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Association between Plasma Transfusion and Clinical Outcome in Critically ill Children at Zagazig University Hospital

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Abstract

Background:*Plasma is frozen for storage to preserve the level of coagulation factors. It is named "fresh-frozen plasma" if refrigerated within 8 hours of collection, and "frozen plasma" if within 24 hours. Currently available evidence derived from retrospective studies suggests that plasma transfusions are independently associated with an increased morbidity and mortality in adults and children. The aim of the study was to decrease morbidity in critically ill children through achieving the following objectives;identification of patient characteristics for plasma transfusions, identification the indications of plasma transfusions in critically ill children, and assessment the effect of plasma transfusion on coagulation tests.****Methods****This was prospective Cohort study which conducted in PICU at Zagazig University Hospital including 54 patients with any eligible patient for whom at least one plasma transfusion was administered on any study day was included unless one of the exclusion criteria exists.* ***Results:****Mean age of studied children 36.8±43 months with range from 40 days to 168 months, 51.9% of them were girls and the mean weight of them is 13±10kg.Common reasons for PICU admission were CNS diseases (29.5%) followed by Respiratory infection and organs failure (24.1%).50 % of plasma transfusion due to bleeding, 40.7% due to hypoalbuminemia, lastly 9.3% of plasma transfusion due to physician conceptions.There is statistically insignificant difference between indication of plasma transfusion and age, sex and children weight, p>0.05.There is statistically insignificant difference between indication of plasma transfusion at different causes and percent of deaths.****Conclusion:*** *Bleeding was the most common cause of plasma transfusion followed by hypoalbuminemia and doctors believes.Plasma transfusion does not statistically affect the mortality, although there was little increase in mortality over the predictive mortality by SOFA score.*

Key words: *plasma transfusions- indications- critically ill children.*

I. Introduction:

In 2008, 4 484 000 plasma units were transfused in the United States. More than 10% of critically ill patients, both adults and children, receive a plasma transfusion during their hospital stay, making plasma transfusion a frequently used treatment modality **(1)**.

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In situations where active bleeding is attributable to a coagulation factor deficiency, plasma transfusions can constitute a life-saving intervention by improving coagulation factor levels. In practice, plasma transfusions are administered mostly to correct abnormal coagulation tests or to prevent bleeding much of the clinical use of plasma lacks objective evidence to support its usefulness. Some authors have shown that transfusing plasma often fails to correct mild coagulation abnormalities [(2)].

In fact, there are little evidence-based data to guide clinicians with regard to appropriate indications for plasma transfusion. Current guidelines are based on a very small number of clinical studies and are derived mostly from experts' opinion, some of whom believe that plasma 'contributes significantly to the morbidity and the mortality resulting from transfusion of blood components' [(3)].

Currently available evidence derived from retrospective studies suggests that plasma transfusions are independently associated with an increased morbidity and mortality in adults and children. Only one prospective study addressed this issue in critically ill adults with haemorrhagic shock and reported an independent association between plasma transfusions and outcomes like MODS and ARDS [(4)].

There continues to be significant use of fresh- frozen plasma (FFP) across a range of clinical specialties in hospital practice. In contrast to red blood cells, data from England and Wales for the use of FFP for transfusion show little change over the past decade with approximately 300,000 units used annually with the latest figures for 2009 showing a 4% annual increase [(5)].

The study aimed towere to identify patient characteristics for plasma transfusions, to identify indications of plasma transfusions in critically ill children and to assess the effect of plasma transfusion on coagulation tests.

II. Patients and Methods

This was a prospective follow-up cohort study of critically ill cases admitted to Pediatrics ICU Department, Zagazig University Hospitals during the period from July 2019 to January 2020.

The study sample composed of 54 critically ill infants and children, their age from 1 month to 14 years.

- **Inclusion Criteria:**

1. Age group of infancy and child hood (from one month to 14years).

2. Newly admitted patients to PICU for any causes either medical or surgical and received at least one plasma transfusion.

3. Male and female with a written informed consent from the parents.

Methods:

All patients incorporated in this study were subjected to the following:

I. Complete history taking regarding:

II. Complete clinical examination (general and systemic):

III. Laboratory investigations including;

- Blood gas estimation of each patient.
- CBC.complete blood count
- Serum calcium, Na, K, creatinine, urea, PT, aPTT, INR, serum albumin, bilirubin, SGOT, SGPT, and CRP.

