**The difference between predicted massive transfusion and actual transfusion in an urban Indian trauma setting: A retrospective cohort study**

**Ruut Seger,1 Monty Khanjanchi,2 Vineet Kumar,3 Mike Mansourati,4 Satish B Dharap,5 Makhan L Saha,6 Martin Gerdin Wärnberg7**

1Corresponding author: Ruut Seger, Global Health: Health Systems and Policy, Department of Public Health Sciences, Karolinska Institutet, 171 77 Stockholm, Sweden, [ruut.seger@gmail.com](mailto:ruut.seger@gmail.com), +46 (0) 761925330.

2DNB General Surgery, Seth GS Medical College and KEM Hospital Mumbai, Acharya Donde Marg, Parel, Mumbai, India 400012, monta32@gmail.com.

3M.D, Department of Surgery, Lokmanya Tilak Municipal General Hospital and Lokmanya Tilak Municipal Medical College, College Building First Floor, Sion, Mumbai, India 400022, drvineetkumar@gmail.com.

4Global Health: Health Systems and Policy, Department of Public Health Sciences, K9, Karolinska Institutet, 171 77 Stockholm, Sweden, mike.mansourati@gmail.com.

5Satish B. Dharap, M.S, Topiwala National Medical College and B.Y.L Nair Charitable Hospital, Mumbai, India 400008, drdharap@hotmail.com.

6Makhan L. Saha, Professor, Department of Surgery, Seth Suklal Karnani Memorial Hospital and Institute of Postgraduate Medical Education and Research, Kolkata, India700020, drmlsaha@yahoo.com.

7PhD, Global Health: Health Systems and Policy, Department of Public Health Sciences, Karolinska Institutet, 171 77 Stockholm, Sweden, martingerdin@gmail.com.

**Word count:** 3052

**Conflicts of Interest and Source of Funding**

The authors do not have any financial or ethical conflicts of interest to declare regarding the contents of this submission. A scholarship was awarded to the main author by the Swedish International Development Agency (SIDA) to finance travel expenses to the study sites in India. The TITCO cohort was funded by the Swedish National Board of Health and Welfare and the Laerdal Foundation.

**Abstract**

*Objective*: The Indian public health system is a low-resource setting and under considerable strain to manage increasing numbers of trauma patients. Mortality in the urban Indian trauma setting is double to that of its high-income country counterparts. More research is needed to understand the reasons behind this disparity. This study aimed to estimate the potential difference between predicted need for massive transfusion (MT) and provided MT in adult trauma patients in an urban Indian setting.

*Design:* A retrospective analysis of the Towards Improved Trauma Care Outcomes (TITCO) in India cohort was conducted. A complete case analysis was conducted using the assessment of blood consumption score to calculate the proportion of patients predicted to need MT. The proportion of patients who received MT based on transfusion data was calculated. McNemar’s two-sided test for paired proportions was used. A p-value < 0.05 was considered significant, and the confidence level was 95 %.

*Setting:* The TITCO cohort included data from trauma patients admitted to four urban Indian public hospitals.

*Patients:* Adult trauma patients in four major urban Indian public hospitals. Patients admitted for burns and those below 15 years of age were excluded.

*Measurements and Main Results:* Of the 6317 patients included, 630 (9∙97 %) were predicted to benefit from MT. However, only 6 (0∙095 %) received one. The difference between these two proportions was statistically significant (p < 0∙001).

*Conclusions:* There is a substantial discrepancy between predicted needs and provisions of MT, indicating an unmet need of MT.

**Introduction**

Trauma fatalities account for 9 % of the world’s deaths, superseding the number of deaths caused by HIV/AIDS, tuberculosis, and malaria combined, disproportionately affecting low- and middle-income countries (LMICs) (1). Haemorrhage is one of the leading causes of preventable death among trauma patients (2-4). Up to 5 % of trauma patients require massive transfusions (MTs), defined as the administration of ten or more units of packed red blood cells (PRBCs) within 24 hours of injury (5).

India is an LMIC that lacks a structured trauma care system and where blood products remain a scarce commodity (6-10). There is a sizeable gap in supply and demand, as India lacks approximately four million units of blood per year according to World Health Organization estimates (9). The in-hospital mortality in an urban Indian trauma setting has been found to be twice that of high-income equivalents, and inadequate resuscitation and bleeding control of haemorrhaging patients have been found to be the main cause of preventable deaths (11, 12). To the best of our knowledge, there are no previous studies mapping the use of MT in this or setting. The absence of information relating to the high in-hospital trauma mortality in the Indian public health system remains a significant barrier to the future improvement of its trauma care outcomes. This study aimed to estimate the potential difference between predicted need for MT and provided MT in adult trauma patients in an urban Indian setting.

