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Transfusion Practice and Costs in a Tertiary Pediatric Intensive Care Unit

Referans Üçüncü Basamak Pediatrik Yoğun Bakım Ünitesinde Transfüzyon Uygulaması ve Maliyetleri

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ABSTRACT

Aim: In this study we aimed to evaluate transfusion related costs in a pediatric intensive care unit, taking into consideration previously defined transfusion indications, evidence-based transfusion evaluations and clinical transfusion practices.

Material and Method: Seventy six patients that received a blood transfusion in our tertiary referral centre's pediatric intensive care unit between January 2017 - January 2018 were included in the study. Transfusion related costs and total healthcare costs were retrospectively collected. Consumables (blood transfusion set, apheresis set etc.), immunohematological tests and blood transfusion procedure related costs were separately evaluated, an overall transfusion cost per patient was estimated and proportioned to the total health care cost per patient.

Results: The ratio of transfusion related costs within total healthcare costs was found to be 3.24%. The median total healthcare cost and transfusion related cost were 5478.76 Euros (IQR=11280.02) and 130.57 Euros (IQR=354.86), respectively. A significantly strong positive correlation was detected between the number of transfusions and total healthcare cost ($r:0.674$, $p<0.01$). Although the median costs of the patients administered split blood were lower, the difference was not statistically significant.

Conclusion: There are no studies evaluating blood transfusions and costs in pediatric intensive care units in Turkey. More detailed studies are needed to examine transfusion costs and the diversity of blood product transfusions in intensive care units.

Keywords: Pediatric intensive care unit, blood transfusion, transfusion cost, pediatrics

ÖZ

Giriş: Bu çalışmada, çocuk yoğun bakım ünitesinde transfüzyonla ilişkili maliyetleri, daha önce iyi tanımlanmış kan transfüzyon endikasyonlarını ve transfüzyon uygulamalarını; pediatrik transfüzyon kararı verme için kanıta dayalı değerlendirmeyi dikkate alarak tartışmayı amaçladık.

Gereç ve Yöntem: Bir yıllık dönemde (Ocak 2017-Aralık 2017) çocuk yoğun bakım ünitesinde kaldığı süre boyunca kan bileşenleri ile transfüzyon yapılan 76 hasta çalışmaya dahil edildi. Çocuk yoğun bakım ünitesinde tedavi gören çocuklara yönelik sağlık hizmetleri için transfüzyonla ilişkili maliyetler ve toplam maliyet hastane bilgi sistemi kullanılarak toplandı. Sarf malzemelerine (kan transfüzyonu ve aferez setleri gibi), immünohematolojik testler ve kan transfüzyonu prosedürlerine bağlı olarak transfüzyonla ilişkili maliyetler ayrı ayrı ele alındı ve her hasta için transfüzyon maliyeti tahmin edildi ve sonuç olarak sağlık hizmetlerinin toplam maliyetine oranlandı.

Bulgular: Transfüzyona bağlı maliyetin toplam sağlık hizmeti maliyetine oranı %3,24 olarak bulundu. Hastane maliyeti ve transfüzyonla ilişkili maliyet için medyanlar sırasıyla 5478.76 euro (IQR=11280.02) ve 130.57 euro (IQR=354.86) idi. Transfüzyon sayıları ile çocuk yoğun bakım ünitesinin hastaneye yatış maliyeti arasında anlamlı ve güçlü bir pozitif korelasyon tespit edildi ($r: 0,674$, $p<0,01$). Çalışmamızda bölünmüş kan uygulanan hastaların ortalama değerleri daha düşük olmasına rağmen anlamlı bir fark bulunmadı.