IV. Outcome of the patients:

A- The primary outcome was the primary indication for the first plasma transfusion and the coagulation tests before plasma transfusion. We considered only plasma transfusion, not Cryoprecipitate, albumin, or infusion of specific coagulation factors.

Clinical indications were categorized as following;

- **Mild bleeding**;
- **Moderate and critical bleeding**
- **No bleeding**, no planned surgery (hypovolemia, abnormal coagulation tests. Factor or component replacement. at high risk of bleeding due to non-surgical reasons, etc.)

B- `The secondary outcome was the changes in coagulation tests that occurred after the first plasma transfusion including PT, aPTT, INR.

STATISTICAL ANALYSIS

All data were collected, tabulated and statistically analyzed using SPSS 20.0 for windows (SPSS Inc., Chicago, IL, USA). Quantitative data were expressed as the mean ± SD & (range), and qualitative data were expressed as & (percentage). **Kruskallwallius test** was used to compare between more than two groups of non-normally distributed variables post hoc test was used to define significant between each groups. **paired test** was used to compare between two dependent variables of normally distributed variable. while **Wilcoxon Signed Ranks Test** was used to compare between two dependent variables of non-normally distributed variables. Percent of categorical variables were compared using **Chi-square test or Fisher eact test when appropriate.** All tests were two sided. p-value< 0.05 was considered statistically significant (S), and p-value ≥ 0.05 was considered statistically insignificant (NS). **ROC curve** to draw roc curve ; the true positive rate (Sensitivity) is plotted on (y) axis and false positive rate (100-Specificity) on(x) axis

III. Results:

Table (1): Socio-demographic characteristics and BMI of studied group (n=54).

Variables		
Age Per Months		
Mean ± SD	36.8±43	
Median(range)	22(40 days-168)	
Weight kg		
Mean ± SD	13±10	
Median(range)	10.5(3-60)	
Sex		
Boys	26	48.1%
Girls	28	51.9%

This table illustrates;mean age of studied children 36.8±43 months with range from 40 days to 168 months, 51.9% of them were girls and the mean weight of them is 13±10 kg.

Table (2): Frequency distribution of reasons of PICU admission (n=54).

Causes	**No**	**%**
CNS	**16**	**29.5**
Convulsion	13	24.1
Encephalopathy	2	3.7
Intracranial hemorrhage	1	1.9
Respiratory infection	**13**	**24.1**
Pleural effusion	2	3.7
Bronchopneumonia	1	1.9

Bronchiolitis	10	18.5
Meningitis	**5**	**9.3**
Septic shock	**1**	**1.9**
Hemorrhagic shock	**1**	**1.9**
Organs failure	**13**	**24.1**
Renal	8	14.8
Hepatic	4	7.4
Heart failure	1	1.9
GE with dehydration	**5**	**9.3**

Table (2): Shows the common reasons for PICU admission, CNS diseases represented (29.5%) followed by Respiratory infection and organs failure (24.1%).

Table (3): Frequency distribution of indication of plasma transfusion (n=54).

Item	No	%
Indication of plasma transfusion		
Bleeding	27	50.0
Hypoalbuminemia	22	40.7
Physician conceptions	5	9.3
Degree of Bleeding		
Mild	1	1.9
Moderate	20	37
Critical	6	11.1

This table shows that;50% of plasma transfusion due to bleeding, 40.7% due to hypoalbuminemia, lastly 9.3% of plasma transfusion due to physician conceptions.

