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Reporting transfusion-related acute lung injury cases

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Abstract:

BACKGROUND: Transfusion-related acute lung injury (TRALI) is a rare but potentially fatal complication of blood product transfusion. It is felt worldwide that TRALI is an underrecognized and underreported entity because of lack of awareness.

AIM: The purpose of this study was to report all cases of TRALI diagnosed in a tertiary care hospital over a 5-year period.

MATERIALS AND METHODS: This is a retrospective review of all TRALI cases reported from January 2011 to December 2015. All TRALI cases were identified from a manual review of reported transfusion reaction forms. For detailed information of all TRALI cases, medical record charts of patients were reviewed. The record of donors implicated in TRALI cases was derived from blood bank system.

STATISTICAL ANALYSIS USED: The rate of TRALI cases per 1000 blood products transfused was computed by dividing the transfusion reactions by total number of all blood units transfused.

RESULTS: Total number of transfusions during the study was 291,041. Six cases of TRALI were reported during this period. Rate of TRALI per 1000 units transfused was 0.02%. The mortality associated with TRALI was 33.3%. TRALI occurred following the transfusion of fresh-frozen plasma in one patient, packed red blood cells in two patients, and a mixture of blood components in three patients. In all cases, the donors were male.

CONCLUSION: The rate of TRALI reported to our blood bank was found to be 0.02%, which is very low as compared to international data. This is the first comprehensive study on TRALI from the country and a step forward to create awareness about the importance of diagnosing and reporting TRALI.

Keywords:

Reporting, transfusion reaction, transfusion-related acute lung injury

Introduction

Transfusion-related acute lung injury (TRALI) is a syndrome characterized by the development of new-onset acute respiratory distress with hypoxemia (SpO_2 <90% on room air) during or up to 6 h after completion of a blood transfusion. According to the International Society of Blood Transfusion hemovigilance definition, TRALI is a clinical diagnosis. The presence of antihuman leukocyte antigen (HLA) or antihuman neutrophil antigen (HNA) antibodies in donor(s) or confirmation of cognate antigens in recipient is not required for diagnosis. TRALI should be considered whenever a patient develops hypoxemic respiratory insufficiency during or shortly after transfusion of any blood product. The clinical findings in TRALI include dyspnea, hypoxemia, and bilateral pulmonary edema. Other reported findings are hypotension, tachycardia, and fever(1–2°C rise from baseline). Characteristic chest X-ray results show bilateral patchy infiltrates with alveolar and/or interstitial patterns. The chest X-ray may indicate noncardiogenic pulmonary edema without cardiac enlargement or other evidence of

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fluid overload. Treatment includes ventilatory and hemodynamic support.[1,2]

There are two pathophysiological mechanisms for TRALI. The first is immune-mediated TRALI, which is related to the infusion of donor antibodies (anti-HLA or anti-HNA) that recognize leukocyte antigens in the transfusion recipient.[3] The second proposed mechanism for TRALI, also called the two-hit theory or two-event model, is nonimmune mediated. It suggests that recipient's neutrophils must be primed by a preexisting clinical condition. These primed neutrophils when exposed to bioactive substances in the transfused product trigger an inflammatory response in the lung alveoli which causes pulmonary edema.[2,3]

All blood products have been associated with TRALI. Products with high-plasma content such as fresh-frozen plasma (FFP), apheresis platelet concentrates, and whole blood have been associated with the greatest risk.[3,4] TRALI is attributable to anti-HLA antibodies in the plasma of multiparous females or donors who have received previous transfusions.[5]

TRALI is a rare but potentially fatal complication of blood product transfusion. Approximately 5%–10% of cases are fatal in spite of aggressive supportive care.[6] The incidence has been reported to be 1 in 2000–7500 transfusions.[7] However, it is felt worldwide that TRALI is an underrecognized and underreported entity because of lack of awareness.[8]

The aim of this study was to report all TRALI cases that presented over a 5-year period. The diagnosis and reporting of TRALI will allow a better understanding of the incidence, clinical course, and associated mortality of this reaction. Furthermore, by identifying cases of TRALI, steps can be taken to prevent further cases of TRALI by investigating donors involved in these cases and deferring them from further donations if they are found to be implicated.

Materials and Methods

The study was conducted at blood bank of a tertiary care hospital from January 2011 to December 2015. According to the hospital's policy, it is mandatory to report each and every untoward event that occurs during or after blood transfusion not related to patients underlying illness. In this retrospective review of TRALI cases, the record of the total number of transfusions was obtained from electronic blood bank information system. All TRALI cases were identified from manual review of reported transfusion reaction forms. The record of donors implicated in TRALI cases was derived from blood bank system. Rate of TRALI cases per 1000 blood products was computed by dividing the transfusion reactions by total number of all blood units transfused. All cases in which there was an evidence of circulatory overload were excluded from the study.

