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The outcome of acute kidney injury in critically ill children with septicemia

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Abstract:

Acute kidney injury is common in critically ill children admitted to intensive care unit. Sepsis remains a significant risk factor and it is the leading cause of acute kidney injury in critically ill children. The aim of the study is to evaluate the outcome of AKI in critically ill septic children. Sixty eight patients, who met criteria of sepsis and related syndromes, were classified into two groups (AKI and non- AKI groups). Patients with AKI are much younger than those without AKI. Hypervolemia is present in about 28% of patients with AKI and the pulmonary oedema is pesent in about 6% of those patients. Patients with AKI need more support as regard to inotropes, mechanical ventilation and the need for RRT [P value< 0.05] than patients without AKI. Patients with AKI have a higher PRISM score [20 vs.9] and a higher mortality rate [62% vs.8%] than patients without AKI.

In conclusion, AKI is common among critically ill children and early diagnosis is vital to prevent and decrease associated morbidity and mortality.

Key words: Acute kidney injury, Creatinine, Sepsis.

INTRODUCTION

Sepsis is one of the leading causes of death among children even in developed countries. (Kawasaki, 2017)

Acute kidney injury is common in critically ill children admitted to intensive care unit. The etiology of acute kidney injury is multifactorial and the incidence varies between 1 and 41% Alkandari et al., 2011 and Krishnamurthy, 2013 probably due to the different definitions used in clinical studies.

Sepsis remains a significant risk factor and it is the leading cause of acute kidney injury in critically ill children (Shalaby et al., 2014). There is an association of acute kidney injury with sepsis in 48.2% and 66.7% progress to septic shock (Consuelo et al., 2012).

The aim of this work is to study the outcome of AKI in critically ill septic children as regard mortality, length of hospital stay, inotropic and ventilatory support, severity of AKI, complications and the need for renal replacement therapy.

MATERIALS AND METHODS

This is a prospective observational study that was conducted in Pediatric Intensive Care Unit(PICU) and emergency room inSohag University hospital, Upper Egypt from July 2015 to December 2016.

Sixty eight children with septicemia were included in this study. Sepsis was diagnosed according to the definitions of the American College of Chest Physicians/Society of Critical Care Medicine modified specifically for pediatrics. , Goldstein et al., (2005).

AKI was defined using the serumcreatinine according to the Kidney Disease Improving Global Outcomes (KDIGO) guidelines for acute kidney injury published in 2012.The staging system defined AKI as: stage 1 --- serum creatinine increase >0.3 mg/dLor 150---200%increase (1.5- to two-fold) from baseline; stage 2 --- serum creatinineincrease >200---300% (two- to three-fold) from baseline; stage 3 --- serum creatinine increase >300% (> three-fold) from baseline.

Inclusion criteria:

All Children < 12 years of age admitted to the emergency room and Pediatric intensive care unit, and meeting criteria for septicemia were included in the study.

Exclusion criteria:

- Neonates (age less than 28 days)
- Children with a history of kidney disease.
- Children with evidence of kidney disease

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Clinical data were collected (demographic, diagnosis on admission,inotropic drugs, length of stay and outcome).For each patient, the severity of illness was calculated using thePRISM III (Pediatric risk of mortality) score of Pollack et al., (1996).

Informed consents to participate in the study were obtained from all subjects' parents. The study wasapproved by Sohag University Ethical Committees.

Laboratory Methodology:

Assay of Serum Creatinine:

Serum creatinine levels were measured by using the kinetic spectrophotometric method according to Jaffe´method without deproteinization, Mazzachi et al., (2000). This is a compensated method based onmanufacturer's instructions (Roche Diagnostics GmbH, Mannheim, Germany).