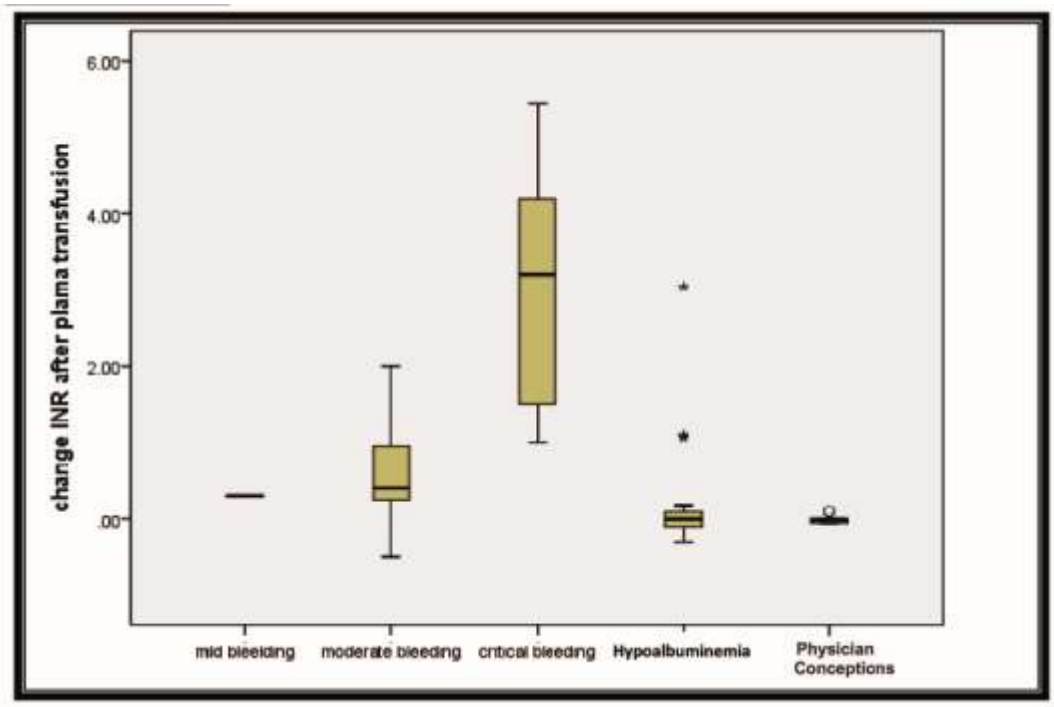

Figure (1): Box plot shows changes of INR value after plasma transfusion as regard the reason of plasma transfusion.

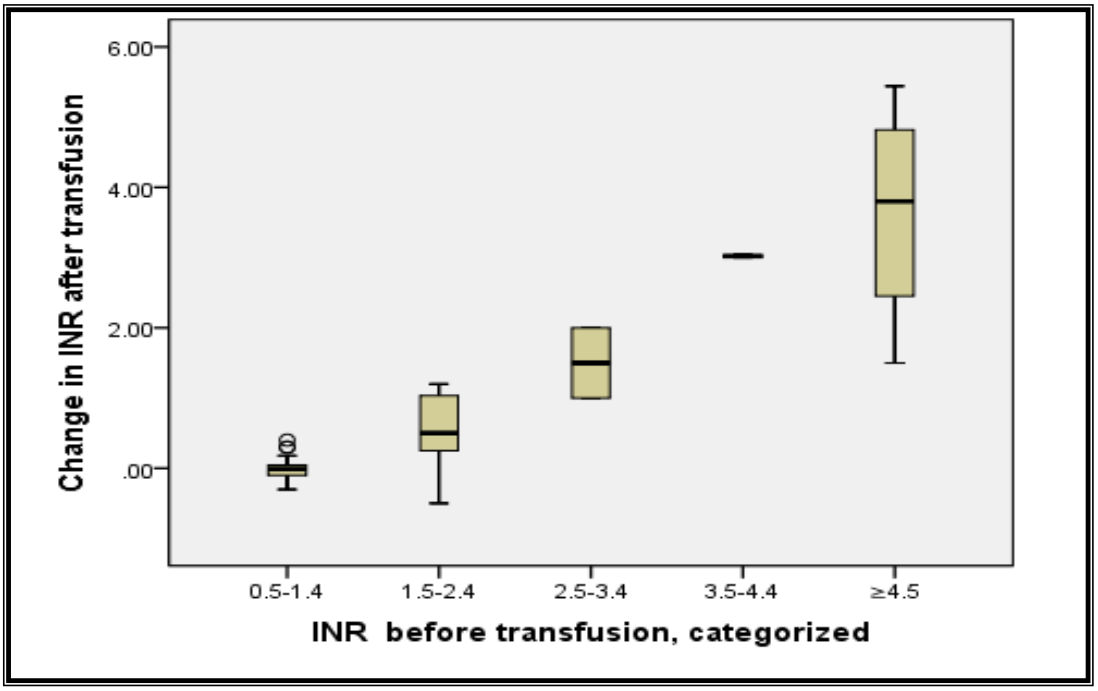

Figure (2): Box plot shows changes of INR value after plasma transfusion as regard the INR category before transfusion.

