Kidney Injury Molecule as A Urinary Biomarker in Kidney Injury in Critically Il Infants

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Abstract

Kidney injury (KI) is a major contributor toward infants mortality and morbidity and is associated with greater long-term risk of chronic kidney disease.The current diagnostic approach of KI is based on an acute decrease of GFR, as reflected by an acute rise in serum creatinine (SCr) levels and/or a decline in urine output over a given time interval, Recently several biomarkers have been proposed for the diagnosis of KI and these are in various stages of development and validation. to evaluate kidney injury molecule (KIM) as an early urinary marker for prediction of acute renal injury in infants.a comparative cross sectional study was performed on 2 groups: cases group included 30 critically ill infants who were suffering from a variety of critical conditions with mean age 6±2.1 months, their sex distribution was 40% males and 60% females. Another group (control group) of 20 healthy control subjects matched the first group in age and gender. The time period of this study was between august 2016 to august 2017. All patients were subjected to complete maternal history taking, full clinical examination and laboratory investigations including CBC, CRP, Na, K, cord PH, Urea and serum creatinine were measured since the first 24hrs (1st sample) of admission and serum creatinine was repeated after 48 h of admission (2nd sample). Critically ill infants were sub sequently discriminated ,within 48 hour of admission ,according to the criteria proposed by the AKIN ,into neonates with KI (group 1A) and infants without KI (group 1 B) , Comparative data were collected between first and second samples of hematologic investigations, renal functions , Na, K, cord pH, CRP and blood culture growth in all studied critically ill infants, cases without KI and cases with AK. Another comparison of KIM, creatinine was done between first and second samples in all studied critically ill infants , with KI and without KI. It was revealed predominance of female sex with no significant difference between groups of the study regarding age, length, and weight. No significant differences were found in hematologic investigations, renal functions, Na, K or blood culture growth at diagnosis between cases and controls as well as between critically ill infants with and without KI. It was reported significant change in creatinine level in second sample between KI patients and patients without KI and also it was revealed significant increase in KIM concentration in first sample. As well as KIM level was significantly higher in second when compared to first sample in critically ill patients with KI. KIM is a sensitive urinary biomarker in early detection of KI in infants.

Keywords: Acute kidney injury (AKI), kidney injury molecule (KIM-1),Complete blood count (CBC), C-reactive protein (CRP), Glomerular filtration rate (GFR) , Acute kidney injury network (AKIN), (AUC) area under ROC curve , Receiver operating characteristic curve (ROC).

1. Introduction

Kidney damage (KI) Previously, babies is intricate issue that fails to offer a uniform presentation [15].

Clinical indications suggesting ki happen late, yet the pathology might rapidly Advance should intense renal disappointment. Presently those analysis from claiming ki is dependent upon those expanded levels from claiming serum creatinine utilizing serial estimations furthermore on oliguria [1].

Those promptly analysis from claiming ki will be vital in the start from claiming therapy; however, the evaluation about diminished kidney work on the support for serial creatinine estimations is deferred [13].

Serum creatinine as a utilitarian kidney marker doesn't show kidney tissue injury; it best measures the amassing of the endogenous marker Concerning illustration an outcome of diminished glomerular filtration rate (GFR). [13].

On account of the occurrence of ki may be at present secondary and the result stays poor, researches have kept tabs looking into identikit new biomarkers fit to suspect the ki analysis in hours alternately much times When a pee yield decrease or SCr. Augment might be distinguished. Promptly ki analysis might bring out new perspectives Previously, restorative possibilities. Moreover, the information of novel serum Also pee biomarkers might transform those methodology to ki Furthermore camwood assistance will separate the middle of distinctive reason for made ki What's more actualizing preventive intercessions [2].

New markers for KI, for example, NGAL (neutrophil gelatinase-associated lipocalin), KIM-1 (kidney harm atom 1), and IL-18 (interleukin 18), assessed both done serum or urine, have favorable element over serum creatinine Eventually Tom's perusing straightforwardly reflecting damage of the kidney. NGAL, known as lipocalin 2, Furthermore at first portrayed Concerning illustration a oncogene communicated by numerous mankind's cells, including epithelial phones Also neutrophils [3].

KIM-1 may be very nearly only communicated on the apical surface of proximal tubule units Similarly as An light of injury, and its outflow doesn't vanish until those harm is completely determined [8].

