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ORIGINAL ARTICLE

Transfusion Related Acute Lung Injury (TRALI): A Single Institution Experience of 15 Years

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Abstract Transfusion related acute Lung injury (TRALI) though a serious blood transfusion reaction with a fatality rate of 5–25 % presents with acute respiratory distress with hypoxaemia and noncardiac pulmonary oedema within 6 h of transfusion. In non fatal cases, it may resolve within 72 h or earlier. Although reported with an incidence of 1:5000, its true occurrence is rather unknown. Pathogenesis is believed to be related to sequestration and adhesion of neutrophils to the pulmonary capillary endothelium and its activation leading to its destruction and leaks. The patient's underlying condition, anti-neutrophil antibody in the transfused donor plasma and certain lipids that accumulate in routinely stores blood and components are important in its aetiopathogenesis. Patient's predisposing conditions include haematological malignancy, major surgery (especially cardiac), trauma and infections. The more commonly incriminated products include fresh frozen plasma (FFP), platelets (whole blood derived and apheresis), whole blood and Packed RBC. Occasional cases involving cryoprecipitate and Intravenous immunoglobulin (IVig) have also been reported. We present a 15 year single institution experience of TRALI, during which we observed 9 cases among 170,871 transfusions, giving an incidence of 1:19,000. We did not encounter cases of haematological malignancy or cardiac surgery in our TRALI patients. Among the blood products, that could be related to TRALI in our patients included solitary cases receiving cryoprecipitate, IVIg, and recombinant Factor VII apart from platelets and FFP. All patients were treated with oxygen support. Six patients required mechanical ventilation. Off label hydrocortisone was given to all patients. There were no cases of fatality among our patients.

Keywords Adverse blood transfusion reaction · Transfusion related acute lung injury (TRALI) · Anti-neutrophil antibody · Damaging lipid in stored blood

Introduction

Transfusion related acute lung injury (TRALI), though rare, is a potentially fatal adverse blood transfusion reaction. It presents with acute respiratory distress characterized by sudden, albeit transient, non cardiac pulmonary oedema on chest radiogram, temporally occurring during or within 6 h of blood or component transfusion. Hypoximea is the essential consequence. The condition requires immediate detection and prompt treatment can be life saving.

Reported to occur with frequency of 1:5000 patients receiving blood or components, it is believed to be the fourth most common adverse transfusion reaction [1] and the third leading cause of mortality, reported in USA [2].

Nested control studies show that the vulnerable groups of patients include patients with haematologic malignancy undergoing induction chaemotherapy, those undergoing coronary bypass surgery [3]. Other antecedent events have included major surgery, massive transfusion (replacement of total volume for 4 days) and cytokine administration (Granulocyte Colony Stimulating Factor, GCSF). In

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addition, patients receiving fresh frozen plasma (FFP) for coumadin reversal, plasmapharesis for Thrombotic Thrombocytopaenia (TTP) and those with wide spread endothelial cell activation due to infections are considered more susceptible for TRALI [4].Pathogenesis of TRALI centers around neutrophil sequestration in pulmonary microcirculation and adherence to alveolar endothelium followed by its activation and leaks either by an immune reaction between neutrophil antigens and anti-neutrophil antibody or by a non-immune mechanism prompted by release of oxidases and damaging response modifier lipids that accumulate in routine storage of blood [3, 5, 6].

We present a 15 year (1999–2013) single institution experience with TRALI, during which we encountered 9 cases among 170,871 transfusions. The presentation's objective is to point out (a) that its prevalence in our experience (1: 19,000) is much lower than the oft reported incidence of 1:5000 (b) With awareness of the caring team for its prompt recognition and immediate management, there was no mortality or significant morbidity in our cases (c) Even among the small number of cases (only nine) who came into our observation, the disease conditions that are suspected to predispose a patient to TRALI are somewhat different (d) a brief review of information available in the literature about this rare and oft overlooked condition is, called for.

