Role of platelet count as an early prognostic indicator on pediatric intensive care unit outcomes

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Abstract

Background: Thrombocytopenia has been shown to be an independent predictor for mortality and prolonged hospital staying in critically ill pediatric intensive care unit patients (PICU)

Aims: Evaluating the relationship between platelet counts at admission, platelet course, length of hospital staying and outcomes.

Method: Prospective Observational Study.

Population: All patients admitted more than four days in pediatric intensive care unit at El Gala Teaching Hospital over the course of one year.

Results: Thrombocytopenia detected in 30% of patients on admission. Mortality was higher in thrombocytopenic than non- thrombocytopenic patients (64.1% vs. 30.8%, p= 0.000 respectively). Length of PICU staying was found to be statistically significant in thrombocytopenic patients (p= 0.004). MV, CVC and coagulopathy were found to be significant risk factors for thrombocytopenia. Leukocytosis, increased ALT, AST, BUN, Cr, total bilirubin, PT, PTT and INR were found to be statistically significant in thrombocytopenic patients. There was highly statistically significant difference was found between mortality and low platelet count on1st, 4th, 7th day of admission.

Conclusion: Thrombocytopenia and falling of platelet counts are associated with increased risk of mortality and prolonged hospital staying.

Key Words: thrombocytopenia; pediatric intensive care unit; outcomes; platelet count.

تاثير عدد الصفائح الدموية كمؤشر مستقبلى مبكر على نتائج الحجز فى وحدة الرعاية المركزة للاطفال

الخلفية: يعد نقصالصفائح الدموية متنبا مستقلا لمعدل حالات الوفاة ومدة الحجز للحالات الحرجة فى وحدة الرعاية المركزة للاطفال.

الهدف: تقييم العلاقة بين نقصالصفائح الدموية عند دخول المستشفى وحدوثة اثناء الحجز وفترة الاقامة فى المستشفى والنتائج المرتبة على الحجز.

المرضى وطريقة العمل: قد اجريت دراسة ملاحظاتية متابعة على الاطفال المحجوزين فى وحدة الرعاية المركزة لمستشفى الجلاء التعليمى لمدة تزيد عن اربعة ايام على مدار عام خلال الفترة بين ابريل ٢٠١٧ الى مارس ٢٠١٨.

النتائج: وقد وجد ان نسبة نقص الصفائح بين الاطفال عند بدء الحجزفى وحدة الرعاية مركزة٣٠% وارتفاع معدلات الوفاة ومدةالحجز فى المستشفى بين الاطفال المصابين بنقص الصفائح عن الاطفال الغير مصابين، وقد وجدت علاقة ذات دلالة احصائية بين عدد من عوامل الخطورة مثل استخدام التنفس الصناعى والقسطرة الوبدية المركزية واضطراب تخثر الدم وارتفاع عدد كرات الدم البيضاء والبروتين التفاعلى نسبة اليوريا والكرياتنين ووظائف الكبد ونسبة الصفراء فى الدم وسرعة النزف وحدوث نقص الصفائح الدموية، من خلال متابعة عدد الصفائح الدموية اثناء فترة الحجز تبين وجود علاقة ذات دلالة احصائية بين ارتفاع معدلات الوفاة ونقص الصفائح الدموية عند بدء الحجز واليوم الرابع والسابع من الحجز.

الاستنتاج: نقص الصفائح الدموية عند الحجز او حدوثة اثناء فترة الحجز يعد موشر مبكر وهام لزيادة معدلات الوفاة ومدة الاقامة فى وحدة الرعاية المركزة للاطفال.

الكلمات المفتاحيه: نقص الصفائح الدموية، نتائج الحجز،عدد الصفائح الدموية، وحدة الرعاية المركزة للاطفال.

Introduction:

Thrombocytopenia is defined as platelet count less than 150× 109/L, commonly occur in critically ill intensive care unit (ICU) patients, mainly results from diminished production, increased platelets consumption or both as in sepsis and malignancy (Amarpreet et.al., 2015). Prevalence of thrombocytopenia in intensive care unit ranging from 13% to 58% depending on severity of disease (Yilmaz et.al., 2013). The platelet count, was not only related to homeostasis disorders, but also considered a good predictor for ICU outcome due to dynamic nature of daily platelet counts (Russul et.al., 2012). Many studies use thrombocytopenia as a prognostic marker in ICU patients and found negative correlation between thrombocytopenia, duration of ICU stay and mortality (mortality rate 31%- 46% in thrombocytopenic patients vs 16%- 20% non-thrombocytopenic patients) (Agrawal et.al., 2008).

