

Citation: Mauka WI, Mtuy TB, Mahande MJ, Msuya SE, Mboya IB, Juma A, et al. (2018) Risk factors for inappropriate blood requisition among hospitals in Tanzania. PLoS ONE 13(5): e0196453. https://doi.org/10.1371/journal.pone.0196453

Editor: Halvard Bönig, German Red Cross Blood Donation Center, GERMANY

Received: September 12, 2017

Accepted: April 15, 2018

Published: May 17, 2018

Copyright: © 2018 Mauka et al. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Data Availability Statement: The study dataset is from a parent study conducted by the Ministry of Health through the Tanzania-National Blood Transfusion Services and the data are under restriction imposed by Institutional Review Board of National Transfusion Services. Data can be requested from Program Manager of the Tanzania-National Blood Transfusion Services, Dr. Magdalena Lyimo (magdalena.lyimo@gmail.com), or from the corresponding author.

Funding: The authors received no specific funding for this work.

RESEARCH ARTICLE

Risk factors for inappropriate blood requisition among hospitals in Tanzania

Wilhellmuss I. Mauka^{1¤a}*, Tara B. Mtuy^{1¤c}, Michael J. Mahande¹[®], Sia E. Msuya^{1®}, Innocent B. Mboya¹, Abdul Juma^{2®}, Rune N. Philemon^{1¤b}

1 Department of Epidemiology and Biostatistics, Institute of Public Health, Kilimanjaro Christian Medical University College, Moshi, Tanzania, 2 National Blood Transfusion Services, Dar es Salaam, Tanzania

• These authors contributed equally to this work.

¤a Current address: Northern Zone Blood Transfusion Services, Moshi, Tanzania

¤b Current address: Department of Paediatrics, Kilimanjaro Christian Medical Centre, Moshi, Tanzania ¤c Current address: Department of Clinical Research, London School of Hygiene & Tropical Medicine, London, United Kingdom

* wilhemauka@yahoo.com

Abstract

Background

Blood is a critical aspect of treatment in life saving situations, increasing demand. Blood requisition practices greatly effect sufficient supply in blood banks. This study aimed to determine the risk factors for inappropriate blood requisition in Tanzania.

Methods

This was a cross sectional study using secondary data of 14,460 patients' blood requests from 42 transfusion hospitals. Primary data were obtained by using cluster-sampling design. Data were analysed using a two-level mixed-effects Poisson regression to determine fixed-effects of individual-level factors and hospital level factors associated with inappropriate blood requests. P-value <0.05 (2-tails) was considered statistically significant.

Results

Inappropriate requisition was 28.8%. Factors significantly associated with inappropriate requisition were; reporting pulse rate and capillary refill decrease the risk (RR 0.74; 95% CI 0.64, 0.84) and (RR 0.73; 95% CI 0.63, 0.85) respectively and the following increased the risk; having surgery during hospital stay (RR 1.22; 95% CI 1.06, 1.4); being in general surgical ward (RR 3.3; 95% CI 2.7, 4.2), paediatric ward (RR 1.8; 95% CI 1.2, 2.7), obstetric ward (RR 2.5; 95% CI 2.0, 3.1), gynaecological ward (RR 2.1; 95% CI 1.5, 2.9), orthopaedics ward (RR 3.8; 95% CI 2.2, 6.7). Age of the patient, pallor and confirmation of pre-transfusion haemoglobin level were also significantly associated with inappropriate requisition. Majority of appropriate requisitions within the wards were marked in internal medicine (91.7%) and gynaecological wards (77.8%).



Competing interests: The authors have declared that no competing interests exist.

Conclusions

The proportion of inappropriate blood requests was high. Blood requisition was determined by clinical and laboratory findings and the ward patients were admitted to. Adherence to transfusion guidelines is recommended to assure the best use of limited blood supply.

Background

In Sub Saharan Africa (SSA), blood and blood components transfusion have become a common practice especially in contemporary medicine, aiding in life saving situations [1,2]. This has resulted in an increasing demand of safe blood and its products especially among children and mothers during and after delivery [3–7]. Due to an increase in demand, scarcity of blood in blood banks is eminent [8,9]

Ineffective blood transfusion services have been contributing to maternal mortality in sub-Saharan Africa [10] as 25% of maternal mortality is attributed to obstetric hemorrhage [11]. SSA is facing a weak blood donation infrastructure which is compounded with social-economic challenges [12–14]. In addition to these factors, blood requisition practices can exacerbate insufficient blood supply in blood banks [15–17], depending on adherence to transfusion guidelines. Furthermore the effect of over-ordering of blood, results in increased and unnecessary patient costs including costs of blood and testing prior to transfusion (e.g. grouping and cross-matching) [18,19].

WHO guidelines on clinical use of blood and blood products has been adopted by several countries including Tanzania [20–22]. The guidelines are evidence based so that those who are in need of blood should have access to blood transfusion. This study aimed to determine the proportion and risk factors associated with inappropriate blood requisition among hospitals in Tanzania in 2013.

Methods

Data source

The parent study was carried out in Tanzania from June 17th through September 27th 2013. The study population included all patients' blood transfusion requests submitted at hospital blood banks during the study period. Sampling and data collection procedures are explained in detail elsewhere [23].

The study protocol was reviewed and approved by the Tanzania National Institute of Medical Research, the Zanzibar Medical Research and Ethics Committee (ZAMREC) and the Institutional Review Board at Centers for Disease Control and Prevention (CDC).

Current study

Study design and population. This was a secondary data analysis of a hospital based cross sectional survey. The analysis included all patients' blood transfusion requests for whole blood (WB) and packed red blood cells (PRBC), submitted to hospital blood banks during the study period. Requests for blood grouping without cross-matching test were excluded from analysis.

Sample size and power

This study involved 14,460 blood requests from 42 transfusion hospitals that met the current study criteria, to estimate the overall proportion of inappropriate transfusion with 95% confidence

with margin error of $\pm 2\%$. The sample size had a power more than 99% to detect a 5% difference in the proportion of inappropriate requisition.