TRALI definitions vary by organizations. We diagnosed TRALI according to the definition of International Society of Blood Transfusion Working Party on Hemovigilance (June 2013) and the Canadian Consensus Conference as "a new onset acute lung injury (i.e., non-cardiogenic pulmonary edema) with hypoxia (Pa02 / Fi02 < 300 mm Hg or Oxygen saturation is < 90% on room air or other clinical evidence), bilateral infiltrates on frontal chest radiograph, no evidence of left atrial hypertension (i.e. circulatory overload) and no temporal relationship to an alternative risk factor for acute lung injury (ALI) occurring during or within 6 hours of completion of transfusion. (all five criteria should be met)."[9] Possible TRALI is defined the same way as TRALI except that there is a temporal relationship to an alternative risk factor for ALI. The alternative risk factors for ALI include factors causing direct lung injury (aspiration, pneumonia, toxic inhalation, near drowning, and lung contusion) and factors causing indirect lung injury (severe sepsis, shock, acute pancreatitis, cardiopulmonary bypass, multiple trauma, burn injury, and drug overdose).[9]

TRALI imputability was graded as definite (certain), possible (alternative risk factor for ALI present), probable (likely), unlikely (doubtful), and excluded. "TRALI imputability would be "Probable" if cases did not meet the criteria for definite or possible TRALI, but due to a high index of clinical suspicion, TRALI could not be excluded from the differential diagnosis.[10]

When a TRALI case is suspected, it is documented in patient's medical record chart, and the case is further evaluated. Patient details including age, sex, primary diagnosis, and history of previous transfusions are noted. The duration of time between transfusion of each blood component and onset of symptoms is noted. Management data including the administration of oxygen support, fluid resuscitation, invasive and/or noninvasive mechanical ventilation, admission to an Intensive Care Unit (ICU), and use of inotropes/vasopressors are collected. All blood components transfused within 6 h before the onset of the reaction are evaluated. The type of blood donation (i.e., directed or regular allogenic or autologous), type of blood component, and volume of blood component received are noted. All the associated donors are traced. The gender, pregnancy, and/or transfusion history of the associated donors are sought. Type of donor, i.e., first-time or repeat donor, is noted. Records of transfusion reactions linked to prior donations by the

associated donors are also retrieved. The study was reviewed and granted exemption by the Institution's Ethical Review board [3467-Pat-ERC-15].

Results

Total number of transfusions given during the study was 291,041. Of the total transfusions, 109,140 (37.5%) were packed red cells, 105,938 (36.4%) platelets, 59,954 (20.6%) FFP, and 16,009 (5.5%) cryoprecipitate transfusions. The majority of the transfusions were given to hematology/oncology patients (28.6%). The other major hospital areas utilizing blood components were emergency department (15%), internal medicine (8%), cardiac surgery (7.2%), and orthopedics (6%).

Six cases of TRALI were reported during the study period. Rate of reporting TRALI per 1000 units transfused was calculated to be 0.02%.

Blood products implicated in TRALI included packed red cells only in two patients, FFP only in one patient, and a mixture of blood components in the rest three patients.

TRALI cases

The patient characteristics are given in Table 1. The male: female ratio was 5:1.

The clinical and radiological findings and TRALI probability are mentioned in Table 2. The cases were differentiated from transfusion-associated circulatory overload as jugular venous pressure was not raised in any patient and there was no rise in blood pressure.

Donor details

In all cases, the donors were male. All of them were first-time and replacement donors. Previous history of transfusion was not present in any of the donors.

Discussion

TRALI is a rare complication of blood transfusion which is associated with high mortality.[11] This study from a developing under-resourced country sheds light on six reported cases of nonimmune-mediated TRALI over a period of 5 years.

The incidence of TRALI reported in the literature is quite variable.[12] TRALI incidence in this study came out to be 0.02/1000 blood products transfused. German hemovigilance data reported TRALI rates as 1:285,000 for packed red cells.[13] Serious Hazards of Transfusion reported TRALI frequency of 0.6 per 100,000 components issued.[14] An overall low incidence of TRALI cases reported in this study may be attributable to the fact that TRALI is still an underrecognized and underreported entity due to lack of awareness.

Because of our donor demographics (99% of the donor population is male), it was of no surprise that in our study population all the donors implicated in TRALI cases were male which is in contrast to the literature that states that plasma from multiparous female donors is the usual cause for TRALI.[15] Implication of male donors in all cases is suggestive that all cases were nonimmunological in nature.

