Incidence and pattern of 12 years of reported transfusion adverse events in Zimbabwe: a retrospective analysis

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Background. Haemovigilance hinges on a systematically structured reporting system, which unfortunately does not always exist in resource-limited settings. We determined the incidence and pattern of transfusion-related adverse events reported to the National Blood Service Zimbabwe.

Materials and methods. A retrospective review of the transfusion-event records of the National Blood Service Zimbabwe was conducted covering the period from 1 January 1999 to 31 December 2011. All transfusion-related event reports received during the period were analysed.

Results. A total of 308 transfusion adverse events (0.046%) were reported for 670,625 blood components distributed. The majority (61.6%) of the patients who experienced an adverse event were female. The median age was 36 years (range, 1-89 years). The majority (68.8%) of the adverse events were acute transfusion reactions consisting of febrile non-haemolytic transfusion reactions (58.5%), minor allergies (31.6%), haemolytic reactions (5.2%), severe allergic reactions (2.4%), anaphylaxis (1.4%) and hypotension (0.9%). Two-thirds (66.6%) of the adverse events occurred following administration of whole blood, although only 10.6% of the blood was distributed as whole blood. Packed cells, which accounted for 75% of blood components distributed, were associated with 20.1% of the events.

Discussion. The incidence of suspected transfusion adverse events was generally lower than the incidences reported globally in countries with well-established haemovigilance systems. The administration of whole blood was disproportionately associated with transfusion adverse events. The pattern of the transfusion adverse events reported here highlights the probable differences in practice between different settings. Under-reporting of transfusion events is rife in passive reporting systems.

Keywords: transfusion reactions, blood transfusion, haemovigilance, adverse events.

Introduction

Blood transfusion is a routine, life-saving medical intervention which is generally regarded as safe when done appropriately. Sometimes, however, blood transfusion is associated with significant clinical risks. These risks can be broadly classified as infectious or non-infectious complications[1]. Several strategies have been put in place to minimise the risks of transfusion and ensure the optimally safe and appropriate use of blood and blood components. These strategies include, but are not limited to, the use of voluntary non-renumerated blood donors, stringent selection of blood donors, screening of donated blood for transfusion-transmissible infections using sensitive assays, regular quality control on blood units, leucoreduction techniques, blood management, hospital transfusion committees and haemovigilance[2-4]. These strategies have significantly improved the safety of blood, especially with regard to infectious risks. Infectious risks associated with blood transfusion have decreased significantly due to early detection of infectious agents and improved donor screening[5,6]. However, newer risks and threats still remain.

Despite the general decrease in transfusion risk, bacterial contamination remains a leading cause of infectious transfusion-related morbidity and mortality[6-8]. In addition, the significance of non-infectious risks in transfusion medicine is on the rise and these risks are often associated with significant morbitity and mortality[5,6,9,10].

Although strategies to minimise transfusion risk have been fully implemented in most developed countries, they are considered to be too expensive to implement in most resource-limited settings, including Zimbabwe.

Nevertheless, continued surveillance of the whole transfusion chain, which includes assessing information on unexpected or undesirable effects resulting from the use of blood transfusions and preventing their occurrence and recurrence, is a necessity regardless of the strategies implemented[11,12]. These sets of activities are collectively referred to as haemovigilance and they help to keep these risks in check. Efficient reporting of suspected transfusion events is a key haemovigilance activity in transfusion medicine.

There is a general paucity of information about the risks of transfusion in resource-limited settings including the sub-Saharan Africa region. Zimbabwe has yet to establish a systematic, formalised haemovigilance system. However, the national blood transfusion service (i.e. National Blood Service Zimbabwe [NBSZ]) receives voluntary, unsolicited reports of transfusion events from hospitals and transfusing centres. The purpose of this study was to estimate the incidence and pattern of transfusion-related adverse events reported to the national blood transfusion service.