Study variables. The dependent variable in this analysis was inappropriate blood request, a binary response (yes/no), determined through relevant criteria (Fig 1) [24,25]. Independent variables were socio-demographic characteristics (age and sex of the patient and hospital areaurban/rural). Pre-admission history (admitted ward, diagnosis, underlying cause of anaemia), pre-transfusion laboratory test (pre-transfusion haemoglobin level-Hb) and vital signs (blood pressure, pulse rate, respiratory rate), patient pre-transfusion signs and symptoms (active bleeding, consciousness, cardiac failure, cold extremities, decreased capillary refill, respiratory distress, large liver or spleen, pallor and tachycardia), and transfusion information (number of units requested/ issued/ not, transfused/not, cross-matched).

Data processing method. All data were extracted from survey database (Excel spread-sheet) into Stata version 13.1 Stata-Corp LP, for cleaning and further analysis (Fig 2).

Data description. The data were hierarchical or multilevel structures such that blood requests were nested within patients and patients nested within hospitals, and hospitals nested within clusters. Thus requests of the same patient were more similar among each other than requests from different patients. Furthermore, individual patients within the same cluster (hospitals) could be more similar to each other than patients among all hospitals and variance of observations might not be constant across risk factors.

Data analysis. Data were summarized into frequency, median (IQR) and percentages. Clinical presentation of the patients and inappropriate blood requests were described considering clustering effect to get average distribution percentage between and within the hospitals. Bivariate analysis was done for testing association between main outcome (inappropriate requesting) and potential exposures (risk factors). Chi-square test of independence was used.

Multilevel mixed-effects generalized linear model was used to test the effect size of individual and hospital factors on inappropriate blood request and estimate the between-cluster variability of effect of inappropriate blood request [26–29].

Univariate multilevel analysis. The analysis involved all variables associated with inappropriate blood request in the bivariate analysis (p < 0.05).

The request was considered inappropriate if:

1. Ordering of blood was without pre-transfusion hemoglobin level and any clinical findings* recorded

2. Had pre-transfusion hemoglobin level but without any clinical condition#/ findings recorded with the following categories;

Age group	Hemoglobin level
0-1month	> 8.5 g/dl
1month to <5 years	>4 g/dl
>=5 years	>5 g/dl

*Pulse rate, respiratory rate, pallor, peripheral capillary refill or blood pressure *Pregnancy, for surgical procedure or active bleeding

Fig 1. Criteria for assessment of inappropriate requisition of PRBC/Whole blood.

https://doi.org/10.1371/journal.pone.0196453.g001



Fig 2. Data sampling process.

https://doi.org/10.1371/journal.pone.0196453.g002

Multivariable multilevel analysis. The analysis involved entering all the variables with P-value <0.05 in univariate analysis. Backward a two-level mixed-effects Poison regression was done in order to determine the factors which significantly predict the risk of inappropriate blood request with probability of elimination at 0.05.

To test the significance of clusters (hospitals) on inappropriate requests, the empty model (a model with only outcome of interest but without any explanatory variables) was run with cluster and then an empty model without clusters.

Then a multilevel multivariable model was computed to account for the hierarchical structure of the data and clustering of responses at the different levels. Six models were run, whereby models 2–6 were compared against the empty model by deploying Akaike Information Criterion.

Intra-Class Correlation (ICC) was used to determine the proportion of the variance that is due to clusters. ICC was calculated using between-cluster variance and within-cluster variance (Π^2 /3). This was used to compare the successive models by looking at the decline of the ICC to explain the variability in risk of inappropriate request. The model was checked for possible confounders and interaction for covariates by using Likelihood Ratio test.

Complete case analysis was used as variables with the greatest missing data could still hold minimum sample size required, hence the study had sufficient power for identifying potential differences.

Ethical consideration. Ethical clearance was obtained from the Kilimanjaro Christian Medical College Research Ethical Committee and permission to use the data from the parent study was obtained from National Blood Transfusion Services. Confidentiality of participants' information was assured using participant identification numbers.

Results

Baseline characteristics of patients

Blood requests from 11,189 patients were ordered from hospital blood banks. Among 10,544 patients whose ages were recorded, the median age was 25, ranging from 6 to 38 years. Among

Median (IQR) n (%)	
25 (6-38)	
86 (80-102)	
6 (4.4-8.6)	
2,264	(21.5)
1,143	(10.8)
1,627	(15.4)
2,245	(21.3)
1,475	(14)
686	(6.5)
485	(4.6)
619	(5.8)
	·
4,155	(37.3)
6,998	(62.7)
	·
8,555	(76.5)
2,634	(23.5)
	·
3,044	(21.1)
11,416	(78.9)
	·
3,743	(33.5)
1,566	(14)
1,083	(9.7)
1,393	(12.5)
977	(8.7)
1,574	(14.1)
853	(7.6)
2,092	(16.9)
353	(2.9)
283	(2.3)
75	(0.6)
54	(0.4)
684	(5.5)
7,924	(64)
908	(7.3)
1,453	(13)
2,691	(24.1)
3,323	(29.8)
281	(2.5)
141	(1.3)
<u> </u>	(1.3) (20.3)
	Median (IQR) n (%) 25 (6-38) 86 (80-102) 6 (4.4-8.6) 2,264 1,143 1,627 2,245 1,475 686 485 619 4,155 6,998 3,044 11,416 3,044 11,416 3,743 1,566 1,083 1,393 977 1,574 853 2,092 353 2,092 353 2,092 353 2,092 353 2,092 353 2,092 353 2,092 353 2,092 353 2,092 353 2,092 353 2,092 353 2,092 353

Table 1. Baseline characteristics of patients (11,189).

