SHORT COMMUNICATION

TRANSFUSION-RELATED ACUTE LUNG INJURY IN A PAEDIATRIC INTENSIVE CARE UNIT OF PAKISTAN

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Background: Transfusion-Related Acute Lung Injury (TRALI) is a major cause of transfusion-related morbidity and mortality in the intensive care unit setting. There is a paucity of such data from Pakistan. The purpose of this study is to assess the incidence and outcome of TRALI in critically ill children admitted in a pediatric intensive care unit (PICU) of Pakistan. **Methods**: This is a retrospective cohort study of all critically ill or injured children who developed TRALI or "possible" TRALI after blood transfusion based on Canadian Conference Consensus criteria in a closed multidisciplinary-cardiothoracic PICU from January 2012 to June 2016. The demographic, pertinent clinical data, transfusion-related variables and outcome of all cases of TRALI were recorded. **Results:** Of total 2975 admissions in the PICU during study period, 35.8% (1066) received 5124 blood components. Eleven cases developed TRALI in our cohort. The incidence of TRALI was 1.03% per patient transfused and 0.19% (19/100,000 per blood product transfused). Median age was 8 (range 1–14) yr., 70 % (n=8) were male. Mean PRISM-III score was 16.3±6.7. Mean time interval for onset of TRALI was 2.73±1.67 hr. The postoperative cardiac surgical and hematology-oncology patients were most common categories (63.6%). Plasma and platelets were the most commomly identified trigger of TRALI. The case-specific mortality was 63.6% and the overall mortality was 10.7% (p<0.0001). **Conclusion:** The incidence of TRALI in critically ill children is low, but is associated with high mortality. Critically ill children with high PRISM-III score, postoperative cardiac surgical and hematology-oncology patients are often affected by TRALI.

Keywords: Transfusion; Critically ill child; TRALI; Outcome; Incidence; Acute Lung Injury

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INTRODUCTION

Blood product transfusion is a commonly employed life-saving procedure in critically sick patients. According to an estimate, around 49% of children admited in multidisciplinary paediatrics intensive care unit (PICU), received at least one blood product during their hospital stay. This percentage increased to 78% of children admitted in cardiac PICU.[1,2]

Blood transfusion, however, is not free of risks and is associated with multiple known and emerging complications. These complications are broadly classified into infectious and non infectious complications. With the advent of proper screening practices, the incidence of tranfusion related infectious complications has significantly reduced.[3] The major burden of morbidity and mortality secondary to blood transfusion is largely accounted by the severe non infectious transfusion related complications.[4]

Transfusion related acute lung injury (TRALI) is one such complication which is now emerging as the leading cause of tranfusion related morbidity and mortality. According to the definition proposed by Canadian Conference Consensus (CCC) and National Heart, Lung, and Blood Institute (NHLBI), TRALI is defined as an acute lung injury occurring during or within 6 h after a transfusion, with a clear temporal relationship to transfusion.[5] The term "possible " TRALI is used when TRALI occurs in the presence of alternate risk factor for acute lung injury such as cardiac surgery (cardiopulmonary bypass), severe sepsis, pneumonia, hematological malignancy and mechanical ventilation.[6,7]

Since TRALI poses a major threat to post transfusion critically ill patients, it is extremley important to estimate the disease burden in order to take effective measures to prevent and treat it. Multiple studies have been conducted to report the incidence and overall disease outcome of TRALI in adult population. However, little data is available for the paediatric population.[8,9] We therefore conducted this study to determine the incidence and overall outcome of TRALI in critically ill children, in a tertiary care hospital.

MATERIAL AND METHODS

We retrospectively reviewed the medical record of all critically ill children who developed TRALI in closed multidisciplinary-cardiothoracic pediatric intensive care unit (PICU) of Aga Khan University Hospital (AKUH) from January 2012 to June 2016. AKUH is a tertiary-care, university hospital with 8-beded multidisciplinary and cardiothoracic intensive care unit with annual admission of around 600 patients.