Sonuçlar: Türkiye'de çocuk yoğun bakım ünitelerinde kan transfüzyonlarını ve maliyetlerini değerlendiren çalışma bulunmamaktadır. Yoğun bakımlarda transfüzyon maliyetlerini ve kan ürünü transfüzyonlarının çeşitliliğini inceleyen daha ayrıntılı çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Çocuk yoğun bakım ünitesi, kan transfüzyonu, transfüzyon maliyet, pediatri

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INTRODUCTION

Blood transfusion - a special type of tissue transplantation, is one of the most common clinical treatment applications. The World Health Organization (WHO) Global Database on Blood Safety (GDBS) reports that 92 million units of blood were donated in 2011 (1). Transfusion rates for blood components in hospitalized children remains uncertain (2). Although mostly used for life-saving interventions, unnecessary use of blood transfusion may be life-threatening. Pediatric transfusion guidelines are limited and differ in applications. However, it is widely utilized by pediatricians owing to its effect on both oxygen transport capacity of erythrocytes and its hemodynamic benefits (3). Pediatric transfusion guidelines differ from adults mainly due to the differing growth and development stages of children. The formation of pediatric transfusion guidelines is difficult due to limited data on transfusion indications and their outcomes. Therefore, transfusion decisions generally rely on the clinical findings (4). Although not widely accepted as standard practice in children, patient blood management (PBM) is an evidence-based practice that aims to improve patient outcomes by maintaining hemoglobin concentration, optimizing hemostasis, and minimizing blood loss (5). Complications caused by unnecessary transfusions and the treatment of these complications leads to direct and indirect financial burden (6). In addition to the avoidance of transfusion-related adverse events, PBM also supports cost-effectiveness by reducing transfusion-related costs (7-9).

In this study we aimed to evaluate transfusion related costs in a pediatric intensive care unit (PICU), taking into consideration defined transfusion indications, evidence-based transfusion evaluations and clinical transfusion practices (10).

MATERIAL AND METHOD

This retrospective cost analysis study was conducted at a tertiary pediatric centre's PICU. Data of children aged 1 month to 18 years admitted to PICU between January 2017 and January 2018 were included in the study. The study was approved by the local ethics board (Date: 2019, Decision No: 358). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. Due to national regulations, regional blood centres run by the Turkish Red Cross provide all blood products except for granulocyte concentrations collected by apheresis at the hospital's apheresis centre.

Splitting of transfusions into smaller amounts using a sterile connector (Terumo BCT, Japan) and gamma irradiation, when required, was conducted at the hospital's transfusion centre. All transfusions were given to critically ill children in a level 3 PICU.

Transfusion related and total cost data were obtained from the hospital information system (HIS) database. Data collected and analysed included patients' age, gender, length of hospitalization, patient comorbidities, indication for PICU admittance, type of blood component transfused and blood type.

Consumables (blood transfusion set, apheresis set etc.), immunohematological tests and blood transfusion procedure related costs were separately evaluated, an overall transfusion cost per patient was estimated and proportioned to the total health care cost per patient.

Statistical Analysis

SPSS Statistics (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY, USA) software was used for statistical analysis. Nonparametric tests (Mann-Whitney U test, Kruskal-Wallis test, Chi-square analysis, Spearman correlation analysis) were used because the data were not normally distributed (Shapiro-Wilk Test).

RESULTS

During the study period, blood transfusions were performed in 76 of 210 (36.2%) patients interned in the PICU. Demographic data, diagnosis at hospitalization and indication for PICU admission of 76 patients included in the study are given in **Table 1**. A total of 388 blood components were transfused. Of these, 217 were red blood cell (RBC) concentrates, 112 were apheresis platelet concentrates (APC), 6 were granulocyte concentrates (GC), 51 were fresh frozen plasmas (FFP), 1 was cryoprecipitate (Cryo) and 1 was whole blood (WB). Blood component splitting was performed in 150 of RBCs (69%), 60 of APCs (53%) whereas 32 of FFPs supplied from the regional blood center were pediatric bags (**Figure 1**).

The most common indication for RBC transfusion was high risk of developing symptomatic anemia with a hemoglobin <7 g/dL without any other medical treatment likely to correct the anemia, followed by symptomatic anemia. The most common indication for thrombocyte transfusion was active bleeding or <50 $\times 10^9/l$ before a surgical procedure, followed by Plt <20 $\times 10^9/l$.