**Materials and Methods**

**Study design**

This was a retrospective observational analysis of the observational Towards Improved Trauma Care Outcomes in India (TITCO) cohort (11).

**Setting**

The TITCO database includes a total of 16047 trauma patients enrolled in four Indian teaching and referral hospitals from October 2013 to December 2015. The units included are the Apex Trauma Centre of the All-India Institute of Medical Sciences (AIIMS), New Delhi; Lokmanya Tilak Municipal General Hospital (LTMGH), Mumbai; King Edward Memorial hospital (KEM), Mumbai; and Seth Sukhlal Karnani Memorial Hospital (SSKM), Kolkata. The centres are located in megacities (Kolkata, Mumbai and Delhi) and are classified as free to the public, charging only nominal fees.

**Participants**

The database included patients who arrived alive to the emergency departments of the participating hospitals with a history of injury sustained in a road traffic accident, railway accident, fall, or assault or with burns and who were subsequently admitted to inpatient care. The additional eligibility criteria for this study population were age ≥ 15 years and a complete record of clinical data required for the intended analyses. Patients with burns were excluded because they often arrive with similarly deranged vital signs as patients with traumatic haemorrhage but require different resuscitation schemes (13).

**Variables**

The primary outcome was defined as the difference between the proportion of adult patients predicted to receive MT and the proportion of patients who did receive MT.

To estimate the proportion of patients predicted to need MT, the assessment of blood consumption (ABC) score was used. The ABC score is based on four dichotomous non-laboratory parameters. These include a penetrating injury mechanism, arrival systolic blood pressure of 90 mmHg or below, arrival heart rate of 120 beats per minute or greater, and findings indicating a positive focused assessment for trauma (FAST) examination. Each parameter yields one point if the abovementioned criteria are met and zero if they are not. A total score of two or more was set to indicate the need for MT (14).

The number of units of red blood administered within the first hour and between one and 24 hours was used to determine the proportion of patients who subsequently received MT. Age, sex, and mechanism of injury in addition to the variables included in the ABC score were presented to characterize the study sample.

**Data sources**

Data were collected on admission through direct observation by independent trained on-site observers who worked in eight-hour shifts during days, evenings, and nights. For patients admitted outside of these hours, data were retrieved retrospectively from patient records. Data were uploaded continuously and were subjected to regular quality controls by senior researchers.

When the FAST examination was not reported as “positive”, relevant free text terms were used to identify indications of free fluid in the abdomen, pelvis, or pericardium. In the main analysis, we used computed tomography (CT) and intraoperative findings to code FAST as positive or negative when FAST data were missing. We coded FAST as positive when splenic or liver lacerations, haemopericardium, haemoperitoneum, or injury of mesenteric arteries was found on CT or intraoperatively.

**Bias**

To reduce measurement bias, data collectors underwent training, and two on-site quality control visits were conducted during which submitted data were cross-checked with patient records revealing no major discrepancies in documentation. The data collectors all had a master’s degree in health sciences and were not affiliated with the hospitals in which they were working.

Injury severity bias is a recognized problem in trauma data sets, and survival bias may play a role in trauma-related transfusion medicine as well (15, 16). There was a considerable amount of missing data in our cohort, and in order to minimize the effects of injury severity bias and account for as many patients as possible in the analysis, missing FAST variables were substituted by corresponding CT and intraoperative findings.

**Study size**

Based on previous research, it was assumed that 10 % of patients would be predicted to need MT (14, 17-19). In contrast, based on clinical experience from the study setting, we anticipated that a maximum of 5 % would actually receive one. Assuming that 10 % (~ 1600 patients) would be predicted to need MT and 5 % (~ 800 patients) would receive one, the sample size needed to detect this difference with 80 % power based on a two-sided paired comparison of proportions, i.e., a two-sided McNemar’s test, would be 369 patients, setting alpha to 5 % and beta to 20 %. Since all complete observations in the cohort were included in the analysis, we could reliably conclude that the study was powered to detect the difference between the proportions at the 80 % level.

**Statistical methods**

All statistical analyses were performed in R, a free open-source software for statistical computing and graphics (20). Qualitative sample characteristics were presented using number and percentage, whereas quantitative sample characteristics were presented as the median, the 25th and 75th percentiles, and the minimum and maximum values.

