients experience various physiological changes during transfusion; however, most of these changes are non-harmful and are often linked to pre-existing conditions or comorbidities rather than true adverse transfusion reactions (ATRs) [6]. In response, many countries have established haemovigilance networks tailored to their health systems to monitor and address ATRs effectively. A haemovigilance system is defined as a structured surveillance framework that oversees the entire transfusion process, from donor to recipient, aiming to enhance safety, efficacy, and quality in blood transfusion practices [6,7]. Blood transfusion is a resource-intensive intervention that demands substantial government funding and efficient management. For example, during 2018/2019, the average cost of a single unit of blood product was $240.90 [7]. In Iran, the blood supply relies on voluntary donations and aims for national self-sufficiency in blood products. However, with an aging population, the demand for transfusions is rising dramatically. Older adults (>65 years) require up to 20 times more transfusions compared to individuals under 41 years of age [8]. Given its high costs, limited availability, and potential risks, physicians strive to optimize blood transfusion practices, ensuring its use is reserved for situations where its benefits clearly outweigh its risks. This study focuses on the effects of blood transfusion in patients with acute and chronic burns who require hospitalization. Its primary goals are to evaluate patients' health outcomes and establish optimal transfusion practices, enabling the prompt identification of adverse effects and ensuring the best possible treatment strategies.

2. Materials and Methods

In this cross-sectional study, medical records of all patients hospitalized at Imam Musa Kazim Hospital, Isfahan, were studied over five years from 2015 to 2020. All the required information about the patients with acute and chronic burns, including admission records, were collected and analyzed separately. Information related to the manifestation of blood transfusion was extracted from transfusion data sheets and patients' files. FNHTRs and anaphylactic reactions were diagnosed based on clinical symptoms, including fever, chills, and rashes, after ruling out other potential causes such as bacterial contamination, medication-induced reactions, and underlying conditions. Allergic reactions were classified into two forms: urticaria, presenting as mild itching and skin rash, and anaphylaxis, characterized by severe systemic symptoms such as bronchospasm, hypotension, and shock. The urticarial form usually causes mild itching and is not accompanied by fever or other severe symptoms. Anaphylactic reactions are more severe forms of allergic reaction—their clinical features include shock, loss of consciousness, and hypotension. The allergic reaction was differentiated from the anaphylactic reaction by the absence of systematic demonstration, such as bronchospasm. The FNHTR was defined as a body temperature rise of >1ºC or more, with or without chills and rigor associated with transfusion. In suspicion of bacterial sepsis, the remaining bag volume was sent for blood culture, and results were correlated with the patient's culture reports. The TRALI was recognized in patients with acute respiratory distress within 6 h with two-sided respiratory distress infiltrates on chest X-rays. The TRALI was differentiated from TACO on the basis of blood pressure, volume status of patients, and response to diuretics. The hypotensive reaction was specified by an isolated decrease in systolic BP<80mmhg or diastolic BP of >30mmhg within one hour of transfusion. The pulmonary edema in TRALI was presented without cardiac failure, while pulmonary edema in TACO was cardiogenic and improved by diuretic therapy. Per standard protocols at the blood bank, a blood sample and a transfusion request form were submitted for any required blood components. Each patient was assigned a unique requisition number, regardless of name, age, or gender. The hospital laboratory required the confirmed blood sample and the completed transfusion request form. The attending physician had to complete and sign this form thoroughly. Upon receipt, laboratory technicians verified the accuracy of the information on the blood sample and the request form. Then, the lab technician confirmed and signed the requisition number of any blood components, including details written on the blood bags, cross-match label, and transfusion requisition form. The assigned number, time of issuance, and all relevant details were recorded in the blood bank's official documentation. The blood bank reported all the ATRs. The form included patient and component details, the start time of blood transfusion, the amount of blood volume transfused, and the time when the transfusion was stopped due to an ATR. Clinical signs and symptoms were carefully recorded, including fever, chills, seizures, hypotension, hypertension, rash, and respiratory distress. The classification of transfusion reaction, whether immediate or delayed (with or without evidence of hemolysis), was determined by its association with patient symptoms. Any ATR that occurs within 24 h is classified as an acute transfusion reaction. The specific type of reaction was determined by analyzing the patient's signs and symptoms.