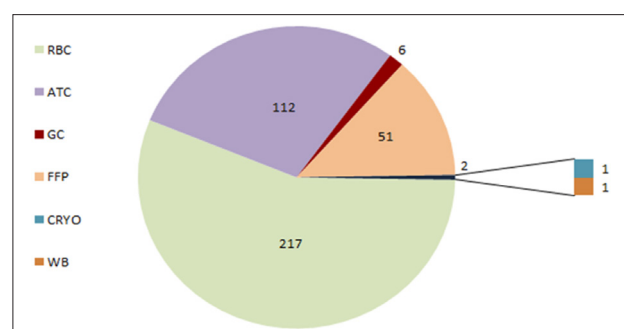


Figure 1. Blood components transfused in PICU patients

RBC: Red Blood Cell, ATC: Apheresis Platelet Concentrates, GC: Granulocyte Concentrates, FFP: Fresh Frozen Plasmas, CRYO: Cryoprecipitate, WB: Whole Blood



Tablo 1. Diagnosis, blood groups, demographic characteristics of patients

Demographics		n=76
Gender		n (%)
Male/Female		36 (47.4)/40 (52.6)
Age		Median; (IQR)
Months		12; (26)
Hospitalization time		Median; (IQR)
Day		16 (30)
Primary Diagnoses		n (%)
Chronic lung disease		7 (9.2)
Cardiovascular disease		11 (14.5)
Hematological-Oncological		11 (14.5)
Metabolic Disease		13 (17.1)
Healthy Child (without chronic disease)		7 (9.2)
Norological disease		27 (35.5)
PICU admission diagnoses		n (%)
Respiratory failure		29 (38.2)
Cardiac failure		13 (17.1)
Septic Shock		17 (22.4)
Metabolic Crisis		5 (6.6)
Post-operative surgery		1 (1.3)
Norological disease		11 (14.5)
Length of stay		n
Day		12/9
Blood groups		n (%)
A Rh+		25 (32.9)
B Rh+		13 (17.1)
O Rh+		23 (30.3)
AB Rh+		3 (3.9)
A Rh-		3 (3.9)
B Rh-		2 (2.6)
O Rh-		6 (7.9)
AB Rh-		1 (1.3)

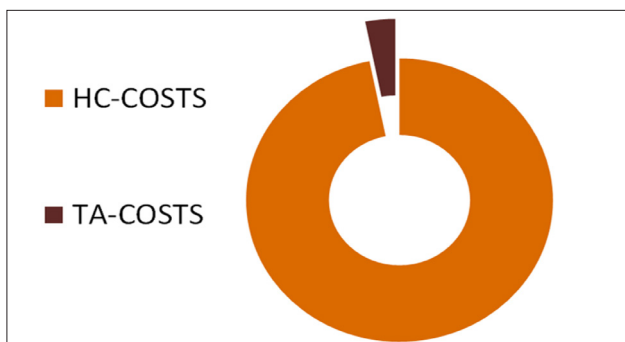


Figure 2. Healthcare costs and transfusion-associated costs proportions

HC: Healthcare, TA: Transfusion-associated

Average hemoglobin and hematocrit levels in patients receiving RBS transfusion were 6.90 ± 0.80 ve 21.31 ± 2.79 respectively. Average thrombocyte count of patients receiving thrombocyte transfusion was 19406 ± 8601 . Average fibrinogen level in patients receiving FFP transfusion was 160 ± 61 and average neutrophil count in patients receiving granulocyte transfusion was <500 cells/l.

Transfusion related costs were calculated taking into account blood transfusion sets, apheresis sets, blood type grouping, cross typing, coombs test and transfusion related procedures (**Table 2**). The ratio of transfusion cost to total health care cost was found to be 3.24% (**Figure 2**).

Patients were grouped according to the ratio of transfusion related cost to total health care cost: group 1 (0-5%), group 2 (5-10%), group 3 (10-15%) and group 4 (>15%). The number of patients per group was 63.2% (n=48), 13.2% (n=19), 11.8% (n=9) and 11.8% (n=9) respectively.