The main analysis was a complete case analysis, where observations with missing covariate values were excluded. The main analysis was thereafter conducted in two steps by first calculating the proportion of patients predicted to need MT on the basis of having an ABC score of two or more (a) and the proportion of patients who actually received MT on the basis of transfusion data in the TITCO cohort (b). The primary outcome was then calculated by subtraction, (a) – (b). The difference between (a) and (b) was formally tested using McNemar’s two-sided test for paired proportions with a 95 % confidence interval (CI), and statistical significance was indicated by a p-value < 0∙05.

In addition, we quantified the unmet need for MT by dividing the number of patients who received MT (b) by the number of patients predicted to need MT (a) and subtracted this number from 1, reporting it as a percentage. We estimated a 95 % confidence interval for the unmet need using an empirical bootstrap approach, drawing 1000 samples of the same size as the original sample with replacement.

Based on clinical experience in this particular setting, a sensitivity analysis was conducted with a cutoff value of 4 units of PRBCs in 24 hours to define MT. A sensitivity analysis was also conducted by restricting the analysis to FAST-positive patients in whom coding using CT or intraoperative findings was not used.

**Results**

**Participants**

The TITCO cohort included 16047 trauma patients, of whom 6317 (39∙3 %) met inclusion criteria. In total 9730 patients were excluded: 2789 patients were under 15 years of age, 2448 patients were missing clinical data necessary for the analysis (arrival heart rate and blood pressure, type of injury, mechanism of injury, recording of whether FAST was performed, or recordings of blood transfusions given during the first 24 hours), 438 patients were admitted for burns, and 4055 patients did not have a FAST examination, data pertaining to free text FAST findings or any of the previously defined ICD codes necessary for surrogate coding. The final study population size was 6317 (Figure 1).

**Descriptive data**

The median patient age was 30 years (range 15-97, IQR 24-45). A total of 5509 (87∙2 %) patients were male, and 808 (12∙8 %) were female. Patients admitted for road traffic injuries composed 3214 (50∙9 %) of all patients in the study sample. Patients with falls represented 1472 (23∙3 %) of all patients in the sample; assaults, 679 (10∙7 %); railway injuries, 668 (10∙6 %); and another mechanism of injury, 284 (4∙5 %). Blunt trauma was sustained by 5798 (91∙8 %) patients.

A positive FAST examination was found in 728 (11∙5 %) patients, and FAST was coded as positive for 406 (6∙4 %) on the basis of CT or intraoperative findings. At arrival, the median systolic blood pressure was 118 mmHg (range 0-254, IQR 108-128), and the median heart rate was 90 beats per minute (range 0-186, IQR 80-100). A total of 630 (10 %) patients were predicted to need MT on the basis of an ABC score of two or more, and 6 (0∙095 %) patients received one.

In total, 3032 units of PRBC were transfused to the study population, of which 950 (31∙3 %) units were administered to the patient group predicted to need MT. The six patients who received MT were administered 62 units of PRBC in total, receiving on average 10∙3 units of PRBC per patient. One of these patients had an ABC score below two and was therefore not eligible for MT according to the prediction score that we used. The patients who were predicted to need MT but were “left out” received 888 units of PRBC in total. The number of patients who died in-hospital was 1226 (19∙4 %). See Table 1 for patient characteristics.

**Outcome data and main results**

The rate of predicted MT on the basis of an ABC score ≥ 2 was 10% in the study cohort (630 patients), resulting in a proportion (a) of 0∙1. The actual MT rate was 0∙095 % (6 patients), for a proportion (b) of 0∙00095. The primary outcome was then calculated as (a) – (b) = 0∙099 (p < 0∙001, odds ratio (OR) 0∙00160, 95 % CI 0∙00004-0∙00890). The unmet need was 99∙0 % (95 % CI 98∙4-99∙9).

**Other analyses**

In the first sensitivity analyses, the cutoff value for MT was changed to four units of PRBC. The number of patients predicted to need MT remained at 630 (10 %), while the number of patients who actually received MT increased to 272 (4∙3 %). The difference between the proportions (0∙100 – 0∙043) was 0.057 (p < 0∙001, OR 0∙31, 95 % CI 0∙25-0∙37). In this analysis, the unmet need was reduced to 56∙8 % (95 % CI 51∙8-62∙0).