Materials and methods

Data on the number of blood components distributed during the period from 1 January 1999 to 31 December 2011 were obtained from the NBSZ's annual reports. Data on transfusion-related events were collated retrospectively from manual records of all the transfusion adverse events reported to the NBSZ during the same period. As a minimum requirement for inclusion in the study, a report had to have information on the symptoms observed by the clinician during or after transfusion, and either the name or the barcode of the component transfused.

Transfusion adverse events were classified using mainly the UK's Serious Hazard of Transfusion (SHOT) classification scheme[13], with some consultation of the American Association of Blood Banks' (AABB) technical manual[14]. These were comparable with the definitions of the International Society of Blood Transfusion (ISBT)[15]. Cases were classified based on the clinical features presented by the recipient, as well as laboratory findings.

Transfusion adverse events were classified by the first author (NM) and reviewed by the fourth author (MEC). Data were collected and analysed to determine the incidence of various types of transfusion events and the types of blood components involved. STATA Version 12.0[16] was used to perform the descriptive data analysis.

Results

Blood components distributed

A total of 670,625 blood components were distributed during the study period (1999-2011), giving an average yearly distribution of 51,587 (SD=16,023) components. Of these blood components 505,524 (75.4%) were distributed as packed red blood cells, 71,279 (10.6%) as whole blood, 59,762 (8.9%) as fresh-frozen plasma, 27,788 (4.1%) as platelet concentrates, 3,568 (0.5%) as cryoprecipitate and 2,704 (0.4%) as paediatric packs.

Transfusion adverse events

A total of 440 suspected transfusion adverse events (to 0.1% of all the components distributed) were reported to the NBSZ during the study period. Of these reports, 308 met the inclusion criteria and were included in the analysis. The incidence (or reporting frequency) of transfusion events for this period was estimated at 0.46 per 1,000 blood components distributed. The number of reports varied between 6 and 65 cases per year (Figure 1). The majority (61.6%) of the patients who experienced a transfusion-related adverse event were female. The median age was 36 years (range, 1-89 years). The majority of the adverse events occured following transfusion with whole blood (66.6%) and packed red blood cells (20.1%). The frequencies and incidences of transfusion adverse events by each category are shown in Table I.

Acute transfusion reactions

Acute transfusion reactions, occuring within 24 hours after transfusion of blood components, formed the largest category of all the adverse events reported, contributing 212 (68.8%) cases (Table II). The majority of acute transfusion reactions occurred following the adminstration of whole blood (68.4%).

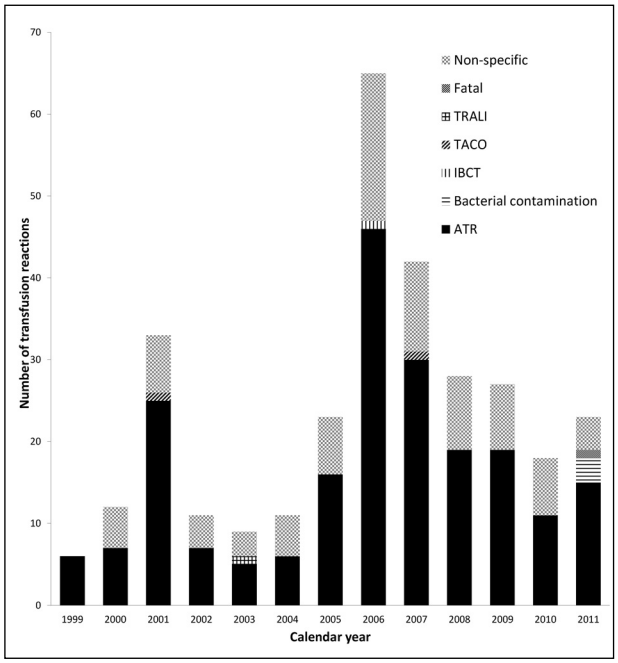

Figure 1 - Distribution of transfusion reactions by calendar year. ATR: acute transfusion reactions; IBCT: incorrect blood component transfused; TACO: transfusion-associated circulatory overload; TRALI: transfusion-related acute lung injury.

Table I - Summary of transfusion reactions over 1999-2011.

