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Original Article

Urinary Protein Biomarkers and Renal Angina Index for Detection of Renal Dysfunction in Sick Full-Term Neonates

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Abstract

Background: By the help of urinary proteins, the mechanism of kidney damage can be understood and diagnosis of renal dysfunction in sick neonates can be reached. **Objective:** Usage of specific urinary proteins to assess renal function in ill full term infants with different early disorders. **Methods:** One hundred full term infants were included in this cross sectional study. They were grouped by Neonatal Therapeutic Intervention Scoring System (NTISS) into 40 healthy infants, 30 infants manifested by clinical signs of moderate disorders of early neonatal period, 19 infants manifested by severe disorders without acute kidney injury (AKI), and 11 infants manifested by severe disorders and AKI. Renal angina index was estimated, albumin/creatinine ratio and the urinary β2-microglobulin (Uβ2-MG) were evaluated. **Results:** Means (± SD) of urinary β2-microglobulin (Uβ2-MG) values, albumin/creatinine ratio (ACR) and renal angina index were significantly higher in severely sick infants with AKI group IIIB (p-value <0.5 and 0.00, 0.00 respectively). ROC curves were plotted for those three parameters to determine the best cutoff for diagnosis of AKI. Uβ2-MG >8961 ug/L exhibited a sensitivity of 100%, specificity 93.88%, ACR level >144.2 mg/g displayed a sensitivity of 81.82% and specificity of 93.88% and RAI >9 demonstrated a sensitivity of 81.82% and specificity of 87.76%. **Conclusions:** Cut off value >9 for RAI can predict the development of AKI in full term infants that is accompanied with complex disorders affecting all structural elements of the nephron, assessed by increased concentrations of urinary protein markers of glomerular (albumin/creatinine ratio) and tubular (β2-microglobulin) malfunction.

Key words: Full-term, renal malfunction, acute kidney injury, proteins, renal angina index.

Introduction

The rate of occurrence of acute kidney injury (AKI) in hospitalized critically sick infants in absence of primary renal disease is high in term and preterm neonates [1]. In infants, AKI prognosis depends on the cause and the degree of kidney injury, non-oliguric AKI has better prognosis than oliguric AKI. Regardless appropriate treatment, mortality rate may range from 25–50% [2], while survivors may suffer from problems in the long run [3]. The diagnosis of AKI is a problem, as diagnosis depends on two functional defects; increase in serum creatinine and decrease of urine output (oliguria). Both are late outcomes of the injury and not predictors for the injury [4]. Recognizing early biomarkers that are able to detect kidney injury before the rise of serum creatinine have been studied in recent decades to improve patient management and patient outcome [5]. Understanding the mechanism and diagnosing renal dysfunction in ill infants may be helped by urinary proteins. Excretion of a protein with high MW is associated with glomerular injury; while excretion of a protein with low MW is related to damage of kidney tubules [6]. Beta-2 microglobulin, is a low molecular weight protein that is freely filtered at the glomerulus and then reabsorbed at proximal renal tubules. Its increased excretion is an early reliable marker for damage of renal tubules [7]. Renal angina is a method used clinically to predict AKI in critically ill neonates [8]. For prediction of infants who are at high risk to develop severe AKI, Renal angina index can be used which can be

calculated in an easy way. It is the product of scores for the risk of AKI and clinical signs of injury as shown in Table 1 [9, 10]. The score ranges between 1and 40 and score more than 8 is considered a cutoff value that predicts renal angina [9, 10].

Thus the aim of this study is to evaluate renal function in full term infants with disorders of early neonatal period by identification of specific urinary protein biomarkers (albumin creatinine ratio & beta-2 microglobulin) and renal angina index.