In the second sensitivity analysis, we omitted patients who were coded positive for FAST on the basis of CT and intraoperative findings. The number of patients predicted to need MT decreased to 508 (8∙0 %), and the number of patients who received MT was 6 (0∙095 %). The difference between the two proportions (0∙080 – 0∙00095) was then calculated to be 0∙079 (p < 0∙001, OR 0∙0059, 95 % CI 0∙0012-0∙017). The unmet need was 98∙8 % (95 % CI 98∙0-99∙8).

**Discussion**

**Key results**

Our hypothesis that there would be an unmet need for MT based on the difference between the predicted need for MT and the actual transfusion rates in this urban Indian trauma population was confirmed. We found a large difference between the predicted need for MT and the actual MT provided. This is the first time that the potentially unmet need for MT has been quantified in a trauma population in this setting.

**Limitations**

Injury severity bias due to missing data from severely injured patients is a recognized problem in trauma databases (15, 21, 22). The degree of “missingness” has been found to correlate with increasing mortality and severity of haemorrhage (15), suggesting that complete data are not always accessible for patients needing MT, thus yielding a proportion of patients predicted to need MT that is falsely low.

In addition, the ABC score was originally developed and validated in a high-income trauma setting with different demographics and patterns of injury mechanism (23) from our study population. Specifically, the proportion of penetrating injury was higher in the reference population (23) compared to the study population. This might indicate differing management requirements and treatment needs of these two trauma populations. The rationale for using the ABC score in this context was that it is based on routinely recorded vital signs and examination results, which are all available in TITCO. Furthermore, the intent was not to validate the score but to use it as an informed basis for identifying patients with substantial bleeding.

**Interpretation**

Trauma care in the Indian public hospital system is ridden with challenges, among them the limited access to resources such as blood components. In high-income settings, the MT rates for trauma patients are reported to be much higher, ranging from 3 % to 24 % (15, 17, 24, 15), which stands in stark contrast to the 0∙095 % found in this study.

One potential explanation for the low number of MTs is that the trauma patients in urban India had less severe trauma than did other trauma populations where MT is more common. Based on available research, however, this explanation appears unlikely (7, 26).

While resource scarcity often dominates the discourse of trauma management in low-income settings, the question of apt resource use also remains. Systems-related opportunities for improvement have been identified as affordable and effective ways to reduce the mortality of patients in an urban Indian trauma setting, where inadequate fluid resuscitation and haemorrhage control have been cited as the main causes of definitely preventable deaths (12).

Considerable wastage has been reported in similar settings due to the excessive demands of cross-matching and preparing blood for patients that is ultimately not utilized due to an overestimation of expected needs (27). Studies from high-income countries have found that physicians consistently overestimate the transfusion needs in trauma settings, and a similar mechanism might manifest here (24). However, entirely different factors might influence estimates and decision making in the opposite direction. In particular, rationing and priority-setting are issues that are addressed on a daily basis in healthcare worldwide, but very little is known about the effects and patterns of bedside rationing in low-resource settings (28).

**Conclusion**

To the best of our knowledge, this study is the first multicentre study estimating the MT needs and rates in an urban low-income trauma setting. A very low rate of MT among trauma patients was identified. The availability of blood components in this setting needs to be quantified. More research is required to delineate clinical decision making and behaviours related to MT and transfusion therapy for trauma patients in this particular demographic setting.

**Acknowledgements**

Thank you to all the TITCO research team members who contributed to the review process and provided valuable input and assistance.

**References**

1 World Health Organization (WHO). Injuries and violence: the facts 2014. Geneva, 2014.

2 Gruen RL, Jurkovich GJ, McIntyre LK, Foy HM, Maier R V. Patterns of Errors Contributing to Trauma Mortality. *Ann Surg* 2006; 124: 37–46.

3 Teixeira PGR, Inaba K, Hadjizacharia P, *et al.* Preventable or potentially preventable mortality at a mature trauma center. *J Trauma* 2007; 63: 1338–47.

4 Montmany S, Pallisera A, Rebasa P, *et al.* Preventable deaths and potentially preventable deaths. What are our errors? *Injury* 2016; 47: 669–73.

5 Cotton BA, Gunter OL, Isbell J, *et al.* Damage control hematology: the impact of a trauma exsanguination protocol on survival and blood product utilization. *J Trauma* 2008; 64: 1173–7.