Transfusion reaction	Frequency (%)	Incidence (per 1,000 components)
Acute transfusion reactions	212 (68.8)	0.32
Bacterial contamination	3 (1.0)	0.0045
IBCT	1 (0.3)	0.0015
TACO	2 (0.6)	0.0030
TRALI	1 (0.3)	0.0015
Fatal	1 (0.3)	0.0015
Unclassified	88 (28.6)	0.13
Total	308 (100)	0.46

Number of distributed blood components: 670,625. IBCT: incorrect blood component transfused; TACO: transfusion-associated circulatory overload; TRALI: transfusion-related acute lung injury.

Table II - Summary of acute transfusion reactions over 1999-2011.

Transfusion reaction	Frequency (%)	Incidence (per 1,000 components)
Anaphylaxis	3 (1.4)	0.0045
FNHTR	124 (58.5)	0.18
Haemolytic	11 (5.2)	0.016
Hypotension	2 (0.4)	0.0030
Minor allergic	67 (31.6)	0.10
Severe allergic	5 (2.4)	0.0075
Total	212 (100)	0.32

FNHTR: febrile non-haemolytic transfusion reactions.

Of the 212 acute reactions, 124 (58.5%) were febrile non-haemolytic transfusion reactions (FNHTR). Most of the cases of FNHTR occurred following transfusion of whole blood (n=80) and packed cells (n=30). Minor allergic transfusion reactions were reported in 67 cases with the majority of cases arising following transfusion of whole blood (55 cases; 82.1%). Five cases were classified as severe allergic reactions.

Eleven cases of acute haemolytic transfusion reaction, representing 5.2% of all acute transfusion reactions, were reported. Of these, five cases occurred following transfusion with whole blood, four with packed cells and in the remaining two, the component transfused was not mentioned in the reports. All the cases of acute haemolytic transfusion reaction showed clinical symptoms consistent with haemolysis. These symtoms included, but were not limited to, pyrexia, rigors, lumbar pain and headache. Two cases were confirmed by a positive direct antiglobulin test, three cases by a fall in haemoglobin concentration and in one case, anti-C and anti-E antibodies were identified. There was no evidence of incompatibility in five of the cases and their classification was made based on the clinical findings, notably evidence of haemolysis in post-transfusion samples. Fresh-frozen plasma and packed cells had been transfused in the two cases (0.9% of acute transfusion reactions) of hypotension that were reported.

Other transfusion adverse events

Three cases of suspected bacterial contamination were reported during the study period, representing 1% of all the adverse events. Coagulase-negative staphylococci were isolated following transfusion of whole blood to a 31-year old female patient with antepartum haemorrhage. The other organisms involved following transfusion with platelet concentrates were only identified as "heavy Gram-positive" and "heavy bacterial contamination". It was not possible to verify the specific strains.

A single suspected case of transfusion-related acute lung injury (TRALI) (0.3%) and two cases of suspected transfusion-associated circulatory overload (TACO) (0.6%) occurred following transfusion of platelet concentrates and whole blood, respectively. It was not possible to ascertain whether any serological investigations had been undertaken since these were not reported. A single case of possible transfusion-related mortality was reported during the period under study. The details of the investigation, laboratory or clinical information for this fatal case were not reported making it impossible to evaluate the causal relationship. There was insufficient information on severity and imputability of all the adverse events.

There was one report of an incorrect blood component transfused (IBCT) (0.3%), in which a 56-year old male patient with blood group A+ was transfused with blood group O+ FFP and developed urticaria.

A total of 89 cases could not be unambiguously allocated into specific categories because case reports only described non-specific clinical features, and as such were classified as non-specific transfusion adverse events. Of the 89 non-specific adverse events, 64 were of acute nature. All these 64 cases occurred within 24 hours following transfusion; however, there was inadequate laboratory and clinical information to classify them further.