2. Subject and methods

This case controlled study was conducted on 30 critically ill infants of both sex admitted to pediatric Intensive Care Unit (PICU) of Baha university hospital. And 20 healthy infants matching the first group in age, sex as a control group. The study was conducted during the period from August 2016 to August 2017.Two samples of blood and urine were obtained day of admission and 48 hours later. Informed consents were taken from the parents of the included infants. The study was approved by the ethical committee of Banha University. Laboratory study was done in Clinical Pathology Department at Benha University.

2.1 Inclusion Criteria

All children who are critically ill treated in the PICU aged from 1 month to 23 months .Critically ill defined as use

of mechanical ventilation, hemodynamic instability or requiring resuscitation or inotropic drugs and admitted to PICU during the study period [7].

2.2 Exclusion Criteria

Children with renal insufficiency (nephrotic syndrome, nephritic syndrome), patients who received hemodialysis, congenital kidney disease, auto immune disease related to kidney, renal malignancy.

The infants were enrolled into two groups:

Group (1) study group:

30 critically ill infants who were at risk to develop kidney injury (KI).

Group (2) control group:

The control group including 20 infants, apparently healthy with age and weight matched with the patient group with no evidence of major illness.

Methods

- History taking covering all aspects.
- Clinical Examination to whole body.
- Laboratory Investigation

Sample collection

- 1 ml of heparinized sterile arterial blood was taken for ABG and was done using 9180 Electrolyte Analyzer.

- 2 ml of blood was taken on ethylene diamine tetra-acetic salt (1.2mg/mL) as an anticoagulant, then was used for complete blood count (CBC) Done by automated hematology analyzer sysmex xs 800 (SN:63387) .
- Two ml of blood was taken on sodium citrate, as an anticoagulant and was used for measurement of PT,PTT Done by CoaDATA4004.
- Two ml of blood was taken on a plain tube (without anticoagulant) for serum separation. The tube was left at room temperature for 30 minutes till coagulation, and then was centrifuged (at 1500 rpm for 15 minutes). The resultant serum was used for clinical chemistry tests: Urea, creatinine, sodium, SGPT SGOT potassium and blood sugar. Done by BT3500.

Biomarker Assay (uKIM)

uKIM was conducted using SunRed Bio (shanghai-china) immunoassay.The outcome was devided into 2 groups, KI and non-KI group on baseline examination and according to the criteria proposed by AKI network in 2007 .

3. Results

The present study was conducted on 30 critically ill infants (18 of them develop KI and 12 did not develop KI). They were 60% females and 40% males . mean weight was 6.1±2.4 kg. In addition to 20 healthy control subjects of matched age and gender. Gender and weight did not differ significantly between both groups.

Table (1) Comparison of demographic, and anthropometric data of all studied groups.

| | | Control N=20 | | Critically ill | | | | | | P^1 | P^2 |
				All cases N=30		Without KI N=12		With KI N=18			
Female	N, %	12	60	18	60	6	54.5	12	61.5	1^Ç	0.736^Ç
Male	N, %	8	40	12	40	5	45.5	6	38.5		
Age (months)	mean±SD	7	2.1	6	1.6	6.4	1.8	6.9	1.6	0.423^ţ	0.747^ţ
	Min-max	35	41	34	40	35	40	34	40		
Length (cm)	mean±SD	42.7	14.1	48.8	1.9	49	2	48.9	1.8	0.066^ţ	0.705^ţ
	Min-max	1.7	52	45.1	51.5	45.8	51.5	45.1	51.5		
Weight (kg)	mean±SD	9.3	2	3.1	3.4	3.1	2.6	3.1	1.5	0.522^ţ	0.955^ţ

SD, standard deviation; min, minimum; max, maximum; KI, kidney injury; ţ, t test; Ç, chi square; p1, comparison between cases and control; p2, comparison between critically ill with and without AKI.