Methods

Subjets

A brief clinical narrative of our nine cases of TRALI is given below and this summarized in Table 1

1. HA, 26 M, had presented with repeated episodes of bleeding and renal impairment at first admission in 1997. Investigations revealed Thrombotic Thrombocytoparnic Purpura (TTP) that subsequently (after three episodes) was found have hereditary TTP with ADAMTS-13 deficiency. HA had been given 43 sessions of Plasmapharesis (2 vol. exchange) with cryo-free fresh frozen plasma (FFP) during the first episode, 3 sessions during the second and 3 sessions during the third episode. He developed TRALI during the first sessions of plasmapheresis in the third episode of recurrent TTP. He was stabilized with appropriate oxygen administration and plasmapheresis was continued.
2. SH, 64F, was a known case of Anti-phospholipid Syndrome (APS) who was taking long term prophylaxis with Coumadin (warfarin) with history of recurrent episodes of cerebral ischaemia. She was given FFP (15 ml/Kg) for quick reversal of Coumadin effect in preparation for emergency appendicectomy for burst appendicular abscess.
3. AA, 18 M, is a patient with Thrombaesthenia (Glanzman's disease) who had been receiving on-demand platelet transfusions (both random and lately single donor apheresis units) since childhood. The episode of TRALI occurred post transfusion with apheresis platelets.
4. MK, 42 M, developed TRALI after planned transfusion with 2 units of Fresh whole blood, 30 ml/Kg of FFP and 6 units of random platelet concentrate following massive packed cell transfusion (with 19 units) given during extensive life saving abdominal surgery for ruptured spleen, liver and torn kidney, consequent to road traffic accident.
5. AL, 27F, had been diagnosed to have Acquired Amegakaryocytic thrombocytopaenia based on complete absence of megkaryocytes in the bone marrow examination performed after failure of response of persistent thombocytopaenia to traditional first line of treatment with steroids and IV immunoglobulin. In addition to immunosuppressive therapy she had been receiving both random and HLA matched platelets on demand. TRALI occurred after completion of one of the sessions of transfusion with random platelet concentrate
6. FH, 57F, was a patient known to have Systemic Lupus Erythmatosis (SLE). She presented with fever and suddenly developing profuse purpura all over the body and multi-site mucosal bleeding. Investigations revealed TTP. She received seven daily sessions of plasmapharesis with cryo-free FFP (2 vol. replacement) to control bleeding and developed TRALI during the fourth session.
7. MA, 11 M, presented with frequent episodes of echymosis and occasional epistaxis and had doubtful history of cerebral hemorrhage at birth. He was diagnosed to have Factor XIII deficiency. He was receiving prophylaxis with FFP infusion (15 ml/Kg) at 1–2 month intervals and developed TRALI after one of these infusions.
8. GM,46F, a known case of vonWillebrand Disease (vWD)- type 2b, received cryoprecipitate (15 units) and Humate-P (80 units/Kg) prior to surgery for severe intra-abdominal haemorrhage for ruptured ectopic pregnancy. TRALI developed almost immediately after evacuation.
9. WA, 24F, presented with massive post partum haemorrhage (PPH) and purpura after evacuation for intrauterine foetal death complicated with pelvic abscess. Diagnosed to have developed Disseminated Intravascular Coagulation (DIC), she was given FFP (25 ml/

Table 1 Clinical narrative of the nine cases of TRALI encountered in our hospital

Name	Age (years) and sex	Nationality	Diagnosis	Product of transfusion	No of units	Single/multiple occasions	Time of TRALI	Time to clear X ray (days)	Year of observation
HA	26 M	Syrian	TTP	Cryo free plasma	43[a] + 3 + 3	Multiple	During transfusion	1	1997[b], 1998, 2005
SH	64 F	Kuwaiti	APS	FFP	4	Single	1 h	2	1999
AA	11 M	Kuwaiti	Thrombasthenia	Plat conc	>45	Multiple	6 h		2000
MK	42 M	Pakistani	RTA, Multiple visceral injury	FFP, WB, Plt, PRBC	4 + 2 + 6 + 19	Single	7 h	2	2004
AL	27 F	Egyptian	Amegakaryocytic thrombocytopenia	Plt conc	>31	Multiple	4 h	3	2006
FH	57 F	Indian	TTP	Cryo free plasma	>[a]	Multiple	During transfusion	2	2007
MA	11 M	Jordanian	Factor XIII deficiency	FFP	>32	Multiple	6 h	1	2009
GM	46 F	Kuwaiti	vWD	Cryo ppt, Humate P	15	Single	Immediate after surgery	2	2009
WA	24 F	Iranian	DIC	FFP, Cryo ppt, rFVIIa	4 + 16 + 5.4 mg	Single	30 min	3	2013