(Continued)

Table 1. (Continued)

Characteristics	Median (IQR) n (%)		
Orthopaedics	34	(0.3)	

*There are missed data

**More than one clinical sign could be presented by on patient

https://doi.org/10.1371/journal.pone.0196453.t001

9,713 recorded haemoglobin levels, the median haemoglobin level was 6g/dl ranging between 4.4 and 8.6g/dl. Of 11,153 patients, more than half 6,998 (62.8%), were females. One-third, 3,743 (33.5%), of patients were from Eastern zone of the country and 853 (7.6%) were from Zanzibar, which had the least number of patients with blood requests. Of 11,153 records, 3,323 (29.8%) patients were admitted in paediatric medical wards followed by adult medical wards 2,691 (24. 1%). From a total of 12,373 reported clinical signs, more than two thirds of patients, 7,924 (64.7%), had pallor, followed by 2,092 (16.9%) with active bleeding and the least reported clinical sign was decreased capillary refill, 54 (0.4%). Patient characteristics are as shown in Table 1.

Distribution of characteristics of blood requests

Underlying causes of anaemia were reported in 9577 requests from 42 hospitals. Of these, 3,483 (37%) requests were due to malaria, 2,363 (24.7%) due to maternal haemorrhage and the least was tuberculosis 151 (1.6%). Among the 42 hospitals, in at least one of their blood requests, 41 (97.2%) had reported malaria and 40 (95.2%) reported maternal haemorrhage as the underlying cause of anaemia (Table 2). Furthermore, within the hospitals which documented the underlying cause of anaemia in at least one of their blood request forms, on average 45.9% of their *requests* were due to malaria, 23.5% due to maternal haemorrhage. The rest of the underlying causes of anaemia are distributed as shown in Table 2.

Pulse rate was recorded in 14,170 requests from 42 hospitals. Overall 64.2% of recorded pulse rates showed signs of tachycardia whereby 97.6% of hospitals had patients with tachycardia in at least one of its blood requests. Within the hospitals, an average of 67.3% of requests which pulse rate recorded revealed signs of tachycardia. Among 8998 requests which recorded patients' haemoglobin levels, 7,917 (79.4%) had anaemia while 1,081 (20.6%) had normal haemoglobin levels.

Different clinical signs were reported in 14,460 blood requests, with more than three quarters of blood requests (85.6%) reported pallor. All 42 (100%) hospitals, reported pallor in at least in one of their blood requests. Within hospitals, on average 81.1% reported pallor in at least one of its blood requests. Other clinical signs are shown in Table 2.

Fig 3, shows the variability of mean haemoglobin level across hospitals among blood requests with an exception of those from neonates. Majority of these blood requests are above the recommended WHO guidelines for minimum level of haemoglobin (4g/dl) for blood requests. The calculated average mean haemoglobin across the hospitals is 6.7 (sd \pm 3.2) g/dl. The graph shows the average mean haemoglobin level for each hospital.

Proportion of inappropriate blood requests

The overall proportion of inappropriate blood requests was 28.8% whereby all 42 hospitals had at least one inappropriate blood request. Within the hospital, an average of 28.9% had at least one inappropriate blood requests (Table 2).

Table 2. Reported clinical presentation of patients' blood requests (N = 14,460).

PLOS

Variables	Overall		Hospitals		Average Within Hospitals		
	n	(%)	N = 42	(%)	(%)		
Underlying the cause of anaemia (n = 9577)*							
Cancer	987	(10.5)	34	(81)	(11.8)		
HIV-related	1,033	(11.0)	33	(78.6)	(12)		
Malaria	3,483	(37.0)	41	(97.6)	(45.9)		
Maternal Haemorrhage	2,363	(24.7)	40	(95.2)	(23.5)		
Non-trauma surgery	555	(5.9)	26	(61.9)	(5.5)		
Sickle Cell Disease	475	(5.1)	35	(83.3)	(6.2)		
Trauma	399	(4.2)	34	(81)	(4.5)		
Tuberculosis	151	(1.6)	30	(71.4)	(2.4)		
Clinical Signs	1	_					
Tachycardia (n = 14,170)*							
No	5,043	(35.6)	41	(97.6)	(35.1)		
Yes	9,127	(64.2)	41	(97.6)	(67.3)		
Tachypnea (n = 14,531)*	1		1				
No	5,164	(36.2)	38	(90.5)	(31.4)		
Yes	9,101	(63.8)	41	(97.6)	(73.4)		
Haemoglobin level (n = 8998) **	1	_					
Normal haemoglobin level	1,081	(20.6)	40	(95.2)	(18.1)		
Anaemia	7,917	(79.4)	42	(100)	(82.8)		
Recorded Clinical Signs (N = 14,460)	1	_					
Cold Extremities							
Yes	3,518	(24.3)	36	(85.7)	(23.7)		
No	10,942	(75.7)	42	(100)	(79.7)		
Capillary refill		-	1				
Yes	3,220	(22.3)	32	(76.2)	(22.9)		
No	11,240	(77.7)	42	(100)	(82.8)		
Tachycardia							
Yes	5,668	(39.9)	41	(97.6)	(32)		
No	8,534	(60.1)	42	(100)	(68)		
Pallor							
Yes	12,379	(85.6)	42	(100)	(81.1)		
No	2,081	(14.4)	39	(95.2)	(19.8)		
Respiratory distress							
Yes	6,331	(43.8)	41	(97.6)	(34.9)		
No	8,129	(56.2)	41	(97.6)	(67.6)		
Inappropriate blood requests (N = 12,204)	*						
No	8,687	(71.2)	42	(100)	(71.2)		
Yes	3,517	(28.8)	42	(100)	(28.8)		

*There are missed data

**Categorization based on age and sex, hence number has decreased for those

https://doi.org/10.1371/journal.pone.0196453.t002

Factors associated with inappropriate blood request

There was a significant association between inappropriate blood request with age group, pallor and type of ward patients admitted to (Table 3). Other factors significantly associated with inappropriate blood requests were; sex, pregnancy, admission due to injury, type of hospital





https://doi.org/10.1371/journal.pone.0196453.g003

ownership, underlying cause of anaemia, surgery on hospitalization, type of surgery, hospital area, malaria, respiratory distress, capillary refill, tachycardia, pallor, cold extremities and heart failure. (Table 3).