2.1. Data Analysis

All Descriptive statistics of study participants' socio-demographic and clinical manifestations were presented in tables and texts. Qualitative data (categorical variables) were presented as frequency and percentages and performed using the Chi-square test. Continuous variables, such Mean (SD), were determined using the independent t-test. Statistical analyses were conducted using SPSS (version 21). A *P*-value < 0.05 was considered statistically significant.

3. Results

From March 2015 to March 2020, 2,086 packed red blood cells were transfused. Of those, 100 (4.79%) lead to ATR. The findings showed that the incidence of transfusion reactions was 2.1%, 1.3%, 0.71%, 0.86%, and 1.3% yearly during this research period. The results illustrated a slight difference in

the incidence of transfusion reactions each year in this study. The present study observed no transfusion reaction with Fresh Frozen Plasma, platelets, and cryoprecipitate. About 51% of burn patients who received blood transfusion suffered 30%-60% burns. Moreover, the frequency of patients with 1%-30% and 60%-90% total body surface area (TBSA) was 31% and 18%, respectively. Surgery (57%) and anemia (43%) were significant reasons for transfusion. In the study, 73% of transfusion reactions were Allergic, followed by 9% TRALI, 7% FNHTR, 5% Dilatory, 4% hemolytic, and 2% TACO (Figure 1). In addition, the highest severity of the reaction was found in Allergic response (14%) (Figure 2). No statistically significant difference was found in the incidence of transfusion reactions in different age groups (P>0.05). In the present study, it was shown that the most prevalent blood group in patients was O+ (42%), followed by A+ (34%), B+ (34%), and AB+ (34%). The current study revealed that the highest rate of transfusion reactions was related to respiratory distress and hematuria, which were 23% and 20%, respectively. Other common symptoms were urticaria, fever, ague, and tachycardia (Table 1). On the contrary, other symptoms such as Oliguria, Anuria, Flashing, Tachypnea, Bradycardia, Abdominal pain, Headache, Chest pain, Hemoglobinemia, and Vomiting were not commonly seen. It can be seen that the most incidence time of the signs and symptoms was up to 5 h (32%), and the least of time was between 4-5 h (3%). Moreover, the exact incidence times were seen in half to 4 h (19%). The data collected in this study regarding the date of intention-packed red blood cells (PRBCs) illustrated that PRBCs aged less than 15 days, 15-30 days, and 30-45 days accounted for 9%, 20%, and 71%, respectively (*P*=0.27). No statistical difference was observed between the ages of PRBCs and clinical effects in burned patients.

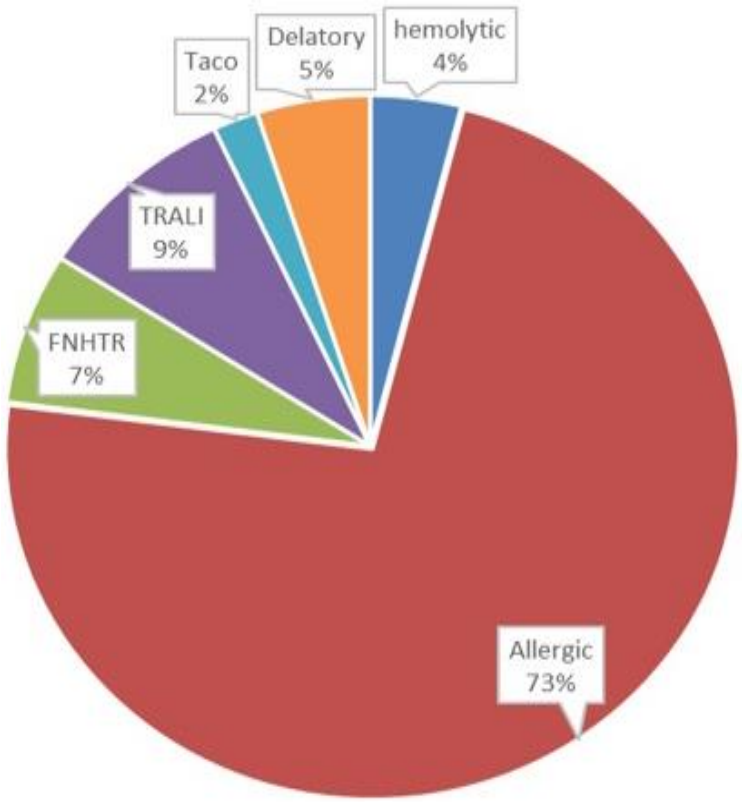

Figure 1. Prevalence of types of adverse transfusion reaction (ATR) from 2015 to 2020
TACO: Transfusion-associated with circulatory overload; TRALI: Transfusion-related acute lung injury; FNHTR: Febrile non-hemolytic transfusion reaction