TTP Thrombotic Thrombocytopenic Purpura, *APS* anti phospholipid syndrome, *FFP* fresh frozen plasma, *VWD* von willebrandt disease, *rFVIIIa* recombinant activated Factor VIII

[a] Each session of plasmapheresis 1.5–2 vol replacements

[b] Three admissions with recurrent TTP

Kg), Cryoprecipitate (14 units), 7 units of packed RBC, and 90 ug/Kg of recombinant activated Factor VII (rVIIa). She developed TRALI soon after control of PPH.

Methods: Diagnostic Criteria

As standard practice in our hospital, the treating clinicians and the nursing staff report all cases suspected of adverse transfusion reactions immediately to the hospital blood bank, followed by event investigation and recording on the standard format, blood sampling and laboratory tests according to a pre-defined d protocol. Detailed review of patient's records, inquiries from the patient and the concerned staff, clinical examination and review of investigations is done by the charge physician/haematologist.

The diagnosis of TRALI, as recommended by the definition of Toronto Canadian consensus conference of 2004 [7, 8] was based on the following criteria in our cases.

(a) Clinically acute respiratory distress manifested by significant dyspnoea with or without tachycardia and cyanosis (our 3 patients showed cyanosis)
(b) Diffuse bilateral pulmonary oedema on chest radiogram in absence of cardiac enlargement and fluid overload with spontaneous clearance of chest X-ray findings in a couple of days, normal echocardiogram and ECG, except sinus tachycardia.
(c) Objective evidence of hypoxia (PaO2/FiO2 <300 mmHg or pulse oxymetry O2 saturation <90 % on room air).
(d) Temporal relationship with transfusion—the episode occurring within 6 h of its completion.
(e) No other evident cause of respiratory insufficiency like volume overload, hypersensitivity reaction, shock, sepsis or drug over dose.
(f) Observations were also directed to record temperature and blood pressure.

All the patients included in the study are those who were investigated, diagnosed and treated prospectively. The data has been stored in the patient files maintained both in the department of medical statistics and in our own haematology unit. The donor details in respect of the offending transfused component were collected from the national blood bank where the donor records are routinely maintained.

Observations

The results of investigations that formed the basis of diagnosis of TRALI on the background of clinical findings in each case are shown in Table 2.

Table 2 Results of investigations that were conducted immediately/soon on suspicion of the occurrence of TRALI

	X-ray chest Pulm oedema	ECHO	Pulse oxymetry Oxygen saturation (%)	Repeat X-ray chest
HA	Bilat' diffuse	N	78	Cleared after 60 h
SH	Bilat' diffuse	N	83	Cleared after 48 h
AA	Bilat' diffuse (Rt. > left)	N	72	Cleared after 48 h
MK	Bilat' diffuse	N	68	Cleared after 72 h
AL	Bilat' diffuse (Rt. > left)	N	88	Cleared after 72 h
FH	Bilat' diffuse (left > Rt.)	N	73	Cleared after 48 h
MA	Bilat' diffuse	N	87	Cleared after 48 h
GM	Bilat' diffuse	N	71	Cleared after 48 h
WA	Bilat' diffuse	N	89	Cleared after 72 h

ECHO: Bed side ECHO cardiogram performed to exclude any cardiac cause of pulmonary oedema especially cardiomegaly or congestive cardiac failure

N: Normal i.e. no evidence of cardiac pathology or CHF accountable for pulmonary oedema

Bilat' diffuse: Bilateral pulmonary infiltration (oedema)

Our nine cases of TRALI were among 170,871 blood and component transfusions giving an occurrence frequency of 1:18,985, that is roughly 1:19,000 transfusions..