Multivariable multilevel analysis

A two-level mixed effects model was used to analyse the effects of patients' individual characteristics and hospital-level factors in determining appropriateness of blood requests. From the empty model, 8% of the total variance in the risk of inappropriate blood request was accounted for by between-hospitals variation of characteristics (ICC = .08, p<0.0001). The between-hospitals variability declined over successive models, from 8% in the empty model to 6% in individual-level only model, but going back to 8% in hospital-level only model and 5% in the combined model. Thus, the combined model of individual-level (request and patient factor), and hospital-level factors was selected for predicting the risk of inappropriate blood request. ICC of 0.05, means 5% of variability of the risk of inappropriate blood request was explained by clusters (hospitals). Difference in hospital settings had little effect on inappropriate blood request (Fig 4).

Effect of individual factors

After adjusting for individual requests and hospital-level factors, reporting patient's clinical signs was highly significantly associated with the risk of inappropriate requisition. Reporting pulse rate decreases the risk by 26% (RR 0.74; 95% CI 0.64, 0.84), and capillary refill by 27% (RR 0.73; 95% CI 0.63, 0.85) compared to not reporting them (Table 4).

We examined inappropriate blood requisition related to surgical operations. Patients who had surgery during their hospital stay had 22% higher risk of inappropriate blood request comparing to those who had no surgery (RR 1.22; 95% CI 1.06, 1.4) (Table 4).

Variables	Inappropriate (N = 11,494)		
	n (%)	P-value	
Sex (n = 12,171)		< 0.0001	
Male	1,410 (31.9)		
Female	2,103 (27.1)		
Age group (years) (n = 11,537)		< 0.0001	
0-4	1,061 (60.8)		
5–14	148 (11.8)		
15–24	466 (24.3)		
25-34	627 (24.3)		
35–44	438 (25.6)		
45–54	201 (23.2)		
55-64	168 (27.2)		
65+	302 (36.1)		
Pallor (n = 12,204)		<0.0001	
Yes	2,094 (19.7)		
No	1,423 (90.4)		
Ward Type (n = 14,585		< 0.0001	
Adult surgery	940 (45.1)		
Adult medical	239 (8.34)		
Paediatric medical	1,038 (35)		
Paediatric surgical	178 (51.9)		
ICU	91 (46.2)		
Obstetrics	747 (29.8)		
Gynaecology	254 (22.2)		
Orthopaedics	22 (47.8)		
Emergency department	1 (14.3)		
Surgery on hospitalization (N = 12,204)		0.002	
Yes	697 (26.4)		
No	2,820 (29.5)		
Type of ownership		< 0.0001	
Government	2,529 (26.7)		
Private	988 (37.8)		
Reported on capillary refill (12,166)		< 0.0001	
No	3,043 (34)		
Yes	461 (14.4)		
Reported on pallor (N = 12,131)		< 0.0001	
No	1,423 (90.4)		
Yes	2,042 (19.3)		
Level of haemoglobin		< 0.0001	
Normal	522 (51.3)		
Anaemia	1,893 (29.7)		
Reported tachycardia (N = 11,976)		< 0.0001	
No	2,439 (38.1)		
Yes	1,004 (18)	1	

Table 3. The variables associated with inappropriate blood request (N = 11,494).

https://doi.org/10.1371/journal.pone.0196453.t003

We analysed the effect of confirming haemoglobin levels when the patient was pale on inappropriate blood requests. Reporting pallor of the patient, and a confirmed laboratory test of

Factors	Model 1 (empty model)	Model 2 (requests factors)	Model 3 (Patients factors)	Model 4 (Hospital factors)	Model 5 (Final with 2 levels)	Model 6 (Final with 3 levels)
ICC	.08	.04	0.6	.08	.05	.05
AIC	15131.27	13268.43	9698.453	15087.61	8519.435	8519.435

Fig 4. Model comparison.

https://doi.org/10.1371/journal.pone.0196453.g004

either low or normal haemoglobin levels decreases the risk by 82% (RR 0.18; 95%CI 0.17, 2.0) and 59% (RR 0.41; 95%CI 0.32, 0.51) respectively compared to not reporting pallor. (Table 4).

We analysed the effect of age group on inappropriate blood requisition. Comparing to age group 0–4 years, patient aged between5 and14 years had 88% lower risk of inappropriate requisition by o 88% (RR 0.12; 95% CI 0.1, 0.15) and those aged 65 years and above had 0.19 (RR 0.19; 95% CI 0.12, 0.28) times lower risk of inappropriate blood requisition, the rest were as shown in the table (Table 4).

Effect of hospital-level characteristics

The study aimed to show if the characteristics of the clusters (hospitals) in which patients were admitted would have an effect on inappropriate blood request, regardless of patients' individual characteristics. After holding constant for the contribution of all the individual request level attributes, there was a significant association between the ward the patient was admitted to and inappropriate blood requisition in those hospitals. Being in surgical wards increased the risk by 3.3 times (RR 3.3; 95% CI 2.7, 4.2), paediatric medical by 1.5 times (RR 1.5; 95% CI 1.0, 2.2), paediatric surgical by almost 2 times (RR 0 1.8; 95% CI 1.2, 2.7) and obstetric ward by 2.5 times (RR 2.5; 95% CI 2.0, 3.1) higher risk of inappropriate blood request compared to being in medical ward. The rest as shown in the table (Table 4).

Discussion

The study involved 11,189 patients from whom 14,460 blood requests were placed in 42 different sampled transfusing facilities (hospitals). Out of those requests, 12,204 were conclusive in determining the inappropriateness of blood request. Of these, 3517 blood requests were inappropriate; a proportion of 28.8%. Similar findings were reported by Cheng and colleagues whereby they reviewed packed red blood cells (PRBC) cross-match requests and found inappropriate ordering was more pronounced for elective than emergency requests by 27.4% [30]. Several studies reported inappropriate requests among other blood components ranging from 22.2 to 42% [31–33]. All these studies show a large burden of inappropriate blood requests leading to unnecessary transfusions.

In this study factors which significantly predicted inappropriate blood requests were; age, not reporting clinical signs of the patient (tachycardia, capillary refill and pallor),confirmation of haemoglobin level, having surgery during the hospitalization period and ward type.