Typically, platelet count of critically ill patients decreases during the first 4 days of ICU admission and reaches a nadir on the day four. This initial decline in platelet count is later followed by an increment (Akca et.al., 2002).

Prolonged and sustained dropping in platelet count over more than 4 days after ICU admission or a decrease in platelet count of >50% during ICU stay is associated with a 4 to 6- fold increase in mortality (Levi and Opal, 2006).

Materials And Methods

This prospectively observational study was conducted in pediatric intensive.

Care unit (PICU) at El Gala Teaching Hospital over a period of one year between April 2017 to March 2018. Parental informed consent was obtained for the study.

The study was approved by ethics committee of General Organization of Teaching Hospital and Institutes and conducted according to Helsinki declaration (2000).

Detailed history including demographic data, place of admission, primary diagnosis, presence or absence of sepsis, bleeding, use of central venous line, the need for platelet or blood transfusion, need for ventilator support and pediatric Risk of Mortality (PRISM) II were recorded for all admitted patients who were staying more than four days. Laboratory data collected at admission i.e. Complete Blood Counts (CBC), C- reactive protein (CRP), Blood Urea Nitrogen (BUN), serum creatinine, serum bilirubin and coagulation profile. Platelets counts were analyzed on the 1st, 4th, 7th day of admission, then twice weekly unless changing from normal limits to critical levels. Children were followed up in order to be checked for clinical improvement or deterioration. Thrombocytopenia was defined as platelet count below 150× 109/ L. The severity of thrombocytopenia was classified as mild, moderate, severe and very severe on the basis of below 150× 109/ L, 100× 109/ L, 50× 109/ L and 20× 109/ L, respectively.

Sepsis was defined in patients had an infection with positive acute phase reactants and raised total leukocyte counts (TLC). Coagulopathy was defined when the activated partial thromboplastin time (aPTT) was 1.5 times the normal reference range for the laboratory with an associated increase in international normalized ratio (INR) more than 1.5. Bleeding was defined as an episode resulting from a fall in Hemoglobin level more than 2 g/dL within 24 hours, episodes require transfusions.

Statistical Analysis

Data was analyzed using statistical package for social sciences (SPSS.V-15). Mean or median was used for continuous variables depending on the distribution of values. Associations between the outcome of critically ill children and various variables were estimated using Fisher's Exact Test and Chi- Square Tests or Mann Whitney test. A p value of< 0.05 was considered to be statistically significant.

Results:

Out of the 148 total admissions in PICU during the period of study, 130 patients were included their age ranged from 0.14 to 8 years with mean (2.21± 1.8) years. Sixty were females (46.2%) and seventy were males (53.8%). Patients from emergency department (65.4%) had more admission than patients from pediatric ward (34.6%). Thrombocytopenia reported in 30% of patients on admission. Mild, moderate, and severe thrombocytopenia was presented in 59.0%, 38.5%, and 2.5% of patients respectively. Mean duration of PICU stay was 11.95± 5.35 days (range 5-28 days). Respiratory disease was the most common cause (44.6%) for admission while the other causes were neurological disease (14.6%), gastroenterology (11.5%), cardiovascular disease(13%), sepsis (7.6%), inborn error of metabolism (4.6%), diabetic ketoacidosis (1.3%), cystic fibrosis (1.5%), hemolytic uremic syndrome (0.7%) Table (1).

Table (1) Clinical features of patients in Pediatric Intensive Care Unit (n= 130).