Although the number of cases in our study is too small, yet it may be observed that there is no consistency in age and gender, indication for transfusion, the kind and number of component units transfused or the number of exposures (single or multiple occasions). The time to symptoms of TRALI varied from a few minutes (during transfusion) to 7 h. The chest radiogram cleared in 2–3 days in all cases.

All patients recovered with prompt management of ARD with oxygen support. Six patients, including three with cyanosis, were put on mechanical ventilation. All were given off- label, hydrocortisone. Two patients developed fever and were given antipyretics. No patient developed hypotension and none received diuretics.

Fortunately, there were no fatalities in our cases.

The information about the particular blood components transfused in our nine TRALI patients is contained in Table 1.

Figuring incidence for particular components as causative of TRALI from merely nine cases will not be meaningful. However, it was observed that among our nine patients, TRALI occurred following FFP in four patients, platelet concentrate in two patients, and cryoprecipitate in one patient. In the remaining two patients, no one specific component could be incriminated because of almost simultaneous emergency transfusion with more than one component in these patients.

The year-wise distribution of various blood components transfused during the period of study is shown in Table 3. It also shows the number of adverse transfusion reactions against each component, with a separate mention of the number of patients who developed dysponea or respiratory difficulty. All such patients were carefully examined clinically for bronchospasm, evidence of fluid overload and accompaniments of hypersensitivity reactions and were specifically investigated for evidence of TRALI according to the accepted criteria. Only nine cases could be proved to have TRALI.

Some authors [7] suggest that If one or more ALI factors are present in a patient considered to have TRALI, the diagnosis of "Possible TRALI" could be given. But, most other workers believe that it may not be recommendable as it introduces an element of significant subjectivity. We have included only those patients who strictly fulfilled all the recommended criteria of TRALI and have avoided considering doubtful patients as "Possible TRALI". However, we did pay particular attention to the patients who developed dyspnoea either as the sole or combined manifestation of transfusion reaction and excluded those patients who showed positive auscultatory findings of bronchospasm, fluid over load or accompaniments of hypersensitivity reactions and those who on further investigations did not show evidence of diffuse pulmonary oedema and hypoxia (PaO2/FiO2 <300 mmHg or pulse oxymetry O2 saturation <90 % on room air).

Discussion

Bilateral pulmonary oedema resulting from blood transfusion was first described by Barnard [9]. However, Popovsky et al. [10] recognized this as a distinct clinical entity as an adverse transfusion reaction in 1983 and coined the term Transfusion "Related Acute Lung Injury"—TRALI. In 1985, they described the minimum diagnostic features and pathogenetic considerations of this condition [11]. However, It is only in 2004 that the EuropeanHaemovigilance Network (EHN) and the Canadian Consensus Conference [7] proposed the criteria for the diagnosis of TRALI. This included (a) active respiratory distress

Table 3 Various blood components transfused and the number of adverse reactions recorded against each component, with special mention of reactions manifesting with dyspnoea/respiratory difficulty