Findings show the blood requests for children below 5 years were at higher risk of being inappropriate comparing to other age groups. This was contrary to a systematic review study which reported inappropriate requests were higher at the older age of 65 years and above compared to ages below that [34]. In Tanzania as other tropical countries, malaria infections among under-

PLOS ONE

Characteristics	Crude	e	Adjusted	
	RR (95% CI)	P-value	RR (95%CI)	P-value
LEVEL 1				
Tachycardia				
Not-Reported	Baseline		Baseline	
Reported	0.40 (0.36, 0.45)	< 0.0001	0.74 (0.64, 0.84)	<0.0001
Capillary refill				
Not-Reported	Baseline		Baseline	
Reported	0.51 (0.39, 0.49)	< 0.0001	0.73 (0.63, 0.85)	<0.0001
Surgery during hospitalization				
No	Baseline		Baseline	
Yes	1.16 (1.02,1.3)	0.02	1.22 (1.06, 1.4)	0.006
Pallor #Haemoglobin level ^a				
Effect of haemoglobin level				
Not reporting pallor	Baseline		1.27 (1.03,1.58)	0.028
Reporting pallor	0.18 (0.17,0.2)		0.18 (0.17,2)	<0.0001
Effect of reporting pallor	·			
Normal haemoglobin level	Baseline		0.41 (0.32,0.51)	<0.0001
Anaemia	0.65 (0.58,0.72)		0.55 (0.49, 0.63)	<0.0001
Age (years)	·			·
0-4	Baseline		Baseline	
5-14	0.15 (0.13, 0.18)	< 0.0001	0.12 (0.1, 0.15)	<0.0001
15–24	0.33 (0.29, 0.37)	< 0.0001	0.15 (0.1, 0.22)	< 0.0001
25-34	0.32 (0.29, 0.35)	< 0.0001	0.15 (0.1, 0.22)	<0.0001
35–44	0.34 (0.30, 0.38)	< 0.0001	0.17 (0.11, 0.25)	< 0.0001
45–54	0.29 (0.25, 0.34)	< 0.0001	0.16 (0.1, 0.24)	< 0.0001
55–64	0.34 (0.29, 0.4)	< 0.0001	0.16 (0.1, 0.25)	< 0.0001
65+	0.42 (0.37, 0.48)	<0.0001	0.19 (0.12, 0.28)	<0.0001
LEVEL 2				
Ward type				
General surgery	4.9 (4.2–5.7)	< 0.0001	3.3 (2.7-4.2)	<0.0001
Adult medical	Baseline		Baseline	
Paediatric medical	4.5 (3.9–5.2)	< 0.0001	1.5 (1.0-2.2)	< 0.045
Paediatric surgical	5.5 (4.5-6.7)	< 0.0001	1.8 (1.2–2.7)	<0.008
Intensive Care Unit	3.3 (2.6–4.3)	< 0.0001	1.9 (1.3–2.7)	<0.001
Obstetrics	3.4 (3.0-4.0)	< 0.0001	2.5 (2.0-3.1)	<0.0001
Gynaecology	2.7 (2.3–3.3)	<0.0001	2.1 (1.5–2.9)	<0.0001
Orthopaedics	4.3 (3.1-7.4)	< 0.0001	3.8 (2.2–6.7)	<0.0001
Emergency department	1.3 (0.2–9.2)	0.8	1.8 (0.2–12.9)	0.566

Table 4. Crude and adjusted regression of risk inappropriate blood requests among patients' blood requests (N = 7201).

Variables were adjusted for age, haemoglobin level, and surgery during hospitalization, reported tachycardia, capillary refill, pallor and ward type. ^a Interaction between reporting pallor and haemoglobin level

https://doi.org/10.1371/journal.pone.0196453.t004

fives is highly associated with anaemia [35,36], possibly contributing towards the increase demand for blood transfusion and hence higher chances of inappropriate blood requisitions [37,38].

The most important clinical signs to document are features of heart failure; decrease in capillary refills and increase in pulse rate. If these signs are well examined and documented, it would decrease the risk of inappropriate request and eventually inappropriate transfusion. These clinical signs have been the main indicators of transfusion in clinical settings [39,40], especially among children below five years [6,41].

This study has revealed that blood requests in which pallor is documented have decreased risk of inappropriate blood requests. Furthermore, when pallor is confirmed with haemoglobin level the risk of inappropriate request decreased significantly rather than when haemoglobin level only is used as an indicator for blood request. This is supported by several studies whereby it was found that a majority of inappropriate transfusions occurred among patients in which haemoglobin level was the only indicator for transfusion [42–44]. Since blood transfusions rely solely on the condition of the patient which is based on clinicians' findings, we would then expect clearer documentation on these findings for those issuing the blood to make the best decision [45].

Having surgery during hospitalization had an effect on inappropriate blood request. Patients who had surgery had a sixteen times higher risk of their request being inappropriate than those who had no operation. Perioperative surgeries have been associated with over ordering of blood, consequently leading to wastage of blood [16,46,47]. Overall, surgical patients are more likely to be inappropriately transfused comparing to medical patients which has been associated with high mortality and morbidity [42,48]. This could be contributed by a perception that all surgical cases would need blood in some way. Furthermore bloodless surgery requires availability of proper infrastructures which are limited in developing countries [49].

This study further demonstrated being in surgical wards increased the risk of inappropriate blood requisition compared to being in medical wards and furthermore being in paediatric surgical wards. Similar findings have been reported on associations between inappropriate transfusion and elective and emergency transfusions in obstetrics, gynaecology and urology departments compared with other departments [30,42]. However in a review by International Consensus Conference on Transfusion Outcomes (ICCTO), there was no difference in inappropriate transfusion among hospital setting (ward type) [34]. Furthermore, we could argue on the basis of the knowledge of the clinician [50] of which this could not be ascertained in this study.