Methods

Patients and study design: That cross-sectional study included 100 full-term infants; admitted in neonatal intensive care unit, Cairo University Children's Hospital between January 2019 to January 2020 to study the renal function in full-term infants (above 37 weeks) with early neonatal period disorders by the renal angina index and detecting specific protein biomarkers in their urine. They were classified according to Neonatal Therapeutic Intervention Scoring System (NTISS) [11] into 3 groups. Group I (control group) included 40 healthy infants with NTISS score zero. Group II (moderate illness group) included 30 infants manifested with clinical signs of early moderate disorders who have NTISS score 1-9. Group III (severe illness group) included 30 infants manifested with clinical signs of early severe disorders in their first week after birth and have NTISS score 10 or higher then this group is further subdivided into 19 infants without AKI (Group IIIA) and 11 infants with AKI (Group IIIB). Infants with AKI were identified on day 7 according to neonatal KDIGO (Kidney Disease Improving Global Outcomes) criteria of AKI as follows: rise of

Serum creatinine ≥ 0.3 mg/dl within 48 h or rise of serum creatinine ≥ 1.5-1.9 from baseline serum creatinine within 7 days or decrease of urine output ≤ 1 ml/kg/h [12].

Excluded from this study, all preterm neonates less than 37 weeks and neonates with renal or urinary tract anomalies defined by prenatal or postnatal abdominal ultrasound. RAI was calculated as the product of risk of AKI and clinical signs of injury scores, as shown in Table 1 [9, 10]. The Apgar score expresses the condition of the infant after birth; it is a standardized tool for assessment and provides a measure to report fetal-to-neonatal transition [13].

Analysis: Venous blood samples were drawn on day three (D3) of life from all infants for complete blood count (CBC), Serum creatinine, Serum urea, Serum electrolytes (Na, K, Ca), C-reactive protein (CRP).Venous or capillary blood samples were obtained for arterial blood gas (ABG). Urine samples were obtained on day three (D3) by sterile pediatric urine collecting bags and was divided into two parts, one for urine analysis and albumin/creatinine ratio and the other was stored for analysis of urinary β2-microglobulin (Uβ2-MG) at -20°C.

Urinary albumin was measured using routine chemistry method; urinary creatinine was measured using Jaffe method and albumin/creatinine ratio (ACR) was calculated by dividing urinary albumin concentration (mg) by urinary creatinine concentration (gm). Uβ2MG was assayed by immunonephlometry using N latex β_2 microglobulin kits (Siemens, catalogue no. OQWU15) on the system BN prospec (Siemens

healthcare diagnostics, Marburg, Germany)

Ethical considerations

The study was approved ethically by Ethical Committee of research for Faculty of Medicine, Cairo University. Informed consent from all parents of the patients was taken prior to clinical data and sample collection.

Statistical analysis

Statistical Package of Social Science (SPSS) Software program was used for data analysis. Mean and standard deviation were used to express Quantitative data (if parametric) while median and interquartile ranges were used to express quantitative data (if non-parametric). Frequencies and percentages were used to express qualitative data. Group comparison was performed using independent sample t-test and one-way ANOVA test (if parametric) and Chi square or Fissure exact test for qualitative ones. Construction of ROC curves was done for beta-2 microglobulin, albumin-creatinine ratio and renal angina index with area under curve analysis. Significant P-value was less than 0.05.

Results

No statistical significant differences was found among the groups as regards sex, gestational age, weight, length, body mass index, consanguinity, amniotic fluid state, gestational diabetes, pregnancy induced hypertension and mood of delivery among the groups (Table 2).

Group of severe illness with AKI (group IIIB) showed significantly more frequent premature rupture of membranes *(P-value=0.011)*, as it was reported in 6 patients (54.5%) while in severe illness without AKI group, it was reported in 9 patients (47.4%), in moderate illness group, it was reported in 13

patients (43.3%) and in the control group, it was reported in 6 neonates (15.0%).

Apgar score mean ± SD at 1 minute was 2.00 ± 1.26 and at 5 minute was 4.64 ± 2.16 in the group of severe illness with AKI. These scores were significantly lower when compared to other groups (P-value= 0.000, 0.000 respectively) (Table 2). The main causes for cases admission were pneumonia (30%), hypoxic-ischemic encephalopathy (31.6%), other causes include congenital heart disease (16.6%), Meconium aspiration syndrome (15%) and Infant for diabetic mother (6.6 %) (Table3).

Infants in the group of severe illness with AKI (group IIIB) had significantly more therapeutic interventions and drug loading (in the form of intensive antibiotic therapy as nephrotoxic aminoglycosides, diuretic drugs, high doses of dobutamine and dopamine and mechanical ventilation) when compared to infants in groups IIIA and II. During management in neonatal intensive care unit (NICU), the mean (± SD) score of NTISS was significantly higher in severe illness with AKI group as the score was 21.73 ± 3.50 points. In group IIIA the score was 13.63 ± 1.77 points, while in group II, the score was 5.53 ± 1.93 points (P-value II-IIIA=0.000, P-value II-IIIB=0.000, P-value IIIA- IIIB=0.000). Urine output mean ± SD (1.89 ± 0.48 ml/kg/hr) was significantly lower in severe illness with AKI group (IIIB) than other groups (P-value=0.014) (Table 4).