Shows there is statistically significant INR change among studied patients received plasma transfusion as regard reason of plasma transfusion and INR interval before plasma transfusion, $p<0.05$.

Post hoc test defined significant INR change after plasma transfusion in patients with moderate& critical bleeding, $p<0.05$ but not significant in other groups, $p=0.95$.

Post hoc test defined significant difference between each INR interval before plasma transfusion p<0.05 except (2.5-) interval and (0.5, 1.5, 3.5, ≥4.5) p>0.05.

Table (4): Comparison aPTT change among studied patients received plasma transfusion as regard reason of plasma transfusion and aPTT interval before plasma transfusion :(n=54)

Item	Change in aPTT after plasma transfusion			W	p
		Mean ± SD	Median (Range)		
According to Indication of plasma transfusion					
Mild*		23	23	0.1	0.013
Moderate	0	9.1±11.7	8.5(-21-32)		
Critical		15.5±25.5	6.5(-6-66)		
Hypoalbuminemia	2	2.9±8.9	0.5(-9 -30)		
Physician conceptions		2.8±6.3	1(-1 -14)		
According to aPTT interval before plasma transfusion					
20-	6	0.73±4.7	1(-9-14)	7.7	0.001
40-	9	8.4±10.2	8(-21 -25)		
60-		16.8±14.7	18(-3 -32)		
80-		15±14.1	15(5- 25)		
≥100*		66	66		

***Excluded from analysis**

Table (4):Shows there is statistically significant aPTT change among studied patients received plasma transfusion as regard reason of plasma transfusion and aPTT interval before plasma transfusion, p<0.05.

Post hoc test defined significant difference between hypoalbuminemia and moderate bleeding p=0.003

Post hoc test defined significant difference between aPTT interval (20-) and (40-, 60-, 80-) p<0.05

Table (5): Relation between indication of plasma transfusion and age, sex and children weight (n=54)

	Bleeding						Hypoalbuminemia		Physician conceptions		KW	p
	Mild		Moderate		Severe							
Age	3		32.7±48.4 10.5 (1.3-168)		19.3±27 2.5(1.3-60)		42.9±45.7 27 (1.5-168)		54±13.4 60 (30-60)		7.6	0.06
Weight	3.6		11.4±7.3 10(4-28)		8.5±6.8 5(4-21)		15.1±12.8 5(1-11)		17.2±6.2 20(6.1-20)		5.4	0.14
	No	**%**	**No**	**%**	**No**	**%**	**No**	**%**	**No**	**%**		
Sex											χ^2	
Boys	1	100	8	40.0	4	66.7	10	45.5	3	60.0	=2.8	0.6
Girls	0	0	12	60.0	2	33.3	12	54.5	2	40.0		

KW=KruskallWallius test significant χ^2 Chi square test

Table (5): Shows there is statistically insignificant difference between indication of plasma transfusion and age, sex and children weight, p>0.05.