	FFP			Cryo ppt			PRBC			LRBC			Washed RBC			Plat conc (apheresis)			Plat conc (random)		
	A	B	C	A	B	C	A	B	C	A	B	C	A	B	C	A	B	C	A	B	C
1999	583	4	0	329	1	0	2600	4	1	435	2	0	2	0	0	297	0	0	1213	5	0
2000	745	6	1	116	2	0	2970	5	0	369	3	0	3	0	0	431	2	1	1395	4	0
2001	801	3	0	126	1	0	3101	7	0	493	3	0	5	0	0	633	2	0	1513	3	0
2002	963	7	1	112	3	0	3906	5	1	723	1	0	5	0	0	969	3	1	1990	4	1
2003	997	4	0	182	0	0	4178	8	1	1343	2	0	16	0	0	735	3	0	2331	5	1
2004	1771	3	0	511	2	0	4690	5	0	489	5	0	36	0	0	1339	4	0	2113	6	0
2005	1018	5	1	600	4	0	4897	7	0	5345	2	0	42	0	0	1078	3	0	1310	4	0
2006	1779	5	0	876	2	0	5345	8	0	4912	0	0	5	0	0	1914	5	1	2542	4	0
2007	1619	3	1	628	3	0	4912	6	0	2017	1	1	3	0	0	1877	4	0	1643	4	0
2008	1562	6	0	599	2	1	111	1	0	5484	2	2	13	0	0	2230	3	0	2197	5	0
2009	2054	5	1	894	0	1	109	2	0	5439	3	0	40	1	0	2899	4	0	2224	7	0
2010	2251	3	0	937	0	0	210	3	1	5879	2	0	52	2	0	3742	5	1	2113	3	1
2011	3252	6	0	1131	1	0	193	1	0	6936	2	0	47	1	0	3793	3	0	4494	6	0
2012	2312	4	0	902	1	0	123	2	0	6593	2	1	39	0	0	3813	3	0	2937	4	0
2013	2093	5	1	893	3	0	159	3	0	6986	2	0	15	0	0	3233	4	0	3435	3	0
Total	23,800	69	6	8836	25	2	37,504	67	4	53,433	32	4	323	4	0	28,983	48	4	33,450	67	3

All blood donations collected by the individual hospitals are transported to the National (Central) Blood Bank where these are screened for infective agents, processed for preparation of components, stored and supplied to the individual hospitals according to their daily requirements/demand

FFP Fresh Frozen Plasma, *Cryo ppt* Cryo precipitate, *PRBC* Packed RBC, *LRBC* Leucocyte reduced RBC, *Plat conc* Platelet concentrate

A: Total number of components transfused

B: Number of adverse transfusion reactions (febrile, skin rash, retrosternal/chest constriction feeling, generalised aches and pain, dizziness, anaphylactoid etc.)

C: Number of transfusion reactions presenting as dyspnoea as sole manifestation or as part of other manifestations, but not conforming to criteria of TRALI on investigations

occurring within 6 h of transfusion (b) new bilateral lung infiltration in chest X-ray in absence of cardiac overload or cardiac malfunction (c) evidence of hypoxaemia, PaO2/FiO2 <300 mmHg or O2 saturation <90 % or other clinical evidence (d) absence of any other risk factor of ALI, such as trauma, pneumonia, cardio-pulmonary bypass surgery, burn injury, near drowning, shock or sepsis.

The National Heart, Lung and Blood Institute (NHLBI) working group on TRALI has published a definition of TRALI that additionally includes pulmonary artery occlusion pressure of <18 mm Hg when measured or lack of clinical evidence of left arterial pulmonary hypertension [12]. AABB has also published an Association Bulletin to provide background information and guidance to members regarding TRALI [13]. They emphasize absence of ALI before transfusion as important. However, it is now believed that ALI risk factors may not exclude TRALI as long as the respiratory insufficiency is temporally related to transfusion. It may also be mentioned that although, by definition TRALI temporally occurs within 6 h of transfusion, yet a few cases are reported to have occurred later, even after 48 h [14]. In our cases the maximum time to TRALI was 7 h.

The differential diagnosis of TRALI includes circulatory overload, anaphylactic transfusion reaction, bacterial contamination of transfused products and occasionally acute haemolytic reaction [15, 16]. A valuable clinical feature of TRALI that may be of importance in its differentiation from ALI is the discrepancy between the chest X-ray appearance of pulmonary oedema and absence of auscultatory findings in TRALI. This is explained by the fact that pulmonary oedema in TRALI is due to interstitial infiltration.

TRALI is believed to account for 6 % of all adverse reactions in the Serious Hazards of Transfusion (SHOT) data base and a leading cause of transfusion related death with mortality rate of 5–25 % [1, 6, 15, 16].