Strengths and limitations

This study had a large sample size and is the first to explore the relationship between factors influencing inappropriate blood requests in Tanzania using country sample data. Although this study used all available information from the parent study, some of observations had missing values, which were found to be completely at random. There is a confidence in the generalizability of the results as hospitals were randomly selected. The parent study used design-standardized questionnaires consisting of closed-ended, easy-to-understand questions with appropriate response options. This decreases the likelihood that the interviewer would "interpret" the questions for the subject or will need to "probe" the subject for an appropriate response. Hence, from that it was assumed that observer bias was not a concern.

The study also had some limitations. Firstly, we found some outlier values such as age and haemoglobin level, which in many settings can be verified against the patients' files. However, since we used a secondary dataset, this was not possible. Secondly, the use of secondary data did not allow us to analyse the effects of the various factors that might have influenced inappropriate blood request, such as clinician's knowledge about blood transfusion and the experience on transfusion practices. Lastly, criteria for inappropriate blood requests were a proxy measure from inappropriate blood transfusion.

Conclusions and recommendations

The proportion of inappropriate blood requisition is high which means a majority of transfusions that took place during the study period were unnecessary. The most significant risk factors of inappropriate requisition were; not reporting clinical presentation of the patients (tachycardia, pallor and peripheral capillary refills), and haemoglobin level, age of the patient and type of ward of admission. The combination of both laboratory findings (haemoglobin level) and physical findings (pallor) are necessary for making decisions on appropriate requests.

Due to the high prevalence of inappropriate blood requests there is a need to emphasize hospital transfusion committees to review their local transfusion guidelines and encourage the clinicians to abide to the national guidelines. This may help in making thorough physical and laboratory investigations prior to requesting blood for transfusions.

It is critical that hospital blood banks abide to transfusion guidelines by scrutinizing the blood requests to monitor blood distribution and prioritize requests for those in real need.

Future studies should be done to understand the effects of various factors that might influence inappropriate blood request, such as clinician's knowledge about blood transfusion and experiences of transfusion practices.

Acknowledgments

We extend our sincere appreciation to Tanzania National Blood Transfusion Services for providing the data from parent study those were used in this study.

Author Contributions

Conceptualization: Wilhellmuss I. Mauka, Tara B. Mtuy, Sia E. Msuya, Abdul Juma, Rune N. Philemon.

Data curation: Innocent B. Mboya.

Formal analysis: Wilhellmuss I. Mauka, Innocent B. Mboya.

Methodology: Michael J. Mahande, Sia E. Msuya, Innocent B. Mboya.

Project administration: Tara B. Mtuy, Rune N. Philemon.

Supervision: Rune N. Philemon.

Validation: Rune N. Philemon.

Writing - original draft: Wilhellmuss I. Mauka.

Writing – review & editing: Wilhellmuss I. Mauka, Tara B. Mtuy, Michael J. Mahande, Sia E. Msuya, Innocent B. Mboya, Rune N. Philemon.

References

- Pitman JP, Wilkinson R, Liu Y, von Finckenstein B, Smit Sibinga CT, Lowrance DW, et al. Blood component use in a sub-Saharan African country: results of a 4-year evaluation of diagnoses associated with transfusion orders in Namibia. Transfus Med Rev [Internet]. 2015 Jan 1 [cited 2016 Feb 1]; 29(1):45–51. Available from: http://www.tmreviews.com/article/S0887796314000947/fulltext https://doi.org/10.1016/j.tmrv.2014.11.003 PMID: 25573416
- Roberts DJ, Field S, Delaney M, Bates I. Problems and Approaches for Blood Transfusion in the Developing Countries. Hematol Oncol Clin North Am. 2016; 30(2):477–95. https://doi.org/10.1016/j.hoc. 2015.11.011 PMID: 27040966
- Butler EK, Hume H, Birungi I, Ainomugisha B, Namazzi R, Ddungu H, et al. Blood utilization at a national referral hospital in sub-Saharan Africa. Transfusion [Internet]. 2015 May [cited 2016 Feb 1]; 55 (5):1058–66. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25646993 https://doi.org/10.1111/ trf.13010 PMID: 25646993
- 4. Kerkhoff AD, Lawn SD, Schutz C, Burton R, Boulle A, Cobelens FJ, et al. Anemia, Blood Transfusion Requirements and Mortality Risk in Human Immunodeficiency Virus-Infected Adults Requiring Acute Medical Admission to Hospital in South Africa. Open forum Infect Dis [Internet]. 2015 Dec 1 [cited 2016 Feb 1]; 2(4):10. Available from: /pmc/articles/PMC4693115/?report=abstract