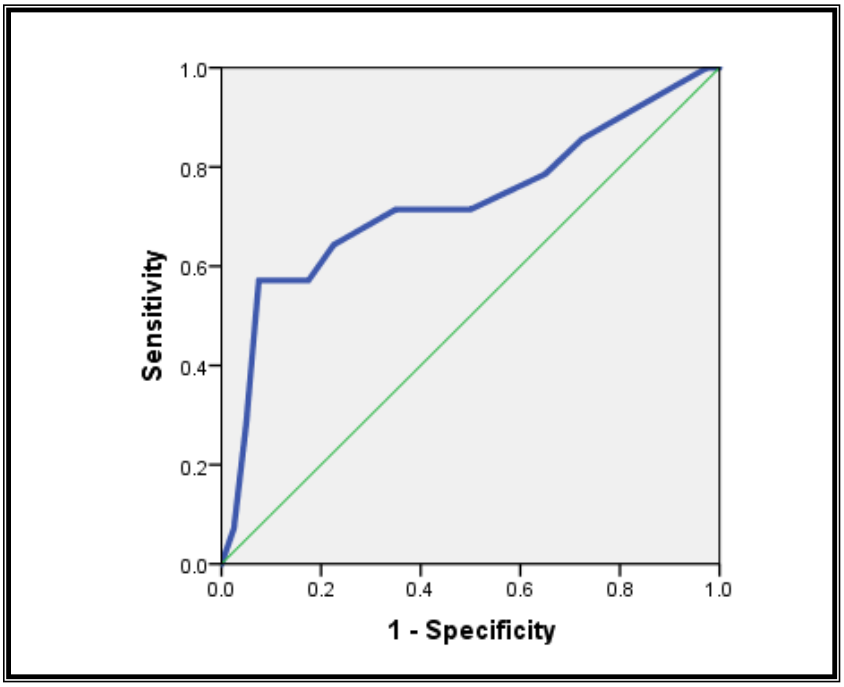

Figure (3): ROC curve to detect area under curve (AUC) to differentiate between deaths and survival in children received plasma transfusion by sofa score.

IV. Discussion

In our study: The mean age of studied children 36.8±43 months with range from 40 days to 168 months, 51.9% of them were girls and the mean weight of them was 13.1kg.

In contrary with our results,study of**Karamet al.,**[6] as they reported that the median age and weight were 1 year (IQR, 0.2–6.4) and 9.1 kg (IQR, 4.0–21.0), respectively. Forty-three percent were males.

The present study shows that the common reasons for PICU admission were CNS diseases (29.5%) followed by Respiratory infection and organs failure (24.1%).

This agreed with a study of **Bo et al.** [7]thesis under the title "Role of probiotics in prevention of ventilation associated pneumonia in PICU".

In our study, 50 % of cases, the indication for plasma transfusion were bleeding whether critical, moderate or mild.

This agreed with **Karamet al.,**[6]that observed the primary indication for plasma transfusion was critical bleeding in 22.3% of patients , minor bleeding in 21.2% , planned surgery or procedure in 11.7% , and high risk of postoperative bleeding in 10.6% .No bleeding or planned procedures were reported in 34.1% of patients.

Our results are supported by study of **Stanworth et al.,**[8] as they reported that the reason was documented as bleeding for 48% of episodes, prophylaxis for a procedure for 15%, and in 36% of cases no procedure was planned and no bleeding was documented as being present.

Our study disagreed with a study conducted by **Palo et al.,**[9]**,**more than 6000 FFP units were tracked to 1159 transfused patients, revealing that FFP was transfused most often in surgical patients, especially cardiac.

Furthermore,**Puetz et al.,** [1] reported that FFP was most commonly administered to children <1 year of age (54%), critically ill children (70%), and those with heart disease (34%). Fifteen percent of FFP-related admissions involved a thrombotic event.

In 2004, **Dzik and Rao,** [10] reported that the most common purpose of plasma transfusion in adults was to "prepare" a patient with an elevated INR for invasive procedures. In 2007, **Lauzier et al.,** [11] also showed that plasma transfusions were often administered to critically ill adults who were not bleeding; 33.7% of plasma orders were for nonbleeding patients with no planned invasive procedures.

In our study; 40.7% of plasma transfusion was due to hypoalbuminemia.

31.8% of hypoalbuminemia was due to renal cause, 18.2% due nutritional and sepsis causes then 13.6% due to hepatic causes and 13.6% due to neurological causes, lastly 4.5% due to heart failure.

It is higher in our study because we are in developing country and sometimes albumin may not be available, beside that malnutrition still a problem in our area, so plasma transfusion solves this problem of hypoalbuminemia.

Also 9.3% of cases received plasma was according to the physicians conceptions and believes. These cases had no bleeding, hypoalbuminemia and were not at risk of invasive maneuvers.

In a study by **Karamet al.,**[(6)]34.1% of cases were without bleeding or planned procedures.From them 68.3% were transfused to correct abnormal coagulation tests, 13.2% were considered at high risk of bleeding due to their medical condition, 12.6% were transfused to treat hypovolemia, and 6.0% 1 were transfused to replace losses (ascites, chylothorax, or antithrombin deficiency).

