24 Transfusion-Related Acute Lung Injury (TRALI) n=10

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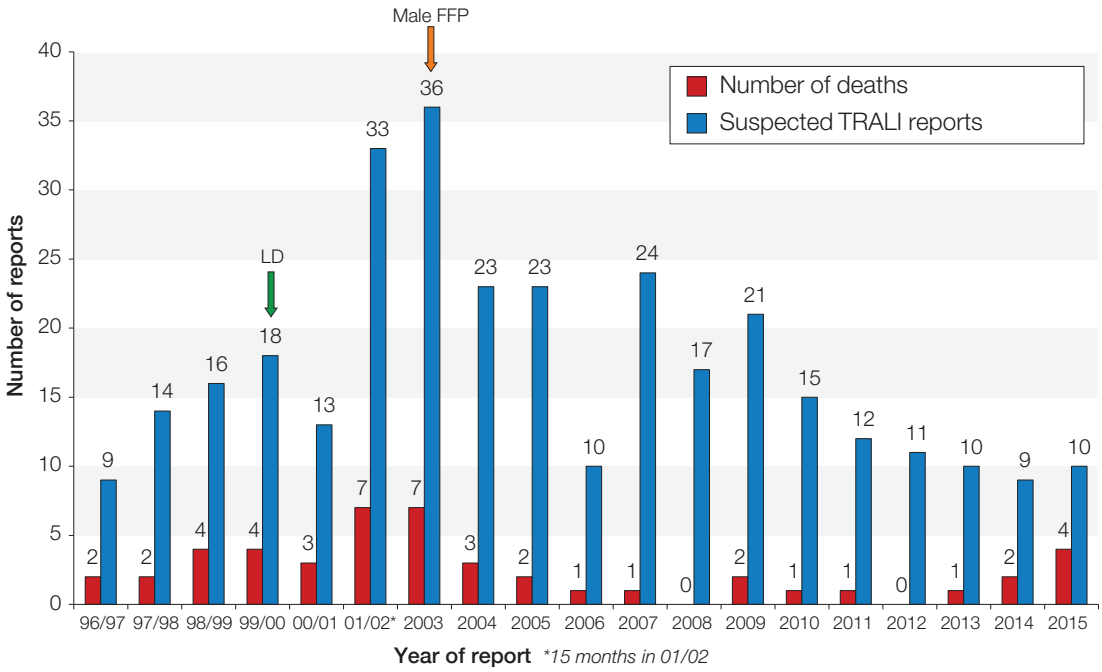
Definition:

Transfusion-related acute lung injury (TRALI) is defined as acute dyspnoea with hypoxia and bilateral pulmonary infiltrates during or within 6 hours of transfusion, not due to circulatory overload or other likely causes.

Ten cases of suspected TRALI have been included in 2015 (9 in 2014). One other case was transferred to another SHOT category (transfusion-associated circulatory overload (TACO)) and a further 4 were withdrawn because they did not fit TRALI criteria and their respiratory deterioration was attributed to another cause.

Figure 24.1: Number of suspected TRALI cases and deaths at least possibly related to TRALI by year of report



LD marks the date when universal leucodepletion was introduced (during 1999). Male FFP (fresh frozen plasma) marks the date (from September 2003) when the Blood Services introduced use of male-only donor plasma for FFP and preferential use of male plasma for suspending pooled platelets. Hospital stocks of female FFP were not recalled at that time.

Patient outcomes

Deaths n=4

Five patients died but 1 death was considered to be unrelated to the transfusion.

Case 24.1: A transplant patient with pneumonia

This patient died following 2 units of red blood cells in optimal additive solution (RBCOA). The patient was already on oxygen for pneumonia post autologous haematopoietic stem cell transplant (HSCT) but deteriorated rapidly 20 minutes after transfusion and died of respiratory failure 7 days later. Serology showed human leucocyte antigen (HLA) class 1 antibodies cognate with the recipient. The event was classified as probable TRALI and it was assessed that TRALI had probably contributed to his death (imputability 2).

Case 24.2: Possible TRALI follows transfusion for a variceal bleed

This patient developed breathlessness 40 minutes following 6 units of red cells, 4 units of fresh frozen plasma (FFP) and 1 pool of cryoprecipitate for a variceal bleed. There was pre-existing fluid overload before transfusion and a chest X-ray before transfusion suggested pneumonia. However antibodies cognate with the recipient were present in one red cell unit and two donors to the cryoprecipitate pool. The case has been classified as possible TRALI and the patient's subsequent death was assessed as possibly related to transfusion (imputability 1).