The incidence of TRALI is generally reported as 1:5000 transfusions. From North America it is reported to vary from 1 in 5000 to 1 in 1323 [3, 5, 11]. A newer report from Quebec mentions the incidence as 1:100,000 [17]. From Europe it is reported a 1.3: 100,000 to 1:7900 [18–20].

However, estimates about its true occurrence are subject to doubt. Firstly, neither the spectrum of clinical manifestations nor the associated laboratory findings of TRALI are independently pathognomic and the condition has remained rather nebulous. Secondly, the clinical as well radiological chest findings of TRALI are transient and the possibility of a missed diagnosis in many patients who ve survive is quite strong. Thirdly, except for measurement of hypoxaemia (PaO2/FiO2), no objective laboratory investigations were included in the criteria for diagnosis, hence leading to considerable subjectivity in its diagnosis. Lastly, some cases of the otherwise acute lung injury (ALI) unrelated to transfusion could have been coincidently become apparent after transfusion and thus mistaken for TRALI [16].

The Australian Red Cross Blood Service reported nine suspected cases of TRALI over a 27-month period from March 1999 to June 2001 [4].In our study, we encountered nine cases over 15 years. These nine cases were observed among 170,871 transfusions suggesting an incidence of 1:19,000. It may be mentioned that we followed the policy of conscious donor selection in avoiding female donors, particularly with history of multiparity since 2005 especially for plasma and platelet collection.

Nested control studies in the literature show that two groups of patients are at greater risk for TRALI [3], that is patients with haematologic malignancy on induction chaemotherapy and patients with cardiac disease undergoing by-pass surgery. Amongst our nine subjects, there was no case of either haematologic malignancy or cardiac surgery. However, it may possibly be because of the cases in our study being too small. Van Burun et al. [21] from their retrospective study showed that among the patients who developed TRALI, antecedent events included major surgery, infections (bacterial and viral), massive transfusion (replacement of total volume for 4 days) and cytokine administration (Granulocyte Colony Stimulating Factor, GCSF). In addition, patients receiving fresh frozen plasma (FFP) for coumadin reversal, plasmapharesis for Thrombotic Thrombocytopaenia (TTP) and those with wide spread endothelial cell activation due to infections are considered more susceptible for TRALI [6, 21, 22]. In our study, the patients who developed TRALI included those with TTP, APS, thrombaesthenia, Multiple visceral trauma, amegakaryocytic thrombocytopaenia, Factor XIII deficiency, vWD and DIC.

Pathogenesis of TRALI still remains largely uncertain [23, 24]. However, it is postulated that TRALI is caused by two independent events. The first event that is pivotal is related to the underlying clinical condition of the patient that has the priming effect for sequestration of neutrophils in pulmonary microcirculation and their adhesion to the endothelium [3, 5, 6].This is amply supported by the post mortem pathological findings from fatal cases of TRALI that exhibit crowding of neutrophils and their extravasation into interstitial tissue and air spaces, along with hyaline membrane formation and destruction of pulmonary architecture. On electron microscopy, the neutrophils show degranulation and focal direct contact with denuded stretches of capillary endothelium [5, 23, 25]. Transfusion is the second event that involves the activation of the adherent neutrophils leading to oxidative burst and the release of other damaging response modifiers, with resultant endothelial cell damage and leaks. This may happen by two mechanisms; immune-based and non-immune. In the former, the transfused donor anti-neutrophils antibodies (leukoagglutinins) bind to the recipient's neutrophils adherent to the pulmonary endothelium, resulting in activation and release of oxidases and other response modifiers. The incriminating antibodies are usually found in the donor's transfused component, but less often recipient's antibodies reacting with donor neurophils have also been implicated [11, 26–28]. Popovsky and Moore [11] demonstrated anti granulocyte antibodies in 89 % of TRALI patients and antibodies to HLA antigens in 65 %, most commonly directed to HLA class I, HLA class II antigens and neutrophil specific antigens particularly HNA-3a [21, 29–32]. Female donors with history of previous pregnancy have shown HLA antibodies with an overall prevalence of 24 %, increasing with more number of pregnancies [32, 33]. The non-immune mechanism that triggers activation of sequestrated adherent neutrophils and damage to the endothelium is believed to due to the presence of several lipophilic substances consisting of a mixture of lysophosphatidyl cholines (Lyso-pcs) which accumulate during routine storage of blood. These compounds provide oxidative burst and activate the primed adherent neutrophils to capillary cytotoxic effect leading to leaks [3, 5, 6, 23, 34].