- Du Pont-Thibodeau G, Harrington K, Lacroix J. Anemia and red blood cell transfusion in critically ill cardiac patients. Ann Intensive Care [Internet]. 2014 Jan [cited 2016 Feb 1]; 4:16. Available from: /pmc/articles/PMC4085735/?report=abstract https://doi.org/10.1186/2110-5820-4-16 PMID: 25024880
- Kiguli S, Maitland K, George EC, Olupot-Olupot P, Opoka RO, Engoru C, et al. Anaemia and blood transfusion in African children presenting to hospital with severe febrile illness. BMC Med [Internet]. 2015; 13:21. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=4313469&tool= pmcentrez&rendertype=abstract https://doi.org/10.1186/s12916-014-0246-7 PMID: 25640706
- Mpoya A, Kiguli S, Olupot-Olupot P, Opoka RO, Engoru C, Mallewa M, et al. Transfusion and Treatment
 of severe anaemia in African children (TRACT): a study protocol for a randomised controlled trial. Trials
 [Internet]. 2015 Jan 29 [cited 2016 Feb 1]; 16(1):593. Available from: http://www.trialsjournal.com/
 content/16/1/593
- Vamvakas EC, Blajchman MA. Transfusion-related mortality: The ongoing risks of allogeneic blood transfusion and the available strategies for their prevention. Blood. 2009; 113(15):3406–17. <u>https://doi.org/10.1182/blood-2008-10-167643</u> PMID: 19188662
- Osei EN, Odoi AT, Owusu-Ofori S, Allain JP. Appropriateness of blood product transfusion in the Obstetrics and Gynaecology (O&G) department of a tertiary hospital in West Africa. Transfus Med. 2013; 23(3):160–6. https://doi.org/10.1111/tme.12028 PMID: 23672710
- Bates I, Chapotera GK, McKew S, Van Den Broek N. Maternal mortality in sub-Saharan Africa: The contribution of ineffective blood transfusion services. BJOG An Int J Obstet Gynaecol. 2008; 115 (11):1331–9.
- Say L, Chou D, Gemmill A, Tuncalp O, Moller AB, Daniels J, et al. Global causes of maternal death: A WHO systematic analysis. Lancet Glob Heal. 2014; 2(6):323–33.
- Allain J-P. Moving on from voluntary non-remunerated donors: who is the best blood donor? Br J Haematol [Internet]. 2011 Sep [cited 2015 Jan 10]; 154(6):763–9. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21539535 https://doi.org/10.1111/j.1365-2141.2011.08708.x PMID: 21539535
- Pule PI, Rachaba B, Gilbert M, Damas M, Habte D. Factors Associated with Intention to Donate Blood: Sociodemographic and Past Experience Variables. Blood Transfus [Internet]. 2014; 2014;7. Available from: http://www.hindawi.com/journals/jbt/2014/571678/
- Mauka WI, Mahande MJ, Msuya SE, Philemon RN. Factors Associated with Repeat Blood Donation at the Northern Zone Blood Transfusion Centre in Tanzania. J Blood Transfus [Internet]. 2015; 2015:6. Available from: http://www.hindawi.com/journals/jbt/2015/717653/
- Arewa OP. One year clinical audit of the use of blood and blood components at a tertiary hospital in Nigeria. Niger J Clin Pract. 2009; 12(4):429–33. PMID: 20329686
- Mwambungu A, Siulapwa N, Mugala D, Chishimba M. Analysis of Blood Cross-match Ordering Practice in Surgical Patients at Ndola Central Hospital. Int J Healthc Sci. 2015; 3(1):278–84.
- 17. Chalya PL, Mbunda F, Mabula JB, Massinde AN. Blood transfusion practice in surgery at Bugando Medical Centre in northwestern Tanzania. Tanzan J Health Res. 2016; 18(1):1–9.
- 18. Ebose EM, Osalumese IC. Blood shortage situation: An audit of red blood cells order and pattern of utilization. African J Biotechnol [Internet]. 2009; 8(21):5922–5. Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L355763959%5Cnhttp://www.academicjournals.org/AJB/PDF/pdf2009/2Nov/Enosolease%5Cnand%5CnImarengiaye.pdf
- Akoko LO, Joseph AB. Blood utilization in elective surgery in a tertiary hospital in dar es salaam, Tanzania. Tanzan J Health Res. 2015; 17(4):1–8.
- 20. WHO. The clinical use of blood in medicine, obstetrics, paediatrics, surgery and anesthesia trauma and burns [Internet]. Geneva; 2001. Available from: www.who.int/bloodsafety/clinical_use/en/
- **21.** MOHCDGCE. Clinical Guideline for Appropriate Use of Blood and Blood Products [Internet]. 2015. 1–69 p. Available from: www.nbts.go.tz/images/pdf/ClinicalGuide.pdf
- 22. MOHSW. Tanzania National Blood Transfusion Services-Guideline policy. 2005;1–13. Available from: ihi.eprints.org/817/1/MoHSW.pdf_(46).pd
- 23. Drammeh B, De A, Bock N, Pathak S, Juma A, Kutaga R, et al. Estimating Tanzania's National Met and Unmet Blood Demand from a Survey of a Representative Sample of Hospitals. Transfus Med Rev [Internet]. 2017 Jul [cited 2017 Aug 10]; Available from: http://linkinghub.elsevier.com/retrieve/pii/ S0887796317300019
- Lackritz EM, Campbell CC, Ruebush TK, Hightower AW, Wakure W, Steketee RW, et al. Effect of blood transfusion on survival among children in a Kenyan hospital. Lancet. 1992; 340(August, 29):524–8. PMID: 1354285
- WHO. The Clinical Use of Blood. 2002;349. Available from: http://www.who.int/bloodsafety/clinical_ use/en/Manual_EN.pdf