Case 24.3: A sick patient with multiple contributory factors

A patient had alcoholic liver disease with encephalopathy and developed hypoxia 30 minutes after a platelet transfusion, but had pre-existing fluid overload and pulmonary effusions. The cause of death was considered to be hepatorenal syndrome. Serology showed HLA class 1 antibodies cognate with the recipient. This case was classified as possible TRALI and death possibly related to transfusion (imputability 1).

Case 24.4: Deterioration following HSCT

A patient with acute myeloid leukaemia (AML) deteriorated during transfusion of the second of 2 units of red cells. The patient was already receiving inotropic support for neutropenic sepsis following an allograft HSCT for relapsed AML. Serology was negative. The case was assessed as unlikely TRALI and death possibly related to transfusion (imputability 1).

Case 24.5: Breathlessness due to myocardial infarction

A patient became breathless 6 hours after a 3 unit transfusion following admission in a state of collapse with a myocardial infarction. Serology was negative. The case was classified as unlikely TRALI and death unrelated to transfusion (imputability 0).

Major morbidity n=4

All had life threatening acute reactions requiring immediate medical intervention. All 4 patients who suffered major morbidity recovered fully from their respiratory events.

Assessment of TRALI

There is no diagnostic test for TRALI and it is difficult to distinguish from other causes of acute lung injury, circulatory overload or infection. Most reported cases are complex with several possible contributory factors. The probability of TRALI has been assessed in each case using the criteria in Table 24.1. Clinical factors considered in assessments include: timing; radiological features; possibility of infection; other risk factors for acute lung injury or acute respiratory distress syndrome; evidence of circulatory overload and/or impairment of cardiac function; pre-existing cardiac, pulmonary, renal, hepatic or other disease and response to diuretics. Serological results are also considered.

Two intensive care specialists and a transfusion medicine expert (TRALI expert panel) assessed clinical details of all National Health Service Blood and Transplant (NHSBT) cases (7 of 10 cases) before laboratory investigation was initiated. Cases were subsequently categorised to take account of the laboratory results (Table 24.2).

Table 24.1: SHOT criteria for assessment of TRALI cases

Probability	SHOT criteria for assessment of TRALI cases
Highly likely	where there was a convincing clinical picture and positive serology
Probable	where there was either a less convincing history and positive serology or a good history and less convincing or absent serology
Possible	where either the clinical picture or serology was compatible with TRALI, but other causes could not be excluded
Unlikely	where the picture and serology was not supportive of the diagnosis

Table 24.2: TRALI case probability (SHOT criteria)

Probability	Number of cases
Highly likely	0
Probable	1
Possible	3
Unlikely	6

Additional information can be found in the supplementary information on the SHOT website www.shotuk.org.

This includes data extracted from individual TRALI questionnaires and the associated laboratory results.

TRALI Table 1 Patient characteristics and component details

TRALI Table 2 Clinical characteristics and radiological features of cases reported as TRALI

TRALI Table 3 Treatment, outcomes, investigation results and likelihood of case being TRALI

Patient characteristics

Age: Ages ranged from 10 to 73 years.

Clinical specialty: The referring specialities were: haematology 4 cases; gastroenterology, cardiology, endocrinology, internal medicine, oncology and emergency department 1 case each.

Clinical presentation

All patients were hypoxic and had bilateral changes on chest X-ray. Six patients were treated in the intensive therapy unit (ITU). Three of these required full mechanical ventilation; duration of mechanical ventilation for these cases was 2 days, 5 days and was not reported in 1 case. Fever was present in 4/9 and hypotension present in 4/8 patients for whom data was submitted.

Laboratory investigations

Complete results were available for all 10 patients. Concordant donor HLA- or granulocyte-specific antibodies were found in 3 cases, the antibody specificities are tabulated below in Table 24.3. Concordant donor antibodies were excluded in 7 cases.

Donor antibody	Concordant antibody specificities	Component	Other risk factors	Outcome
HLA class I	A2	RBCOA	Pneumonia	Death probably related to transfusion
HLA class I and II and human neutrophil antigen (HNA)	B44, Cw5, DR4, DR53, HNA2	Cryoprecipitate: 2 female donors had concordant antibodies RBCOA: 1 female donor had concordant antibodies	Pneumonia, massive haemorrhage, liver disease, fluid overload	Death possibly related to transfusion
HLA class 1	Cw12	RBCOA	Alcoholic liver disease, fluid overload, positive fluid balance	Death possibly related to transfusion

Table 24.3: Concordant donor antibodies 2015: specificities and implicated components

Patients who have suspected TRALI are no longer tested for leucocyte antibodies unless granulocytes have been transfused. This is because all other United Kingdom (UK) blood components are leucodepleted.