The transfusion components that are most commonly implicated are FFP, whole blood platelet concentrates, apheresis platelets and packed red blood cells [6, 11, 15], though other products that is cryoprecipitate [35] and intravenous immunoglobin (IVIg) [36] have also been responsible in some cases. Among our nine patients, TRALI occurred following FFP in four patients, platelet concentrate in two patients, and cryoprecipitate in one patient. In the remaining two patients, no one specific component could be incriminated because of simultaneous emergency transfusion with more than one component as life saving requirement.

Based on the immune based mechanism for aetiopathogenesis of TRALI, several laboratory tests for detection of antigranulocyte antibodies that is granulocyte agglutinin test (GAT) and granulocyte immunfluorescence test (GIFT), neutrophil HNA and neutrophils HLA antigen

characterization in donor and recipient blood and leukocyte cross matching between the recipient and the implicated donor, have also been proposed, but not universally applied [22].

Until recently, the therapeutic approaches to TRALI have been based on intuitive reasoning rather than large scale controlled prospective studies. Firstly, the literature contains only case reports or small series of cases and secondly the episodes generally resolve in less than 72 h in nonfatal cases, often even before a firm diagnosis has been established [5, 6, 15, 16]. However, the recommended management is largely supportive, that essentially involves measures to combat hypoxaemia with oxygen support, including intubation and mechanical ventilation in large proportion of cases. In some patients arterial hypotension may occur that needs judicious non-aggressive use of intravenous fluids and occasionally presser agents when hypotension is profound, prolonged and non-responsive to intravenous fluids [37]. The benefit of corticosteroid therapy is controversial and has been reported in only anecdotal case reports. There is no convincing data to support or to refute the value of such therapy. Therefore its use remains empirical. In our case, we administered corticosteroids (hydrocortisone) to all our patients, in addition to appropriate oxygen therapy. Seven of our patients were subjected to mechanical ventilation. None of our patients developed hypotension. Therefore, none required intravenous fluids or presser agents.

Prevention of TRALI should undoubtedly include minimizing of transfusions by strict application of transfusion guidelines, thus avoiding needless risk exposure. Many transfusion medicine professionals and American and UK blood banks [15, 36] advocate temporary disqualification of donors implicated in TRALI reactions until leukocyte antibody testing is completed. In case, these donors show antibodies to leukocyte antigens HNA-3a, HNA-A2 and HLA-B1, they should remain disqualified for plasma and platelet donations [15, 38, 39].The clinical significance of plasma from multiparous female donors was confirmed by Pilfi et al. [40]. The United Kingdom disqualified all multiparous females form plasma donations, because of the possibility that plasma from multiparous female donors may be the major risk factor for TRALI, although plasma is not disproportionately implicated in other common transfusion reactions [38, 40, 41]. In late 2003, the UK National Blood Service introduced the policy of using only male donors whenever possible to produce FFP [42]. Since much of the data from the literature does not support general disqualification of multiparous female donors at this time, it does not seem prudent to further squeeze the already short pools of donor populations [3, 41]. Exclusion of multiparous women has been estimated to result in approximately 30 % donor depletion [41].

Transfusion with leukocyte depleted and washed cellular components at least for the susceptible patients may reduce the risk of TRALI as washing would help remove antibodies, storage induced lipids and other response modifiers [43, 44]. Similarly, fresher products may be helpful in obviating the effect of lipids accumulating in the prolonged stored blood. Using packed RBC of less than 14 days and platelets of less than 2 days post collection is reported to avert the neutrophil priming activity of these compounds that accumulate on routine storage [45].

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