The blood bank of the hospital is manned by a team of experienced and fully trained medical technologists who work under the supervision of full-time hematologists to provide quality service round the clock. AKUH is a Joint Commission International accredited hospital and our laboratory is certified by College of American Pathologists (CAP). We follow strict transfusion policy in our unit.[10] and we preferentially used male-donor plasma in our PICU. Like other acute transfusion reactions, all cases of TRALI are reported to the blood bank. Blood bank completes transfusion reaction investigation by reviewing patient history and following up on donors and products implicated in each case.

The case definition of TRALI was used based on CCC criteria and TRALI was defined as of acute dyspnea with hypoxia and bilateral pulmonary infiltrates on chest X-ray during or within six hours of end of blood transfusion in the absence of other causes of acute lung injury. The "possible" TRALI was defined as TRALI in the presence of risk factor for acute lung injury. The medical record of children (aged 1 month to 16 years) with TRALI was retrieved by using ICD-9: 518.7 code from our medical record.[6] Data for the total number and type of blood components was retrieved from blood bank record. The following data was collected on structured performa: demographic variables (age, gender), clinical variables (diagnosis, PRISM -III score[11], time of onset hypoxia, need for respiratory support, length of stay and use of inotropes), transfusion-related data (number and type of blood components) and outcome (defined as death or survival of the patient). Descriptive statistics were applied for data analysis. This study was approved by local institutional Ethical Review Committee [4463-Ped-ERC-16].

RESULTS

Out of total 2975 patients admitted to the PICU during the study period, 35.8% (n=1066) received at least one or more blood component transfusion. Forty-one percent (n=1145) were post-cardiac surgical patients. Total number of blood components transfused was 5,727 which included: 1759 (30.7%) packed red blood cells, 2226 (38.9%) fresh frozen plasma, 459 (8%) cryoprecipitate, 1279 (22.3%) platelets and 4 whole blood (0.07%). Eleven patients (1.03% per patient transfused) developed TRALI during the study period. The incidence of TRALI per 100,000 blood components transfused was 19/100,000 (0.19%). The demographic, clinical, transfusion-related characteristics and outcome are described in table-1.

Median age of patients was 8 (range 1–16) years including 8 males and 3 female patients. The mean PRISM-III score was 16.36 (SD 6.77) and the mean time interval to development of TRALI was 2.73 (SD 1.67) hours. All of them were severely hypoxic and demonstrated as mean PaO_2: FiO_2 ratio of 88.72 (SD 72.78). Ten (90.9%) required mechanical ventilation and two patients were advanced to High Frequency Oscillatory Ventilation. Seven (63.63%) patients expired. One patient was not mechanically ventilated because of code status of "Do Not Resuscitate" (DNR). All of our cases were "possible TRALI" because other risk factors for acute lung injurywere present. There was a temporal rise in the incidence of TRALI over the duration of the study. All components of blood are implicated in the development of TRALI in our cohort. However, there was a predominance of plasma and platelets being implicated. The overall mortality of the PICU during the study period was 10.7% and case-specific mortality was 63.6% (p<0.0001).

Table-1: The demographic, clinical, transfusion-related characteristics and outcome of patients who developed TRALI during stay in PICU at AKUH.

Age (Years)	Sex M/F	PRISM-III Score	DIAGNOSIS	Year	Trigger	TIME (hours)	PaO_2/FiO_2 Ratio	Mechanical Ventilation	Outcome (A/E)
10	F	12	Atypical HUS	2012	FFP	3	54	Y	A
6	M	20	S/P Rastelli	2014	WB	1	47	Y	E
11	M	11	AML	2015	PC	1	104	Y	E
1	F	24	Septic Shock	2015	FFP	5	40	Y+HFO	E
9	M	23	THAL, BMT	2015	PLT	2	82	Y+HFO	E
13	M	13	Aplastic Anemia	2013	PLT	5	165	Y	E
2	F	13	SP TOF Repair	2013	CRYO	2	42	Y	E
3	M	14	SP TOF Repair	2014	CRYO	1	51	Y	A
1	F	10	Pneumonia	2016	PC	5	45	Y	E
8	M	15	SP TOF Repair	2016	Mixed	3	51	Y	A
14	M	25	Aplastic Anemia	2016	PLT	3	214	Y	A

Abbreviation: Y-yes; A-alive; E-expired

DISCUSSION

With this study, we report eleven cases of TRALI admitted in multidisciplinary and cardiothoracic PICU in a tertiary care hospital of Pakistan.