Table (2) Comparison of hematologic investigations at diagnosis of all studied groups.

| | | Control N=20 | | Critically ill | | | | | | P^1 | P^2 |
				All cases N=30		Without KI N=12		With KI N=18			
Hemoglobin	Mean± SD	13.5	2.2	14.8	2.6	15.1	2.1	14.7	2.7	0.162ţ	0.708ţ
(g/dL)	Min-max	9	16	9	20	11	18	9	20		
Hematocrit	Mean± SD	38.7	9.1	42.5	8.2	42.9	7.6	42.4	8.5	0.231ţ	0.839ţ
(%)	Min-max	6	50	24	58	31	55	24	58		
TLC	Mean± SD	13.4	3.1	13.7	4	12.8	3.7	13.9	4.1	0.848ţ	0.447ţ
($X10^9$/L)	Min-max	10	20	7	21	7	18	7	21		
Platelet	Mean± SD	244	65	201.1	58.2	208	55.9	199.2	56.9	0.110ţ	0.746ţ
($X10^9$/L)	Min-max	140	340	41	364	70	337	41	364		

SD, standard deviation; min, minimum; max, maximum; KI, kidney injury; ţ, t test; p1, comparison between cases and control; p2, comparison between critically ill with and without AKI.

Table (3) Comparison of routine investigations between first and second samples in studied critically ill infants.

		critically ill infants N=30				P
		First sample		Second sample		
Hemoglobin (g/dL)	Mean± SD	14.8	2.6	13.9	2.2	0.071
	Min-max	9	20	8	21	
Hematocrit (%)	Mean± SD	42.5	8.2	39.3	6.7	0.093
	Min-max	24	58	25	62	
TLC (X10^9/L)	Mean± SD	13.7	4	12.9	3.1	0.101
	Min-max	7	21	5	17	
Platelet (X10^9/L)	Mean± SD	201.1	58.2	196.9	49.6	0.634
	Min-max	41	364	29	349	
Urea (mg/dL)	Mean± SD	32.8	8.9	42.9	12.3	<0.001
	Min-max	14	83	20	101	
Serum Creatinine (mg/dL)	Mean± SD	0.5	0.1	1.1	0.5	0.001
	Min-max	0.3	0.9	0.4	2.5	
	Min-max	22.9	70.25	7.6	49	
Na	Mean± SD	140.2	7	140.2	5.8	0.951
	Min-max	130	154	132	156	
K	Mean± SD	3.8	0.5	4	0.7	0.106
	Min-max	2.9	5	2.4	6	

SD, standard deviation; min, minimum; max, maximum. Numerical data were tested using paired sample t test.

Table (4) Correlation of KIM level with other renal function tests in all critically ill neonates.

	critically ill infants N=30			
	KIM			
	First sample		Second sample	
	r	p	r	p
Serum creatinine	0.322	0.054	0.797	<0.001
Urea	0.228	0.320	-0.063	0.663

Pearson correlation.

4. Discussion

Our study revealed no significant difference between groups of the study regarding age, length, and weight with predominance of female sex.

S.A. Walters et al. [11], found that, there was no statistical significant difference between the studied groups regarding age and sex which was in agreement with our study. Both studies aimed to evaluate the role of kidney injury molecule (KIM) as an early marker for kidney injury (KI) in critically ill infants.

A.I. Lim et al. [10], found in their study that there was no significant difference between both sexes in the group of KI which disagree with our results.

Our study revealed non-significant change in the CBC in KI and patients without KI. And renal functions in our study revealed no significant change between KI patients and patients without KI in the first sample while significant change in creatinine level in second sample.

N.A. Abdelaal et al. [12], in their study found that in the first sample the mean of serum creatinine values were not significantly different between infants with KI compared with infants with no KI and controls, and in the second sample there was a significant increase in serum creatinine in infants with KI when compared with non KI and controls which was in agreement with our results.

Serum creatinine has a delay in rise of as much as 48 h after the injury which was in agreement with our study [14].

This disagreed wit., B.T. Workeneh [15] who reported that there is no statistically significant difference between patients who developed KI and those who did not develop KI at 48 h regarding serum creatinine.

CRP was significantly elevated in critically ill patients with no significant change in Na, K, pH between them and control group or between patients with KI and those without KI.

M.Y. Park et al. [16], in their study found that CRP as a continuous variable was found to be associated with KI which was in agreement with our results Also, Shacham and his coworkers, showed in their studies that studies reported CRP was a significant predictor for KI and clinical outcomes in cardiac surgery which run in line with our results [11].

In our study we found that there was no difference in blood culture in KI or non-KI groups.

Park and his colleagues, found in their study that there was no difference in blood culture or other hematological values in patients of KI which was in agreement with our results [16].

In our study there was a positive correlation between KI and KIM.

A.I. Lim et al. [10] concluded in their study that urinary KIM levels were significantly elevated within few hours after kidney damage which was in agreement with our study.

5. Conclusion

KIM is a sensitive urinary biomarker in early detection of KI in infants.

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