Median total cost and transfusion related cost was calculated to be 5478.76 Euros (IQR: 11280.02) and 130.57 Euros (IQR: 354.86).

When compared to patients with metabolic or neurological disease, those with hematological-oncological pathologies had a statistically significantly higher ratio of transfusion related cost to total health care cost ratio ($p=0.012$). Therefore grouping was conducted as: 1) Patients with hematological-oncological pathologies 2) others. Relationship between cost rates, gender of patients and use of pediatric packs is summarized in **Table 3**.

Tablo 2. Transfusion-associated costs analysis

Costs Data	Costs (=Euro)
Transfusion sets	431.64
Transfusion services	571.19
Crossmatch	617.31
Blood products	16,512.88
Apheresis sets	7,973.47
Total transfusion costs	26,106.51
Total healthcare costs	804,802.38

Tablo 3. Analysis between cost and gender, pediatric blood product and diagnosis

Groups	Transfusion costs		Total costs	
	Median (IQR)	p	Median (IQR)	p
Gender		0.643		0.423
Male	994.87 (2019.17)		36351.53 (77042.52)	
Female	722.03 (2955.52)		31246.23 (39099.1)	
Pediatric packages		0.414		0.362
Used	740.99 (2030.28)		29125.35 (70753.64)	
Unused	3572.23 (5521.71)		48612.34 (210412.52)	
Diagnoses		<0.01*		0.914
Hematological-Oncological	5790.87 (6224.21)		36637.98 (67014.79)	
Other diagnoses	678.15 (1700.14)		33036.93 (70587.48)	

IQR: Interquartile Range



A statistically significant and strong positive correlation was observed between the number of transfusions in PICU and hospitalization costs ($r:0.674$, $p<0.01$). A statistically significant weak positive correlation was found between transfusion cost and hospitalization cost ($r:0.247$, $p=0.032$), and also between age and transfusion related cost ($r:0.227$, $p=0.048$).

While there was a significant and strong positive correlation between length of stay (LOS) and total cost of PICU ($p<0.01$, $r:0.695$), there was no correlation between transfusion related cost and LOS ($p>0.05$).

DISCUSSION

The transfusion of blood and blood products is widely practiced yet rarely discussed as a clinical topic. Whatever the indication, expected clinical improvement, possible alternatives to transfusion and a benefit-risk analysis of transfusion must be performed before a transfusion is performed. Transfusion criteria can vary between clinics. Clinicians in the study centre follow current literature and take into consideration hemodynamic variables and blood parameters of critically ill patients during the blood transfusion decision making process. In a report by the Pediatric Intensive Care Transfusion and Anemia Expertise Initiative (TAXI), a hemoglobin level of <5 g/dl is highlighted as a threshold value due to an increase in mortality below this level, however, there remains uncertainty of the risk-benefit for transfusion when hemoglobin (Hb) is between 5-7 g/dl. In addition, although Hb concentration should be accepted as a measure of the body's oxygen status in critically ill patients, it is important to note that it should not be used alone as an indication for RBC transfusion (11,12).

The most frequently used threshold value accepted for the indication of transfusion, the transfusion rates in critically ill pediatric patients and the amount of incentive clinicians take to decrease complication rates are causes for concern. A multicentered study conducted on adult intensive care units reported that transfusion rates decreased without leading to an effect on general mortality (13). Another study concluded that a lower minimum threshold value could be tolerated when making a decision on RBC transfusion (14). Furthermore, it has been reported that the use of a restrictive transfusion protocol may be a better strategy for prolonging survival (15). The average Hb of patients at transfusion in our study was 6.9 g/dl. We believe the variations in our results are due to the diagnosis of our critically ill patients and their hemodynamic as well as respiratory parameters. As reported in literature, severe anemia ($Hb<5$ g/dl or $Htc<15\%$) is an absolute indication for transfusion due to a significant increase in mortality in these patients (11,12,16). Hemodynamic status is important in critically

ill pediatric patients and therefore the threshold value for transfusion may change. Threshold values may be higher in patients with cardiac pathologies and those with sepsis where an increase in tissue oxygenation is required (17).