Statistical Analysis:

Data was analyzed using Statistical Package for Special Science software computer program version 16.0(SPSS Inc., Chicago, Illinois, USA). Categorical variables were expressed as number (n), percent (%) and were compared using the Chi square test or Fischer's Exact tests, as indicated. Continuous variables were compared using Mann-Whitney test and Kruskal-Wallis ANOVA, as indicated. The associations between variables were assessed by Spearman rank order correlation analysis. P value less than or equal 0.05 was considered statistically significant

Results:

This study included 68 children with septicemia. AKI was developed in 32 (47.06%) out of 68 critically ill patients.**Table** (1) shows the comparison between patients with AKI and those without AKI. It shows that patients with AKI are much younger than those without AKI but no statistically significant difference as regard the gender between the two groups.In

consistence with the definition of AKI used in this study, serum creatinine was significantly increased in critically ill children with AKI (P<0.0001).It shows a statistically significant difference as regard to the estimated GFR (35.68±16.90 vs. 93.63±23.28ml/min/1.7m2) between patients with AKI and those without AKI.

Hypervolemia is present in about 28% of patients with AKI and the pulmonary oedema is pesent in about 6% of those patients. Patients with AKI need more support as regard to inotropes, mechanical ventilation and the need for RRT [P value< 0.05] than patients without AKI. Patients with AKI have a higher PRISM score [20 vs.9] and a higher mortality rate [62% vs.8%] than patients without AKI.

When the KDIGO staging system was applied to the present study, we found totally 32(47%) patients having AKI [8 patients (11.76%) had stage 1; 13(19.12%) stage 2, and 11 (16.18%) had stage 3]as shown in table (2).

Table (2) shows that patients who developed AKI stage3 had the highest incidence of oliguria (72.7%, p = 0.001), hypervolemia (72.7%, p < 0.0001) and pulmonary oedema (18.18%) when compared to AKI stage1&2. Patients who developed AKI stage3 had the highest PRISM score and highest mortality (p = 0.006) when compared to AKI stage1&2.

Table 1: Clinical data of critically ill children (AKI patients vs. non- AKI patients).

	Non AKI	AKI	P VALUE
Number	**36(52.94%)**	**32(47.06%)**	
Age(month)	**29.41±32.16**	**9.34±12.57**	**0.0001**
Highest serum creatinine(mg/dl)	**0.46±0.13**	**1.32±0.89**	**<0.0001**
Estimated glomerularfiltration rate(ml/min/1.73m2)	**93.63±23.28**	**35.68±16.90**	**<0.0001**
Urine output *			
Normal	**36 (100%)**	**22 (68.75%)**	**<0.0001**
Low	**0**	**10 (31.25%)**	
Hypervolemia*			
No	**36 (100%)**	**23 (71.88%)**	**0.001**
Yes	**0**	**9 (28.13%)**	
Inotropes*			
No	**27 (75.00%)**	**11 (34.38%)**	**<0.0001**
Yes	**9 (25%)**	**21 (65.62%)**	
Mechanical ventilation *			
No	**31 (86.11%)**	**12 (37.50%)**	**<0.0001**
Yes	**5 (13.89%)**	**20 (62.50%)**	
Need RRT*			
No	**36 (100%)**	**23 (71.88%)**	**0.001**
Yes	**0**	**9 (28.13%)**	
PRISM III score	**9.64±4.40**	**20.17±6.65**	**<0.0001**
Length of stay (day)	**12.33±5.5**	**9.47±5.35**	**0.007**
Outcome*			
Good	**33(91.67%)**	**12 (37.50%)**	**<0.0001**
Dead	**3 (8.33%)**	**20 (62.50%)**	

***Data are represented as mean and standard deviation except* represented as frequency.**

PRISM III=pediatric risk of mortality, RRT= renal replacement therapy

Table 2: Comparison among stages of acute renal injury (AKI)

Variables	Stage 1	Stage 2	Stage 3	P value
Number	8 (11.76%)	13(19.12%)	11(16.18%)	
Urine output				
Normal	8 (100%)	11 (84.62%)	3 (27.27%)	0.001
Low	0	2 (15.38%)	8 (72.73%)	
Hypervolemia				
No	8 (100%)	12 (92.31%)	3 (27.27%)	<0.0001
Yes	0	1 (7.69%)	8 (72.73%)	
Pulmonary edema				
No	8 (100%)	13 (100%)	9 (81.82%)	0.13
Yes	0	0	2 (18.18%)	
PRISM				
Mean ± SD	15.44±4.74	18.38±5.97	25.73±4.76	0.002
(range)	(9-20.5)	(7-27.5)	(17-30)	
Length of stay (day)				
Mean ± SD				
(range)	11.28±6.63	11.0±5.82	6.36±1.12	0.04
	(4-25)	(3-21)	(4-8)	
Outcome				
Good	4 (50.00%)	8 (61.54%)	0	0.006
Dead	4 (50.00%)	5 (38.46%)	11 (100%)	