Quality of reports

All 308 reports that met the inclusion criteria were subjected to a quality evaluation to establish the completeness of all the information required. Or the 308 reports included in the analysis, 20 (6.5%) were not fully investigated. These investigations were either not completed, referred to the quality assurance department, not reported or not done at all. In 218 (70.8%) of the analysed reports, microbiological investigations were not done. Of these, 50 (22.9%) were not cultured because the unit submitted was vented. In 35 (11.4%) of the reports, it was not possible

to establish whether microbiological investigations were done or not. Pre-transfusion haemoglobin values were not reported in 91 (29.5%) of the cases whilst post-transfusion haemoglobin values were only reported in seven (2.3%) of the cases.

Discussion

Suspected transfusion-related adverse events in Zimbabwe are reported by transfusing centres/hospitals on a voluntary basis. Hospital participation in the surveillance system for the period included in this study was low, constituting approximately 20 percent of all transfusing hospitals. This low participation could be attributed to the passive nature of the surveillance system as well as lack of appropriate legislation for enforcement of reporting.

In this study, a total of 308 transfusion adverse events were suspected and investigated, giving an overall incidence of 0.46 per 1,000 blood components distributed (0.046%). This incidence is comparable to that estimated based on the data given in the South African National Blood Service (SANBS) Haemovigilance Report for 2007[17]. The incidence of transfusion adverse events for South Africa was estimated to be 0.049%. However, the incidence in the present study is very low when compared to rates reported in developed countries. A university hospital in Switzerland documented a global incidence of 4.2 incidents per 1,000 blood components distributed[18]. In France, a reporting rate of 2.5-3 per 1,000 blood components was documented[19,20], while the Quebec haemovigilance system reported a rate of 3.5 per 1,000 blood components transfused[21]. A recent study from a tertiary care hospital in India reported a frequency of 0.5 transfusion reactions per 1,000 blood components issued[22]. Other studies conducted in Sub-Saharan Africa reported very high incidences of transfusion-related adverse events. A tertiary hospital in Nigeria reported a rate of 87 events per 1,000 blood components transfused[23]. Similarly, a rate of greater than 50 adverse events per 1,000 blood components transfused was reported for a teaching hospital in Cameroon[24]. The rates recorded in Nigeria and Cameroon were from prospective studies that focused on a single institution. Differences in study design between the present study and these other studies may partly explain the variability in reporting rates of transfusion events.

The comparison was restricted to systems that monitor all specific major and minor adverse transfusion-related adverse events. The low reporting frequency observed in this study reflects the passive nature of the surveillance system and may be a pointer towards under-reporting of transfusion events. A study carried out in India also noted under-reporting of adverse events as a major concern[22]. Information on the actual number of blood components transfused over a specified period is not currently available in Zimbabwe. The number of blood components issued was, therefore, used as a surrogate measure of consumption. To some extent, this might have over-estimated consumption, possibly resulting in a lower reporting rate estimate. The National Blood Policy of the Republic of Zimbabwe[25] and the Standards for Blood Donation, Processing and Clinical Transfusion in Zimbabwe[26] came into effect in 2010. These guiding documents stipulate that medical officers (treating physicians, transfusing officers) should report all suspected transfusion adverse events to the NBSZ. These guiding documents also call for the formation of Hospital Transfusion Committes whose overall role will be to assess the use of blood and blood components in hospitals. This may improve hospital participation and reporting rates, subsequently uncovering under-reporting.

Of the total 212 acute transfusion reactions, 124 (58.5%) cases were suspected to be FNHTR. This gives an incidence rate of 0.18 per 1,000 blood components, which is much lower than incidence estimates documented in literature[27-29]. Platelet transfusions are more commonly associated with FNHTR[29-33], but that was not the case in this study. This is mainly because few platelet units (1,321; 0.4%) were transfused relative to the other components. None of the components transfused during this period was leucoreduced, and FNHTR observed with whole blood and red packed cells are associated with the involvement of donor leucocytes, pro-inflammatory cytokines and biologic response modifiers[14,34-36]. The use of leucocyte-depleted red blood cells and platelets may reduce the incidence of FNHTR[27-29,37]. However, FNHTR still occur, suggesting the involvement of other mediators. Premedication of recipients with antipyretics, especially those with two consecutive episodes of FNHTR, may also help reduce the incidence of FNHTR[27,38]. This underscores the need for adequate collection of patients' histories, particularly with regard to transfusion episodes and adverse events.

