Research Article

Thrombocytopenia in Children with Severe Sepsis Association with renal function and liver function

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Abstract
Introduction: Sepsis is the clinical syndrome resulting from the inflammatory response of the host against various invading pathogens such as bacterial infections. **Aim of the study:** Our objectives are to study the prognostic value of thrombocytopenia, in critically ill patients with severe sepsis. **Subject and Method:** The present study was conducted on 60 infants and children, who were admitted to PICU of Minia University Children and Maternity Hospital, El-Minia. **Results:** Liver enzymes were significantly higher in the two severe sepsis groups than the controls, as $p<0.001$ in all. **Discussion:** Sepsis is the leading cause of death worldwide in the pediatric population resulting in an estimated 7.5 million deaths annually. **In conclusion:** the existence of thrombocytopenia in critically ill patient is associated with bad prognosis and higher mortality.
Keywords: Thrombocytopenia, renal function, liver function

Introduction
Sepsis is the clinical syndrome resulting from the inflammatory response of the host against various invading pathogens such as bacterial infections. Sepsis can be complicated by hemodynamic instability and multiorgan dysfunction and is associated with hemato-logical abnormalities. Patients with severe sepsis usually develop thrombocytopenia due to various reasons such as disseminated intravascular coagulation (DIC), drug-induced myelosuppression, heparin-induced thrombo-cytopenia (HIT), drug-induced immune destruction, hemodilution, massive transfusion, hemophagocytosis syndrome, and others (Thiele et al., 2013). Thrombocytopenia was defined as platelet count below 150x109/L. Prolonged and sustained thrombocytopenia over more than 4 days after ICU admission or a drop-in platelet count of >50% during ICU stay is related to a 4 to 6-fold increase in mortality (Levi et al., 2006).

Aim of the study
Our objectives are to study the prognostic value of thrombocytopenia, in critically ill patients with severe sepsis. Association with renal function and liver function

Subject and Method
The present study was conducted on 60 infants and children, who were admitted to PICU of Minia University Children and Maternity

Hospital, El-Minya. The study was conducted during the period from February 2018 till October 2018. Also, 30 healthy children were included as control group, they were age and sex matched with the children of the 2 septic groups.
The studied children were divided into three groups:

Group 1 (Thrombocytopenic group):
This group included 30 children. They were 18(60%) boys and 12(40%) girls, with mean age of 9.7±7.5 months.
They were diagnosed with severe sepsis accor-ding to the international pediatric sepsis consensus criteria, 2005, with a platelet count < 150,000\ cmm.

Group 2 (Non-thrombocytopenic group):
This group included 30 children. They were 17(56.7%) boys and 13(43.3%) girls, with mean age of 13.6 ± 13.6 months.

They were diagnosed with severe sepsis according to international pediatric sepsis consensus criteria, 2005, with a platelet count ≥150,000\ cmm.

Group 3 (control group):
This group included 30 apparently healthy children. They were 21(70%) boys and 9 (30%) girls, with mean age of 18.8±11.7 months.

Inclusion criteria:
Children diagnosed with severe sepsis according to the international pediatric sepsis consensus conference, and include the following criteria:

Sepsis plus one of the following: cardiovascular organ dysfunction (septic shock) or acute respiratory distress syndrome OR two or more other organ dysfunctions ***(International pediatric sepsis consensus conference, 2005)***.

Exclusion criteria:
1- Admission to PICU with causes other than severe sepsis e.g. intracranial hemorrhage.
2- Drug induced thrombocytopenia.
3- Hematological malignancy or DIC directly related to a malignant disorder
4- HIT syndrome (Heparin induced thrombocytopenia)

Results:

Table 1: Other laboratory investigations of the three studied groups

	Group A (Thrombocytopenic)	**Group B (Non-thrombocytopenic)**	**Group C (Controls)**	**p**		
	N=30	**N=30**	**N=30**	***A vs B***	***A vs C***	***B vs C***
- RFT **1) Urea (mg/dl)** *Median / (IQR)*	39/ (32-56)	30.5/ (24.5-435)	16/ (12-22)	***0.049****	***<0.001****	***<0.001****
2) Creatinine (mg/dl) *Median / (IQR)*	0.7/ (0.5-0.8)	0.6/ (0.05-0.8)	0.49/ (0.45-0.6)	*0.436*	***<0.001****	***0.001****
- Liver enzymes **1) AST (u/L)** *Median / (IQR)*	152/ (44.3-200.5)	128/ (37.5-222)	30/ (25.8-32.3)	*0.478*	***<0.001****	***<0.001****
2) ALT (u/L) *Median / (IQR)*	105/ (40.5-125.3)	93.5/ (30-134.5)	23.5/ (19.8-28)	*0.375*	***<0.001****	***<0.001****
- CRP (mg/dl) *Median / (IQR)*	96/ (92-192)	72/ (48-96)	6/ (0-6)	***0.003****	***<0.001****	***<0.001****

RFT: renal function tests, AST: aspartate amino-transferase, ALT: alanine amino-transferase, CRP: C-Reactive protein, U/L: unit per liter

- ***Kruskal Wallis test for non-parametric quantitative data (expressed as median) between the three groups followed by Mann Whitney test between each two groups***
- ****: Significant difference at p value < 0.05***
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Table 1 shows that Group A and Group B had both significantly higher renal function tests (serum urea and creatinine) than controls, as p<0.001 in all. Furthermore, Group A had significantly higher urea levels than Group B, as p=0.049.
Liver enzymes were significantly higher in the two severe sepsis groups than the controls, as p<0.001 in all.

CRP was significantly higher in the two severe sepsis groups than the controls as p<0.001 for both. Additionally, CRP was significantly higher in Group A than in Group B, as p=0.003.

Discussion

That the thrombocytopenic group and the non-thrombocytopenic group had both significantly higher renal function tests (serum urea and creatinine) than controls. Furthermore, the thrombocytopenic group had significantly higher urea levels than the non-thrombocytopenic group. Our results were in agreement (Gafter-Gvili et al., 2011) and (Takasu et al., 2013). This can be explained by that sepsis causes a profound alteration of the renal macro- and microcirculation and is characterized by a decreased peripheral vascular resistance, maldistribution of tissue blood flow, and derangement of microcirculatory perfusion (Zarbock et al., 2014). These alterations cause a significant decrease in functional renal capillary density (Donati et al., 2013).

Liver enzymes were significantly higher in the two severe sepsis groups than the controls. Our results were in agreement with (Prin et al., 2015). As the splanchnic blood flow and cardiac output are increased in sepsis but not sufficient to counterbalance the high demands for oxygen and the inability of liver cells to extract oxygen. Vascular mechanisms of defense against portal blood flow reduction are also altered, especially the defective hepatic arterial response (Wang et al., 2014). Hypoxic hepatitis is related to hypoperfusion in the presence of hypovolemia as well as inadequate cardiac output (Henrion, 2012).

That CRP was significantly higher in the two severe sepsis groups than the controls. Additionally, CRP was significantly higher in the thrombocytopenic group than in the non-thrombocytopenic group. And this can be attributed to that CRP is an acute phase reactant synthesized in liver in response to infection or inflammation and its serum concentration can increase up to 1000-fold during acute inflammatory events and correlated well with severity of infection (Povoa et al, 2005). Other studies observed that CRP concentrations at ICU admission were associated with organ dysfunction, increased ICU length of stay, and higher mortality (Fan Shu-Ling et al., 2016).

Conclusion

In conclusion the existence of thrombocytopenia in critically ill patient is associated with bad prognosis and higher mortality.

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