Again this agreed with a study by **Camazine et al., [(12)],** in where 35% of cases not bleeding or procedure were recorded.

There is statistically insignificant difference between indication of plasma transfusion and percent of deaths.

Mortality percent in our study was 25.9 %. This near to the PICU mortality of the study of **Karamet al.,[(6)],** that was 26.9%.

Optimal cut off for sofa score is 5.5to detect deaths. Define fair diagnostic index (AUC 0.7-<0.8) to differentiate between deaths and survival in children received plasma transfusion by sofa score.

The predictive mortality percent using cut off value of SOFA score was 21.5% , so the actual mortality percent was little higher than the predictive mortality by SOFA of the cases on the study received Plasma transfusion .

This agreed with **Biuet al., [(13)],** they found association of Plasma transfusion with worse outcome .

Also **Biu et al., [(13)],** stated that the use of FFP is not without potential danger and it should be used only if indicated.

V. Conclusion:

Bleeding was the most common cause of plasma transfusion followed by hypoalbuminemia and doctorsbelieves.Plasma transfusion does not statistically affect the mortality, although there was little increase in mortality over the predictive mortality by SOFA score.

References:

1. **Puetz J, Witmer C, Huang YS, Raffini L, (2012).** Widespread use of fresh frozen plasma in US children's hospitals despite limited evidence demonstrating a beneficial effect. *The Journal of pediatrics*, 160(2), 210-215.
2. **Vlaar AP, der Maur AL, Binnekade JM, Schultz MJ and Juffermans NP. (2009).**A survey of physicians' reasons to transfuse plasma and platelets in the critically ill: a prospective single-centre cohort study. *Transfus Med*; 19:207–212.
3. **Pinkerton PH and Callum JL. (2010).** Rationalizing the clinical use of frozen plasma. *CMAJ*; 182:1019–1020.
4. **Watson G. A., Sperry J. L., Rosengart M. R., Minei J. P., Harbrecht B. G. et al., (2009).** Fresh frozen plasma is independently associated with a higher risk of multiple organ failure and acute respiratory distress syndrome. *Journal of Trauma and Acute Care Surgery*, 67(2), 221-230.

5. **Holland LL and Brooks JP. (2006).**Toward rational fresh frozen plasma transfusion: the effect of plasma transfusion on coagulation test results. *Am J ClinPathol*; 126:133-9.
6. **Karam O., Demaret P., Shefler A., Leteurtre S., Spinella, et al., (2015).** Indications and effects of plasma transfusions in critically ill children. *American journal of respiratory and critical care medicine*, 191(12), 1395-1402.
7. **Bo L., Li J., Tao T., Bai Y., Ye X. et al., (2014).** Probiotics for preventing ventilator-associated pneumonia. *Cochrane Database Syst. Rev.* CD009066.
8. **Stanworth S. J., Walsh T. S., Prescott R. J., Lee R. J., Watson D., et al., (2011).** A national study of plasma use in critical care: clinical indications, dose and effect on prothrombin time. *Critical care*, 15(2), R108.
9. **Palo R, Capraro L, Hovilehto S, Koivuranta M, Krusius T, et al., (2006).**Population-based audit of fresh frozen plasma transfusion practices. *Transfusion*; 4:1921-5.
10. **Dzik W and Rao A. (2004).** Why do physicians request fresh frozen plasma? *Transfusion;* 44:1393–1394.
11. **Lauzier F, Cook D, Griffith L, Upton J, Crowther M., et al., (2007).** Fresh frozen plasma transfusion in critically ill patients. *Crit Care Med;* 35:1655–1659.
12. **Camazine, Maraya N., Karam, Oliver, Colvin, et al., (2017).** Outcomes Related to the Use of Frozen Plasma or Pooled Solvent/Detergent-Treated Plasma in Critically Ill Children. *Pediatric Critical Care Medicine*, 18(5):e215- e223.
13. **Biu E, Beraj S, Vyshka G, Nunci L and Çina T., (2018).** Transfusion of fresh frozen plasma in critically ill patients: effective or useless? *Open access Macedonian journal of medical sciences*, 6(5), 820.