The established criteria for confirming acute haemolytic transfusion reactions were met for six cases. Classification of the remaining five cases was made based on the clinical findings, notably evidence of haemolysis in post-transfusion samples. These five cases could be a result of the presence of weak antibodies[39,40] or non-immune-mediated haemolysis[9,10,41]. The use of malfunctioning blood warmers, bacterial overgrowth, infusion of blood through small-bore IV needles, or infusion of blood through lines containing hypotonic solutions or incompatible medications are all thought to be reponsible for non-immune-mediated acute haemolytic transfusion reactions[9,42]. The overall frequency of acute haemolytic transfusion reactions,

0.016 per 1,000 blood components transfused, was generally lower than the rates reported in literature[9,37,42,43].

There were few suspected cases of TRALI, IBCT, TACO, bacterial contamination or transfusion-related mortality in this study. TRALI and TACO are difficult to identify and the rates may have been low in our study due to under-reporting because of insufficient recognition and and variable awareness among medical staff. TRALI and TACO are also often confused for each other. The observed clinical features for TACO were sufficient in this study while those for TRALI were borderline.

Under-reporting of bacterial contamination is highly likely since microbiological investigations were not done in most of the suspected cases. A number of suspected transfusion adverse events were submitted without all or some of the samples required for a full investigation to be carried out. A number of these may have been misclassified as FNHTR and/or in the category of non-specific adverse events.

Of the 440 reports received, 132 were not included in the analysis due to incomplete information. This is a real cause for concern since these accounted for 30 percent of all the reported suspected transfusion adverse events. This also reflects the passive nature of the system, in which transfusing centres are not clearly aware of the key information to be reported and the value of such missing information. Most reports are sent in retrospect thereby making and follow-up extremely difficult.

The general quality of the assessed reports was graded as low, as most of them were incomplete making classification difficult. This also made it impossible to grade the adverse events according to severity and imputability. Revising the reporting form and the introduction of a systematic and standardised surveillance system may go a long way in addressing these shortcomings and improving the quality of the data reported. More active participation of hospital transfusion committees would also improve the quality and quantity of reporting.

Although the suspected transfusion adverse events reported may not adequately represent the true picture of the frequency of transfusion events, these data can be useful as some form of signal of the complications occuring in clinical practice. This study therefore serves as a basis for meaningful risk assessment and further research. It also sets the tone for improvement of the current reporting system as well as institution of preventative action required to minimise transfusion-related risks in resource-limited countries.

Conclusions

The reported incidence of suspected transfusion adverse events is generally lower in Zimbabwe than those reported globally in countries with well-established haemovigilance systems. The patterns of the transfusion adverse events reported here highlights the probable differences in practice between different settings. Quality reporting is a key element required for the accurate quantification and characterisation of transfusion-related events. There is need for a more organised, standardised and systematic surveillance system for transfusion adverse events. Education and awareness campaigns for health care professionals are required in order to improve both the quality and quantity of reports.

Authorship contributions

Nyashadzaishe Mafirakureva had full access to all data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. McLeod E. Chitiyo assisted with the classification of cases. All Authors contributed to the design of the study and writing the paper.

Acknowledgements

The research leading to these results received funding from the European Union Seventh Framework Programme (FP7/2007-2013) under grant agreement n° 266194. The authors wish to thank the T-REC (building research capacity for blood transfusion services in Africa) consortium for its support. The views expressed in the manuscript do not reflect the views nor do they imply endorsement of the suggestion by the funders.

The Authors would also like to thank the NBSZ laboratory technical staff who received, investigated and filed the transfusion reaction reports.

The Authors declare no conflicts of interest.

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Arrived: 23 May 2013 - Revision accepted: 24 October 2013
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