Table 1: Patients' characteristics of reported transfusion-related acute lung injury cases

Case	Age (years)	Sex	Diagnosis	Reason for transfusion	Blood product transfused	Interval between transfusion and symptoms
1	21	Male	AML	Low hemoglobin	PRBC	During transfusion
2	6	Male	Tetralogy of Fallot	Postoperative oozing	FFP	0-1 h
3	1	Male	Tetralogy of Fallot	Postoperative oozing	FFP + platelet + PRBC	3 h
4	12	Female	Ileostomy due to ileal perforation	Postoperative anemia	PRBC + FFP	0-2 h
5	22	Male	Relapsed AML	Low hemoglobin	PRBC	During transfusion
6	3	Male	Tetralogy of fallot	Postoperative oozing	CP + FFP	0-1 h

AML = Acute myeloid leukemia, PRBC = Packed red blood cells, FFP = Fresh-frozen plasma, CP = Cryoprecipitate

Table 2: Clinical and radiological findings and outcome of reported transfusion-related acute lung injury cases

Case	Fever/ rigor	Low BP	Shortness of breath	Low pO2	Chest X-ray finding	ICU admission	Other risk factors	Outcome	TRALI imputability
1	Yes	No	Yes	Yes	Not done	No	No	Died	Possible
2	No	Yes	Yes	Yes	Bilateral infiltrates	Already in ICU	Cardiopulmonary bypass	Survived	Possible
3	No	Yes	No	Yes	Subsegmental atelectasis	Already in ICU	Cardiopulmonary bypass	Died	Possible
4	No	Yes	Yes	Yes	Pulmonary infiltrates and interstitial edema with hilar congestion	Yes	No	Survived	Definite
5	Yes	No	Yes	Yes	Increase in the airspace shadowing at the right lung base	Yes	Sepsis	Survived	Possible
6	Yes	No	Yes	Yes	Bilateral infiltrates	Already in ICU	Cardiopulmonary bypass	Survived	Possible

TRALI = Transfusion-related acute lung injury, BP = Blood pressure, ICU = Intensive Care Unit

The patient's age in our study ranged from 1 to 22 years. This reflects the higher propensity of this complication in a younger age group in our population. Interestingly, four out of six subjects belonged to the pediatric age group. In one of the largest report of children diagnosed with TRALI, the age of reported TRALI cases showed a bimodal distribution pattern, with the majority of children being <1 year or >14 years of age.[10]

After reviewing the cases in detail, it was concluded that five patients had "Possible" TRALI because an alternate risk factor for ALI was present in these patients. In one patient, TRALI seemed the likely diagnosis and was labeled as definite TRALI. It is advised that TRALI cases must be interpreted with caution keeping in view the clinical and radiological findings because of the difficulty in establishing the diagnosis with certainty.[16]

Overall, the mortality rate in this study was higher (33%) than the one reported in the literature of around 6%.[17] A plausible explanation to this finding may be that the TRALI cases identified in this study already had a comorbid condition and TRALI was thought to have been only a contributory factor to the death. The comparison of the fatal outcome of TRALI with respect to age group showed a higher mortality rate in adults. We assume that the underlying hematological malignancy in both adult patients resulted in poor outcome.

The striking finding in this study was that an excess risk of TRALI was seen in patients with cardiac surgery and hematological malignancy, indicating that all possible measures should be taken to avoid TRALI to occur in the first place in these two settings. Another study had similarly identified these two groups of patients with hematologic malignancies and cardiac disease at highest risk for TRALI.[18] This highlights that the staff caring for this patient population must be extra vigilant to recognize signs and symptoms of TRALI and start management as early as possible. Another feature seen in our study was that 50% of the TRALI cases were reported from ICU. Increased incidence of TRALI in critically ill patients has been supported by other studies as well.[19]

There are few major limitations of this study; one was that the age of blood product could not be retrieved from the blood bank data. Age of blood components transfused is a major contributing factor for nonimmune-mediated TRALI. The current literature supports more for aged platelet components for nonimmune TRALI. However, there is no definitive consensus for aged red cell and plasma components. Another limitation was that it was a retrospective analysis and the donors implicated in TRALI could not be tested for HLA and HNA antibodies. This database may serve as a tool for further prospective analysis to understand the true incidence of TRALI and aid in educating physicians about diagnosing and reporting TRALI cases. A better awareness of this rare but potentially fatal complication of blood transfusion by healthcare professionals will allow us to understand the true incidence of TRALI in our part of the world.

Conclusion

The rate of TRALI reported to our blood bank was found to be 0.02%, which is very low as compared to international data. This shows that TRALI is underreported in our setting. This report from a developing country has attempted to create awareness about the importance of diagnosing and reporting TRALI cases.

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Conflicts of interest
There are no conflicts of interest.

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