Parameters		Mean±SD Range	NO	%
Age (Year)	Mean±SD	2.15± 1.79		
	Range	0.14- 8		
Sex	Female		60	46.2%
	Male		70	53.8%
Place Of Admission	ER		85	65.4%
	Ward		45	34.6%
Platelet Count At Admission	100 to 149×109 per L		23	59.0%
	50 to 99 × 109 per L		15	38.5%
	< 50 × 109 per L		1	2.5%
Diagnosis	Respiratory Disease		58	44.6%
	Cardiovascular		17	13%
	Central Nervous System		19	14.6%
	Gastroentrology		15	11.5%
	Sepsis		10	7.6%
	Ierm		6	4.6%
	Dka		2	1.5%
	Hus		1	0.7%
	Cystic Fibrosis		2	1.5%
Hospital Stay In Days	<7days	11.95± 5.35	13	10.0%
	7- 14	5- 28	77	59.2%
	>14		40	30.8%
Prism	<8		47	36%
	8		10	7.9%
	>8		73	56.1%

Parameters		Mean±SD Range	NO	%
Outcome	Non- Survivors		53	40.8%
	survivors		77	59.2%
Coagulopathy			15	11.5%
Mechanical Ventilation			44	33.8%
Central Line			33	25.4%
Bleeding			39	30.0%
Platelete Transfusion			11	8.5%
Blood Transfusion			34	26.2%

IERM: Inborn error of metabolism DKA: Diabetic Ketoacidosis HUS: Hemolytic Uremic Syndrome. PRISM II: Pediatric Risk of Mortality II.

Other than cardiovascular disease(p= 0.004) there was no statistically significant association between thrombocytopenia, non- thrombocytopenic patients in various diseases Table (2)/ Figure (1).

Table (2) Comparison of clinical diagnosis between thrombocytopenic and Non-thrombocytopenic patients at admission (n= 130)

Diagnosis	Thrombocytopenic	Non Thrombocytopenic	Test Value*	P-Value
	No.= 39	No.= 91		
Respiratory Disease:	17 (43.6%)	41 (45.1%)	0.024	0.877
Pneumonia	9 (23.1%)	23 (25.3%)	0.071	0.790
Bronchial Asthma	2 (5.1%)	9 (9.9%)	0.244	0.621
Bronchiolitis	5 (12.8%)	7 (7.7%)	0.857	0.355
Larngiomalacia	1 (2.6%)	2 (2.2%)	0.016	0.899
Cardiovascular Disease:	0 (0.0%)	17 (18.7%)	8.382	0.004
Myocarditis	0 (0.0%)	3 (3.3%)	1.316	0.251
Congenital Heart Disease	0 (0.0%)	14 (15.4%)	6.724	0.010
Central Nervous System	7 (17.9%)	12 (13.2%)	0.496	0.481
Coma	4 (10.3%)	8 (8.8%)	0.070	0.791
Convulsion	3 (7.7%)	4 (4.4%)	0.582	0.446
Gastroenterology:	6 (15.4%)	9 (9.9%)	0.807	0.369
Hypernatremic Dehydration	2 (5.1%)	0 (0.0%)	4.74	0.029
Gastroenteritis	4 10.3%)	9 (9.9%)	0.004	0.950
Sepsis	4 (10.3%)	6 (6.6%)	0.516	0.473
IERM	2 (5.1%)	4 (4.4%)	0.033	0.856
DKA	1 (2.6%)	1 (1.1%)	0.387	0.534
Hus	1 (2.6%)	0 (0.0%)	2.351	0.125
Cystic Fibrosis	1 (2.6%)	1 (1.1%)	0.387	0.534

P- value >0.05: Non significant (NS); P- value< 0.05: Significant (S); P- value<0.01: highly significant (HS) *: Chi- square test IERM: Inborn error of metabolism DKA: Diabetic Ketoacidosis HUS: Hemolytic Uremic Syndrome.

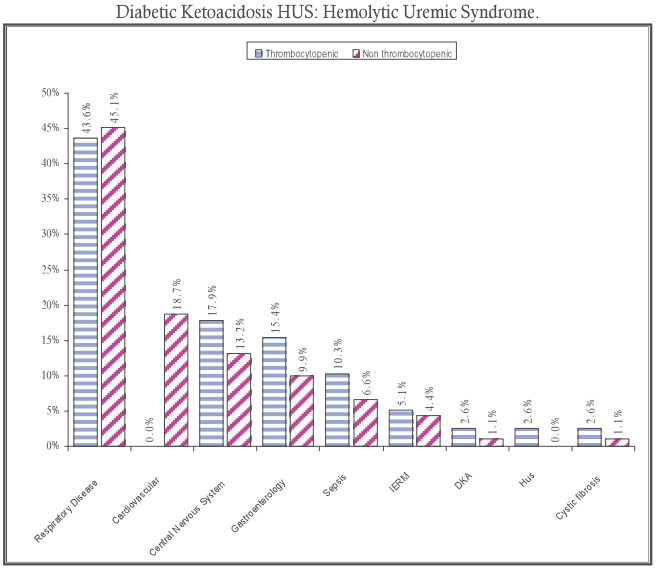

Figure (1) Disease in thrombocytopenic and non- thrombocytopenic patients.