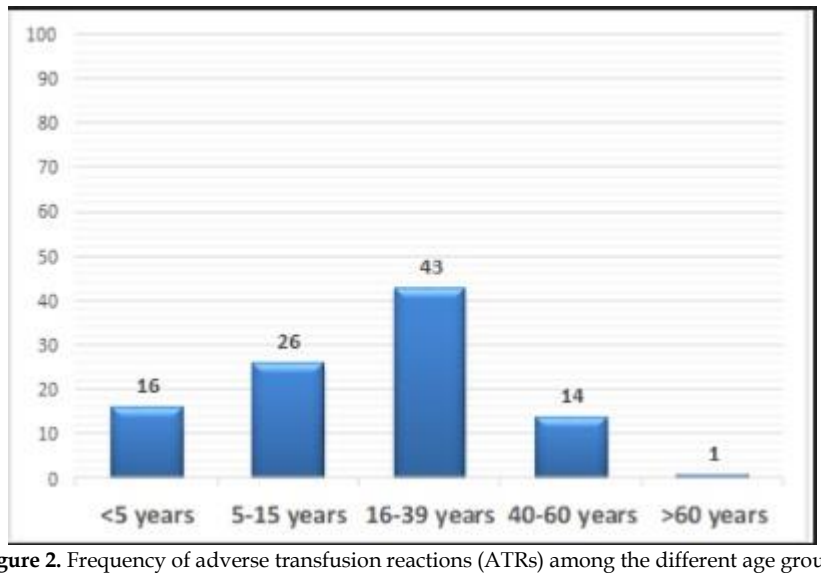

Figure 2. Frequency of adverse transfusion reactions (ATRs) among the different age groups

Table 1. Characteristics of the recipients with recognized adverse transfusion reaction (ATR)

Symptoms	Hemolytic	Allergic	FNHTR	TRALI	TACO	Delayed	Total	Percent
Fever	2	8	6	0	0	0	16	%16
Hemoglobinuria	0	5	1	4	0	3	13	%13
Hemoglobinemia	0	6	0	2	0	0	8	%8
Headache	0	2	1	1	0	5	4	%4
Restless	0	12	1	1	0	0	14	%14
Abdominal pain	0	2	0	0	0	0	2	%2
Flashing	0	2	1	1	1	0	5	%5
Hematuria	0	13	0	4	0	3	20	%20
Vomiting	1	4	0	0	0	0	5	%5
Ague	1	9	3	2	1	0	16	%16
Urticarial	2	12	1	2	0	0	17	%17
Respiratory	1	18	0	3	1	0	23	%23
Chest pain	1	0	2	1	1	0	5	%5
Itching	1	9	0	0	0	0	10	%10
Tachypanea	0	7	0	0	0	0	7	7%
Tachycardia	1	11	1	2	1	0	16	%16
Bradycardia	0	8	0	0	0	0	8	%8
Oliguria	0	1	0	0	0	0	1	%1
Anuria	0	0	0	1	0	0	1	%1

TACO: Transfusion-associated with circulatory overload; TRALI: Transfusion-related acute lung injury; FNHTR: Febrile non-hemolytic transfusion reaction

4. Discussion

In this cross-sectional study, based on adverse blood transfusion analysis of five years from burn patients, the incidence rate of ATR was 4.79%. A systematic review study has shown that the incidence of blood reactions differs among different countries and even in the same country in the same year. Therefore, the highest rate of adverse effects belonged to Japan (6%), and the lowest reported incidence was in India with 0.03% [9]. In the present study on 2,086 burnt patients, ATR occurred in patients with a mean age of 22.5 years. Anemia, Hypoxia, TBSA, percentage of burn (TBSA), age, sepsis, and need for further surgeries were the essential reasons for blood transfusion in burnt patients. In a similar study in Mashhad, Tavousi et al. showed that most blood reactions were performed in patients between 20 and 25 years old. They also reported that 34.2% of patients with a mean burnt TBSA of 30.5% used at least one of the blood products [10]. Another study by Tichil et al. reported that patients with >20% burnt TBSA received an average of 9.6 units [11]. In addition, other studies revealed that the highest transfusion rate was reported in patients with over >20% TBSA burn