Discussion:

AKI is common among critically ill children and early diagnosis is vital to prevent and decrease associated morbidity and mortality. Sepsis remains a significant risk factor and it is the leading cause of acute kidney injury in critically ill children (Shalaby et al., 2014).

The incidence of sepsis associated AKI is variable. In our study about 47% of the patients have AKI. Riyuzoet al.2017 found an association between sepsis and AKI in 71.03% of the patients admitted to the PICU in his study. Lopes et al, 2009 demonstrated 31.4% the incidence of AKI in septic patients. Oppert et al, 2007 demonstrated 41.4% the incidence of AKI in septic patients while the incidence of AKI in septic patients was 10.3% according to Alkandari et al, 2011. Sood et al, 2014 show the incidence of AKI in patients with septic shock to be 77.6%.This difference can be explained by heterogeneity of patient population, regional differences and sample size can explain this difference.

Our study shows that patients with AKI were younger than those without AKI (P=0.0001). They also had significantly higher needs for vasopressor support and mechanical ventilation. In agreement with our results, Mehta et al, 2012 demonstrated that the young age, shock, sepsis, the need for vasopressor support and mechanical ventilation are risk factors for AKI in critically ill children. Alobaidi et al 2015 also demonstrated that Patients with sepsis-associated AKI are more likely to require mechanical ventilation and hemodynamic support with vasoactive therapy, and to receive large volumes of fluid for resuscitation

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When the KDIGO staging system was applied to the present study, we found totally 32(47%) patients having AKI [8 patients (11.76%) had stage 1; 13(19.12%) stage 2, and 11 (16.18%) had stage 3]. In contrast with Riyuzo et al.2017 who found an association between sepsis and AKI in 71.03% of the patients and he classified his patients according to KDIGO staging system to find 11 patients (14.3%) had stage 1; 23(29.9%) stage 2, and 43 (55.8%) had stage 3.Our results disagree with Kari et al., 2018 who found that AKI affected 511 children (37.4%) of his critically ill children, with (17.8%) classified as stage I (mild), (12.3%) stage II (moderate), and (7.3%) were classified as stage III (severe)

AKI had a major impact on prognosis in critically ill children. As regard to prognosis of AKI, we found that septic patients with AKI had higher PRISM score [20 vs.9] and higher mortality rate [62% vs.8%] when compared to septic patients without AKI. We also found that patients who developed AKI stage3 had the highest PRISM score and mortality (p = 0.006). Comparable to our results, Riyuzoet al.2017 found that the mortality rate was 33%, and it was higher in patients with AKI stage 2 and 3.

Our results agree with Kari et al., 2018 who found that AKI was associated with increased hospital mortality in both PICU and hospital. In-hospital mortality was six times more likely among patients with AKI as compared to patients with normal renal function in his study in Saudi Arabia. Alobaidi et al., 2015 declared that in sepsis-associated AKI, the probability of death was higher in patients classified as stage 3 AKI, when compared with those classified as stage 1.

The mortality in AKI in children also has been reported to vary widely from 16% to 43.8% [Akcan-Arikan et al 2007] [Ghani et al2009]. In our study, it was 62%, which disagree with Ghani et al., 2009 who reported 43.8% mortality in study from Kuwait. Krishnamurthy et al., 2013 reported mortality rate 46.3% in his study in India. These studies used different definitions and criteria. The wide variation in mortality rates across these studies probably reflects the different definitions for AKI used in these studies.

*Conclusion:*AKI is common among critically ill children and early diagnosis is vital to prevent and decrease associated morbidity and mortality.

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