- 26. Barros AJD, Hirakata VN. Alternatives for logistic regression in cross-sectional studies: an empirical comparison of models that directly estimate the prevalence ratio. BMC Med Res Methodol [Internet]. 2003; 3(21):1–13. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid= 521200&tool=pmcentrez&rendertype=abstract
- Diaz-Quijano FA. A simple method for estimating relative risk using logistic regression. BMC Med Res Methodol [Internet]. 2012; 12(1):14. Available from: http://www.pubmedcentral.nih.gov/articlerender. fcgi?artid=3305608&tool=pmcentrez&rendertype=abstract
- Thompson M Lou Myers JE, Kriebel D. Prevalence odds ratio or prevalence ratio in the analysis of cross sectional data: what is to be done? Occup Environ Med [Internet]. 1998; 55:272–7. Available from: http://oem.bmj.com/ PMID: 9624282
- Zocchetti C, Consonni D, Bertazzi PA. Relationship between prevalence rate ratios and odds ratios in cross-sectional studies. Int J Epidemiol. 1997; 26(1):220–3. PMID: 9126523
- Cheng DR, Bajraszewski C, Verma KP, Wolff AM. How appropriately is blood ordered in a rural hospital? Transfus Apher Sci [Internet]. 2013; 48(1):79–82. Available from: <u>https://doi.org/10.1016/j.transci.</u> 2012.06.016 PMID: 22840204
- Lingegowda JB, Jeyakumar JD, Muddegowda PH, Pitchai R, Gopal N, Sinha P. An Audit of Requests for Fresh Frozen Plasma in a Tertiary Care Center in South India. J Lab Physicians [Internet]. 2016 [cited 2017 Jun 20]; 8(1):41–4. Available from: http://www.ncbi.nlm.nih.gov/pubmed/27013812 https:// doi.org/10.4103/0974-2727.176232 PMID: 27013812
- Makroo RN, Raina V, Kumar P, Thakur UK. A prospective audit of transfusion requests in a tertiary care hospital for the use of fresh frozen plasma. Asian J Transfus Sci [Internet]. 2007 Jul [cited 2017 Jun 20]; 1(2):59–61. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21938235 https://doi.org/10.4103/ 0973-6247.33847 PMID: 21938235
- Paramjit K, Sabita B, Gagandeep K, Ravneet K. An Analysis Of The Pattern Of Blood Requisition And Utilization In A Tertiary Care Centre. Natl J Integr Res Med. 2013; 4(2):123–7.
- Shander A, Fink A, Javidroozi M, Erhard J, Farmer SL, Corwin H, et al. Appropriateness of Allogeneic Red Blood Cell Transfusion: The International Consensus Conference on Transfusion Outcomes. Transfus Med Rev [Internet]. 2011; 25(3):232–246.e53. Available from: https://doi.org/10.1016/j.tmrv. 2011.02.001 PMID: 21498040
- 35. Smithson P, Florey L, Salgado SR, Hershey CL, Masanja H, Bhattarai A, et al. Impact of Malaria Control on Mortality and Anemia among Tanzanian Children Less than Five Years of Age, 1999–2010. PLoS One [Internet]. 2015 Jan [cited 2015 Nov 6]; 10(11):e0141112. Available from: /pmc/articles/ PMC4633136/?report=abstract https://doi.org/10.1371/journal.pone.0141112 PMID: 26536354
- 36. Korenromp EL, Armstrong-Schellenberg JRM, Williams BG, Nahlen BL, Snow RW. Impact of malaria control on childhood anaemia in Africa—a quantitative review. Trop Med Int Health [Internet]. 2004 Oct [cited 2016 Jan 9]; 9(10):1050–65. Available from: http://www.ncbi.nlm.nih.gov/pubmed/15482397 https://doi.org/10.1111/j.1365-3156.2004.01317.x PMID: 15482397
- Natukunda B, Schonewille H, Smit Sibinga CT. Assessment of the clinical transfusion practice at a regional referral hospital in Uganda. Transfus Med. 2010; 20(3):134–9. https://doi.org/10.1111/j.1365-3148.2010.00992.x PMID: 20136779
- Bugge HF, Karlsen NCT, Oydna E, Rake MM, Wexels N, Bendabenda J, et al. A study of blood transfusion services at a district hospital in Malawi. Vox Sang. 2013; 104(1):37–45. https://doi.org/10.1111/j. 1423-0410.2012.01628.x PMID: 22765350
- WHO. The Clinical Use of Blood [Internet]. Geneva; 2002. Available from: <u>http://www.who.int/bloodsafety/clinical_use/en/Manual_EN.pdf</u>
- Desalu I, Dada OIO, Ahmed R a, Akin-Williams OO, Ogun H a, Kushimo OT. Transfusion trigger—how precise are we? Intraoperative blood transfusion practices in a tertiary centre in Nigeria. [Internet]. Vol. 18, Transfusion medicine (Oxford, England). 2008. p. 211–5. Available from: http://www.ncbi.nlm.nih. gov/pubmed/18783579
- Mueller Y, Bastard M, Ehounou G, Itama J, Quéré M, de la Tour R, et al. Effectiveness of blood transfusions and risk factors for mortality in children aged from 1 month to 4 years at the Bon Marché Hospital, Bunia, Democratic Republic of the Congo. Trop Med Int Health [Internet]. 2012; 17(12):1457–64. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23051824 https://doi.org/10.1111/j.1365-3156.2012. 03095.x PMID: 23051824
- Barr PJ, Donnelly M, Cardwell CR, Parker M, Morris K, Bailie KEM. The appropriateness of red blood cell use and the extent of overtransfusion: right decision? Right amount? Transfusion. 2011; 51 (8):1684–94. https://doi.org/10.1111/j.1537-2995.2011.03130.x PMID: 21470238
- **43.** Lackritz E., Hightower AW, Zucker J., Ruebush TK, Onudi CO, Steketee R., et al. Longitudinal evaluation of severely anemic children in Kenya: the effect of transfusion on mortality and hematologic

recovery. AIDS [Internet]. 1997; 11(12):1487–94. Available from: http://www.ncbi.nlm.nih.gov/pubmed/9342071 9342071 PMID: 9342071

- 44. Yong M, Riis AH, Fryzek JP, Møller BK, Johnsen SP. Predictors and patterns of red blood cell transfusion use among newly diagnosed cancer patients with chemotherapy-associated anemia in Western Denmark (1998–2003). Clin Epidemiol. 2011; 3(1):91–9.
- 45. Friedman MT, Ebrahim A. Adequacy of physician documentation of red blood cell transfusion and correlation with assessment of transfusion appropriateness. Arch Pathol Lab Med. 2006; 130(4):474–9. https://doi.org/10.1043/1543-2165(2006)130[474:AOPDOR]2.0.CO;2 PMID: 16594741
- **46.** Ayantunde AA, Ng MY, Pal S, Welch NT, Parsons SL. Analysis of blood transfusion predictors in patients undergoing elective oesophagectomy for cancer. BMC Surg. 2008; 8(3):1–7.
- Niraj G, Puri GD, Arun D, Chakravarty V, Aveek J, Chari P. Assessment of intraoperative blood transfusion practice during elective non-cardiac surgery in an Indian tertiary care hospital. Br J Anaesth. 2003; 91(4):586–9. PMID: 14504164
- Hajjar LA, Vincent J-L, Galas FRBG, Nakamura RE, Silva CMP, Santos MH, et al. Transfusion Requirements After Cardiac Surgery. Jama [Internet]. 2010; 304(14):1559. Available from: http://jama.jamanetwork.com/article.aspx?doi=10.1001/jama.2010.1446 PMID: 20940381
- Katsaliaki K. Cost-effective practices in the blood service sector. Health Policy (New York). 2008; 86 (2–3):276–87.
- Wilson K, Macdougall L, Fergusson D, Graham I, Tinmouth A, He PC. The effectiveness of interventions to reduce physician's levels of inappropriate transfusion: what can be learned from a systematic review of the literature. Transfusion. 2002; 42(9):1224–9. PMID: 12430683