Gender and source of admission had no significant correlation with the development of thrombocytopenia. Age, use of central line, mechanical ventilation, elevated biochemical markers as total leucocytic count, blood urea nitrogen, serum creatinine, bilirubin, PT, PTT, INR and positive CRP were found.

statistically significant in thrombocytopenic patients. Coagulopathy were found to be statistically significant risk factors for thrombocytopenia(p= 0.001).

As regarding mortality there was statistically significant difference that was found between thrombocytopenic and non- thrombocytopenic patients (64.1% vs. 30.8% respectively, p= 0.000) as shown in Table (3).

Table (3) Comparison of clinical parameters between thrombocytopenic and Non-thrombocytopenic patients at admission (n= 130).

Parameters		Thrombocytopenic	Non Thrombocytopenic	Test Value	P-Value
		No.= 39	No.= 91		
Age (Year)		2.69± 1.81	1.92± 1.73	2.287	0.024
Sex	Female	18 (46.2%)	42 (46.2%)	0.000*	1.000
	Male	21 (53.8%)	49 (53.8%)		
Hospital Stay (Days)	<7	2 (5.1%)	11 (12.1%)	11.243*	0.004
	7- 14	17 (43.6%)	60 (65.9%)		
	>14	20 (51.3%)	20 (22.0%)		
Place Of Admission	ER	29 (74.4%)	56 (61.5%)	1.983*	0.159
	Ward	10 (25.6%)	35 (38.5%)		
Outcome	Non- Survivors	25 (64.1%)	28 (30.8%)	12.561*	0.000
	Survivors	14 (35.9%)	63 (69.2%)		
Prism	<8	17 (47.2%)	26 (28.9%)	4.126*	0.127
	8	3 (8.3%)	7 (7.8%)		
	>8	16 (44.4%)	57 (63.3%)		
Mechanical Ventilation		19 (48.7%)	25 (27.5%)	5.503	0.019
Central Line		19 (48.7%)	14 (15.4%)	16.015	0.000
Coagulopathy		10 (25.6%)	5 (5.5%)	10.856	0.001
WBCs	Median (IQR)	16 (12- 20)	9 (5- 14)	-4.666‡	0.000
	Range	3.4- 32	3- 26.6		
Hb	Mean± SD	8.38± 1.45	9.56± 1.51	-4.070•	0.000
	Range	5- 12	6.8- 13.4		
CRP	Median (IQR)	24 (12- 48)	12 (6- 24)	- 3.331‡	0.001
	Range	6- 96	6- 96		
Cr	Median (IQR)	0.7 (0.6- 1.1)	0.6 (0.5- 0.7)	- 3.912‡	0.000
	Range	0.4- 4.4	0.3- 6		
Urea	Median (IQR)	32 (25- 56)	26 (18- 28)	- 3.446‡	0.001
	Range	8- 215	0.5- 156		
Ast	Median (IQR)	44 (37- 78)	28 (23- 43)	- 3.957‡	0.000
	Range	17- 416	11- 378		
Alt	Median (IQR)	48 (35- 96)	42 (35- 52)	- 2.379‡	0.017
	Range	22- 356	9- 430		
PT	Mean± SD	14.95± 2.54	13.52± 3.64	2.231•	0.027
	Range	12- 21	12- 36		
PTT	Mean± SD	47.18± 15.13	37.21± 8.32	4.824•	0.000
	Range	33- 89	12- 76		
INR	Mean± SD	1.68±0.89	1.26±0.41	3.693•	0.000
	Range	1- 4	1- 3.1		

Non significant (NS); P- value< 0.05: Significant (S); P- value<0.01: highly significant (HS). *: Chi- square test; •: Independent t- test; ‡: Mann Whitney test.

There was no statistically significant difference found between morality in various diseases and thrombocytopenia Table (4).