6 Garg R. Who Killed Rambhor?: The State of Emergency Medical Services in India. *J Emerg Trauma Schock* 2012; 5: 49–54.

7 Oestern H-J, Garg B, Kotwal P. Trauma care in India and Germany. *Clin Orthop Relat Res* 2013; 471: 2869–77.

8 Joshipura MK. Trauma care in India: Current scenario. *World J Surg* 2008; 32: 1613–7.

9 Marwaha N. Whole blood and component use in resource poor settings. *Biologicals* 2010; 38: 68–71.

10 Bagcchi S. More blood for India. *BMJ* 2014; 349: g7166–g7166.

11 Roy N, Gerdin M, Ghosh S, *et al.* 30-day in-hospital trauma mortality in four urban university hospitals using an Indian Trauma Registry. *World J Surg* 2016; 40: 1299–307.

12 Roy N, Kizhakke Veetil D, Khajanchi MU, *et al.* Learning from 2523 trauma deaths in India- opportunities to prevent in-hospital deaths. *BMC Health Serv Res* 2017; 17: 142.

13 Latenser BA. Critical care of the burn patient: the first 48 hours. *Crit Care Med* 2009; 37: 2819–26.

14 Nunez TC, Voskresensky I V, Dossett LA, Shinall R, Dutton WD, Cotton BA. Early prediction of massive transfusion in trauma: simple as ABC (assessment of blood consumption)? *J Trauma* 2009; 66: 346–52.

15 Trickey AW, Fox EE, del Junco DJ, *et al.* The impact of missing trauma data on predicting massive transfusion. *J Trauma Acute Care Surg* 2013; 75: S68-74.

16 Brown JB, Cohen MJ, Minei JP, *et al.* Debunking the survival bias myth. *J Trauma Acute Care Surg* 2012; 73: 358–64.

17 Burman S, Cotton BA. Trauma patients at risk for massive transfusion: the role of scoring systems and the impact of early identification on patient outcomes. *Expert Rev Hematol* 2012; 5: 211–8.

18 Ogura T, Nakamura Y, Nakano M, *et al.* Predicting the need for massive transfusion in trauma patients. *J Trauma Acute Care Surg* 2014; 76: 1243–50.

19 Ogura T, Lefor AK, Masuda M, Kushimoto S. Modified traumatic bleeding severity score: Early determination of the need for massive transfusion. *Am J Emerg Med* 2016; 34: 1097–101.

20 R Core Team. R: A Language and Environment for Statistical Computing. 2017.

21 Fuchs PA, Junco DJ, Fox EE, *et al.* Purposeful variable selection and stratification to impute missing Focused Assessment with Sonography for Trauma data in trauma research. *J Trauma Acute Care Surg* 2014; 75: 1–13.

22 Rahbar H, Holcomb JB, Study P. Seven Deadly Sins in Trauma Outcomes Research: An Epidemiologic Post-Mortem for Major Causes of Bias. *J Trauma Acute Care Surg* 2013; 75: S97–103.

23 Cotton B a, Dossett LA, Haut ER, *et al.* Multicenter validation of a simplified score to predict massive transfusion in trauma. *J Trauma* 2010; 69 Suppl 1: S33–9.

24 Med P, Clin R, Author NA, *et al.* Clinical gestalt and the prediction of massive transfusion after trauma. 2015; 25: 1–30.

25 Brockamp T, Nienaber U, Mutschler M, *et al.* Predicting on-going hemorrhage and transfusion requirement after severe trauma: a validation of six scoring systems and algorithms on the TraumaRegister DGU. *Crit Care* 2012; 16: R129.

26 Murlidhar V, Roy N. Measuring trauma outcomes in India An analysis based on TRISS methodology in a Mumbai university hospital. 2004; 1383: 386–90.

27 Raghuwanshi B, Pehlajani N, Sinha MK TS. A retrospective study of transfusion practices in a Tertiary Care Institute. *Indian J Anaesth* 2017; 61: 24–8.

28 Defaye FB, Desalegn D, Danis M, *et al.* A survey of Ethiopian physicians ’ experiences of bedside rationing : extensive resource scarcity , tough decisions and adverse consequences. *BMC Health Serv Res* 2015; : 1–8.

29 Cantle PM, Cotton BA. Prediction of Massive Transfusion in Trauma. *Crit Care Clin* 2017; 33: 71–84.

30 Hwang K, Kwon J, Cho J, Heo Y, Lee JC-J, Jung K. Implementation of Trauma Center and Massive Transfusion Protocol Improves Outcomes for Major Trauma Patients: A Study at a Single Institution in Korea. *World J Surg* 2017. DOI:10.1007/s00268-017-4441-5.