A multicentered study of thrombocyte transfusion conducted in 2018 reported that thrombocyte transfusions were mostly indicated for prophylaxis and administered when Plt count was $< 20 \times 10^9/l$ (18). In our study, prophylactic thrombocyte transfusion was administered when Plt count was $< 20 \times 10^9/l$ after considering the clinical status of the patient, requirement for surgery, the presence of major or minor bleeding and requirement for extracorporeal treatment.

An evidence-based RBC transfusion guideline regarding transfusion threshold in hematology-oncology patients was published in 2019 by TAXI. The guideline stated that more data regarding RBC transfusion indications, risks, benefits and transfusion alternatives are required in hematology-oncology patients that require frequent transfusions (19). Our study revealed higher transfusion costs in patients with an underlying chronic disease. Apart from hematological pathologies, the presence of chronic pulmonary disease was found to be associated with higher costs. Lengthy recovery times and frequent hospitalization lead to prolonged hospitalization in these patients. Prolonged hospitalization may increase transfusion requirements especially when sepsis is present. As expected, our study revealed the highest cost in patients with hematological diseases.

In-hospital transfusion reactions were calculated to have cost 933,356 Euros in Holland in 2018, with non-serious reactions making up two-thirds of all transfusion reactions and only a third of reactions leading to an increase in hospitalization length (20). Although the length of hospitalization and care as well as cost including medication may vary, it is estimated that RBC transfusions cost 100,000,000 USD in Turkey per year (21). Some studies have reported that these additional costs may affect the general cost of blood transfusions (22,23). As all blood products did not require irradiation, we excluded intravenous access, management of adverse reactions, nursing care and irradiation costs were excluded in our study. Transfusion related side effects and the cost of their management was not included in our study, involving all patients receiving a transfusion for a period of 1 year. During this time-frame, one patient received intravenous antihistamines due to erythema during erythrocyte transfusion. Hospitalization length was not affected therefore the additional cost was disregarded.

It is important to emphasize that, unlike adults, calculating transfusion requirements in smaller amounts, such as in milliliters versus units may also lead to a decrease in



transfusion related costs. Although the median cost of patients treated with split blood were lower in our study, the difference was not significant. However, the number of non-pediatric blood products in our pediatric centre was low. Statistical analysis could only be performed when the number of non-pediatric blood products are higher.

Patient blood management (PBM) is thought to be beneficial in transfusion practices. This approach entails the prevention of complications, decrease in costs and more importantly the more effective use of the patients blood reserve. A single-centred study from Germany examined the impact of this approach on clinical outcomes and costs. The study reported that PBM combined RBC transfusion with many alternatives leading to improved clinical outcomes and that PBM costs vary between institutes and are determined by the extent to which PBM is utilized (24). It is possible to define blood products and transfusions, ensure their safe application, manage blood transfusion side effects and decrease costs through hospital hemovigilance teams. A study performed in 2016 reported that while not a primary aim of hemovigilance teams, the management and documentation of blood products by these teams lead to advantages regarding costs (25).

CONCLUSION

Blood transfusions, frequently used in PICUs lead to an increase in health care costs. Clinicians and hospitals must be aware of the financial burden they put on their respective health care system. Many clinicians may choose to perform a blood transfusion in critically ill children independent of current guidelines and without performing a risk-benefit analysis due to the ease of access to blood products. Further studies are required to create strong guidelines for clinicians to follow and to accurately define transfusion thresholds as well as risk and benefits of these thresholds. Such guidelines may also aid in decreasing transfusion related and overall health care costs.

Study Limitations:

Some parameters that may effect accurate cost calculation such as intravenous lines, management of adverse reactions, nursing services, irradiation etc were not included in cost calculation. Our study is also limited by a small number of patients and its retrospective design.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was approved by Health Sciences University, Dr. Behçet Uz Children's Diseases and Surgery Training and Research Hospital Ethic Committee (Date: 2019, Decision No: 358).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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