Cumulative serological data

Since 1996 204/324 (63.0%) reported cases have had full laboratory investigation for TRALI. Concordant antibodies were identified in 116/204 (56.9%) of these. The most frequently identified antibody specificities (either alone or in combination with other concordant antibodies) have been HLA-DR4 (22/116 cases, 19.0%), HLA-DR52 (17/116, 14.7%) and HLA-A2 (18/116, 15.5%). All other HLA antibody specificities have been identified in less than 10% of cases. Concordant HNA-specific antibodies, alone or in combination, have been found as follows: HNA-1a (9/116 cases, 7.8%); HNA-2 (2/116, 1.7%); HNA-3a (2/116, 1.7%).

Analysis of reports of 184 complete TRALI investigations between 2001 and 2015 inclusive has shown that the specificities of concordant antibodies were as follows:

Concordant donor antibodies 2001 to 2015 inclusive				
HLA class I alone	**HLA class II alone**	**Both HLA class I and HLA class II**	**Granulocyte-specific antibody (+/– HLA antibodies)**	**None identified**
20/184 (10.9%)	36/184 (19.5%)	27/184 (14.7%)	18/184 (9.8%)	83/184 (45.1%)

Table 24.4: Concordant donor antibodies 2001 to 2015 inclusive

Classification of cases according to Canadian consensus criteria

All 10 reports have also been classified using the Canadian consensus criteria to allow international comparison (Goldman et al. 2005; Kleinman et al. 2004). Using these criteria, no cases were classified as TRALI, 5 as possible TRALI and 5 were classified as not being TRALI (including 2 with antibodies) because there was a history of fluid overload.

Case 24.1 above, further details: Probable TRALI

A 60 year old man with multiple myeloma, day 24 post autologous HSCT and with hospital-acquired pneumonia had been stable, maintaining oxygen saturation of 100% on 3L/minute oxygen. Within 20 minutes of commencing a unit of red cells, respiratory rate increased to 30/minute and oxygen saturation dropped to 70%. Blood pressure fell to 85/49 from 103/59mmHg at baseline and heart rate rose to 180 from 100 beats per minute at baseline. Chest X-ray showed bilateral changes in addition to the previously noted lower lobe pneumonia. The patient was clinically volume depleted and was in negative fluid balance over the previous 24 hours. An echocardiogram pre transplant had shown good left ventricular function. Despite ITU admission and ventilation the patient died 7 days post transfusion. Investigation of the female red cell donor showed HLA-A2 antibodies cognate with the recipient.

Likelihood of TRALI: This was classified as probable TRALI according to SHOT criteria because concordant HLA class I antibody was transfused within 6 hours of his respiratory deterioration and the clinical picture was concordant with the TRALI definition but could also be consistent with infection.

COMMENTARY

Five patient deaths were reported. One was assessed as probably due to TRALI, three as possibly related and one as unlikely to have been caused by TRALI. This is the highest number of reported deaths since the introduction of TRALI reduction measures but it is notable that all cases had alternative, and often multiple, reasons for respiratory deterioration which in most cases were more likely than TRALI. Two of the deaths classified as TRALI according to SHOT definitions because of the presence of antibodies would not have been classified as TRALI under the Canadian consensus definition due to the presence of fluid overload.

Three cases this year were found to have received donations from female donors with concordant HLA-specific antibodies. The implicated component/s were pooled cryoprecipitate and RBCOA in one case and RBCOA only in two cases. Multiple female donors contributing to the cryoprecipitate pool were found to have leucocyte antibodies.

The recommendation from last year's SHOT report for all UK Blood Services to avoid the use of female donor plasma for the preparation of cryoprecipitate thus remains active.

No case of TRALI linked with transfusion of female FFP, apheresis platelets or plasma contribution to platelet pool containing concordant HLA- or granulocyte-specific antibody has been reported to SHOT during the last five years.

References

Goldman M, Webert KE, Arnold DM, et al. (2005) **Proceedings of a consensus conference: Towards an understanding of TRALI**. Transfus Med Rev 19, 2–31

Kleinman S, Caulfield T, Chan P, et al. (2004) **Towards an understanding of transfusion-related acute lung injury: statement of a consensus panel**. Transfusion 44, 1774–1789