[12]. Although burnt TBSA and age are important causes for blood transfusion in burnt patients, less than 7 level hemoglobin (Hb) and < 21 level hematocrit (Hct) are the most common factors for blood transfusion [10]. In the present study, according to the reported adverse blood reactions, the mean level of Hb was 8.3 g/dl, which was the most crucial reason for surgery at 57%, followed by anemia at 43%. In comparison, Curinga et al. reported that the Hb level before transfusion was 8.1 g/dl, and the frequency of anemia was 20%. [11]. Due to a direct correlation between increased risk of infection and the amount of blood transfused, the strategy is based on reducing the blood transfusion rate in patients [11-13]. O'Mara et al. and Losee et al. designed the protocols to reduce adverse blood transfusion in the burn population [11]. These protocols defended hemostasis and techniques in burn grafting and excision to remove the blood transfusion needed, particularly in those patients with the slightest burn. The most extensive study was carried out by Voigt et al., which revealed the benefits of controlling blood transfusion in significantly burned children. The blood transfusion literature confirmed patient safety by decreasing the number of unnecessary transfusions [14]. In the current study, the most ATRs were caused in 53% of patients who transfused >200 ml of blood, and the lowest rate of ATRs caused (14%) was in patients who received <100 ml of blood. It was also illustrated that the storage age of transfused blood was not observed with any meaningful clinical effects. Another similar study by Cartotto et al. presented that the oldest transfused blood is acceptable and has no clinical impact on burn patients, particularly patients with severe thermal injuries [15]. One of the essential points recommended in blood transfusion is to use the blood warmers to help reduce hypothermia and its harmful effects [16]. In this study, the collected data showed six types of reactions, and their frequencies vary in different studies. In our research, the majority of the ATRs were allergic (73%), and the last type of ATRs belonged to TRALI, FNHTR, Dilatory, and TACO reactions, respectively. It was similar to other studies conducted by Gelaw et al. (65%) [17], Hatayama et al. (70%) [18], Oakley FD et al. (45%) [19], and Kumar P et al. (55%) [20], which have shown that allergic reactions were the most common type. On the contrary, other studies have reported that FNHTR reactions were more prevalent among others [21-23]. Hendrickson et al. described TACO reactions as the most prevalent type of reaction [24]. The study showed that 52% of the ATR population (n=100) were males and 48% were females, as previously reported by Prasanna et al. (2019) [25]. There was no statistically significant relationship between sex and the occurrence of ATRs. Monitoring various clinical manifestations of blood transfusion reactions in a timely manner can contribute to a better prognosis [26]. Using blood conservation approaches during surgery can decrease blood loss and prevent unnecessary blood transfusions by clinicians in burnt patients. Better and newer techniques, such as filtering donor leukocytes from packed RBC units and restricting the number of blood products being administered, also decrease ATRs in burnt patients [27].

5. Conclusion

Blood transfusion is a medical method generally suggested as a last resort to rescue patients, particularly burn patients. In this study, we analyzed various factors associated with ATR, including donor-product and recipient-related factors. In addition, it was revealed that most of the ATRs belonged to allergic reactions (73%), while other transfusion reactions were observed in smaller proportions. The solution should be based on strong indications, which involve an extensive evaluation of patients' conditions, such as hemoglobin and platelet blood type, and a history of allergic reactions. Further medical education and adequate awareness of the hemovigilance system among medical staff will likely help reduce ATRs.

Ethical Considerations

Compliance with ethical guidelines

The study was approved by the Ethics Committee of Isfahan University of Medical Sciences (IR.MUI.MED.REC.1399.599).

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Authors' contributions

All authors read and approved the final manuscript.

Conflict of Interests

The Authors declare that there is no conflict of interest.

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