TRALI, although less common, is now emerging as a leading non infectoius complication of blood product transfusion. There is paucity of clinical data on TRALI in the pediatric population and it is mainly limited to case reports, case series and hemovigilance reporting systems.[8,12] According to the hemovigilence reports from UK and Canada, the incidence of TRALI in paediatric population is about 6% of all the adverse reactions post blood transfusion.[11,13] A study conducted in 2015, reported the incidence of TRALI in of about 6.9% per transfused patient and 1.5% per product transfused over a period of four years in PICU settings.[9]

The incidence of TRALI in our heterogeneous cohort was found to be 1.03% per transfused patient and 0.19% per transfused unit of blood. The stark variation in our estimates and what has been previously establishedis of note.[9] TRALI in general is an underdiagnosed and under reported condition.[14] We have a universally accepted definition for TRALI in adult population however no set criterean exists for the paediatric population.[15–17] These discrepencies in guidelines and overall under detectection of the disease leads to lesser people being diagnosed, which could also be attributed to the lower incidence in our cohort. Another factor that could have led to lower incidence in our cohort is the preferential use of male donor plasma, which has been previously associated with a reduction in the incidence of TRALI.[18]

The rate of blood transfusion in our cohort is higher (35.8%) than what has been reported previously.[9] This is most likely due to a higher proportion of cardiac post operative surgery patients in our study. Such patients are predispoed to complications like coagulopathy and thus have higher transfussion requirements.[2]

We did not find any age predilection in our cohort and our patients were distributed across all age groups. This was in contrast to a bimodal age of presentation, as previously demonstrated in a study.[9] We observed TRALI events from all components of blood including whole blood. The risk of TRALI was higher with plasma and platelets than RBC or whole blood, similar to what has been reported previously.[19] All of our PICU patients had high PRISM-III scores, with a mean of 16.36, which put them at risk of developing acute lung injury due to multiple other factors and were thus labelled as “possible” TRALI. About two-third of our cohort were either postoperative cardiac surgical or hemotology-oncolgy patients, who have an increased rate of transfussion, as mentioned.[22] These patients have co morbids like cardiac bypass, sepsis and pneumonia, which in turn puts them at risk to develop acute lung injury. However, these risk factors also support “two-event” hypothesis in the pathogenesis of TRALI, where the first event is the presence of critical illness and blood transfusion serves as the second event.[20]

The mortality rate of patients with TRALI was higher (63.7%) than the overall mortality rate (10.7%) in our cohort (p<0.0001). This finding was in accordance to what has been demonstrated previously; where TRALI was associated with high mortality rate both in adult and paediatric population (63.7%).

This is first such study from Pakistan to report the incidence of TRALI and its outcomes from a tertiary care hospital based PICU with multidisciplinary patients. Some of the weaknesses of our study include it being a retrospective study based on patients from a single center. We were also unable to establish a an association between the volume of blood being transfused and development of TRALI.

CONCLUSION

We found that the incidence of TRALI in critically ill children is lower than previously reported, but is associated with a high mortality rate. Critically ill children with high PRISM-III score, postoperative cardiac surgical and hematology-oncology patients have the higher likelyhood of getting affected by TRALI.

AUTHORS' CONTRIBUTION

MTJ: Conception of idea, manuscript writing; ZD: data collection; QA and HJ review manuscript; FKM: Transfusion Specialist critical review; AH: Guarantor of manuscript

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