Serum Creatinine (median IQR) demonstrated a statistical significant difference between groups (P-value I-II=0.001, P-value I–IIIB=0.000, P-value II-IIIB=0.001, P-value IIIA-

IIIB=0.001). In addition, blood urea (median IQR) displayed significantly higher levels in the group of severe illness with AKI (group IIIB) (P-value I–IIIA=0.001, P-value I–IIIB=0.000, P-value II-IIIB=0.000, P-value IIIA-IIIB=0.000). However, serum Calcium (mean ± SD) showed significantly lower levels in severe illness with AKI group (IIIB) (P-value I-II=0.007, P value I–IIIB=0.002, P IIIA-IIIB=0.007)

Also it was demonstrated that Albumin/creatinine ratio (mean ± SD) showed a statistical significant difference between groups, as it was higher in patients with AKI than patients without AKI (233.90 ± 91.08 and 99.32 ± 30.28 respectively, P- value=0.000) (Table 5). There was a statistical significant difference between patients with and without AKI as regards urinary β2-MG (mean ± SD) as higher values were observed in patients in AKI group (IIIB) (15079.93 ± 3207.6 and 3494.22 ± 3097.94 respectively, P-value= 0.000)

Construction of ROC curves was done for Albumin-creatinine ratio and urinary β2-MG to establish the best cutoff values for diagnosis AKI. As regards albumin/creatinine ratio, area under curve (AUC^{ROC}) was 0.955 and using a cutoff value of >144.2 mg/g demonstrated a sensitivity of 81.82% and specificity of 93.88%. Regarding urinary β2-MG, AUC^{ROC} was 0.994 and using a cutoff value of >8961 ug/L displayed a sensitivity of 100.0% and specificity of 93.88% (Fig.1)

Statistically higher values of renal angina index score (mean ± SD) were observed in patients with AKI in comparison to patients without AKI (11.82 ± 5.60 and 3.67 ± 3.46 respectively, P-value <0.05). Construction of ROC

curve was done for renal angina index to establish the best cutoff for diagnosis AKI. AUC^{ROC} was 0.911 and using a cut off value of >9 gave a sensitivity 81.82%, specificity 87.76%, positive predictive value 60.0 and negative predictive value 95.6 (Fig.2).

Discussion

AKI, in the present study, affected 11 (18.3%) neonates among the 60 studied cases, 8 (72.7%) of them were males and 3 (27.3%) were females; male-female ratio was 2.6:1 with male predominance. This was in agreement with Askenazi et al., they found in a study included 58 ill full term that AKI affected 9 (15.6%) neonates, 7 (77.8%) were males and 2 (22.2%) were females which was close to our data [14].

In our study, neonates from severe illness with AKI group (group IIIB) appeared to have significantly more drug loading and therapeutic interventions than neonates in groups IIIA and II; they received antibiotic therapy as nephrotoxic aminoglycosides, diuretic drugs, high doses of dopamine and dobutamine, and required mechanical ventilation. During NICU management, the average value of NTISS score was 21.73 ± 3.50 points in group IIIB, 13.63 ± 1.77 points in group IIIA, 5.53 ± 1.93 points in group II with P-value =0.000 among different groups. This reflects the degree of suffering of this group from the severity of the already present disorders and also from the long period of intensive therapy that reflected on the extent of kidney damage.

Also the same findings were reported by a study that included 205 term infants that found the same relationship between the intake of inotropic drugs as high doses of dopamine and

dobutamine, diuretics and central nervous system drugs and the rate of occurrence of AKI. As during treatment in NICU, NTISS values in group IIIB were 18.8 ± 4.51 points, while in group IIIA, values were 12.3 ± 4.12 points and in group II values were 5.0 ± 1.48 points with P-value < 0.05 among the groups [6].

Renal dysfunction can be assessed by the already established markers serum creatinine and urine output. As regards urine output (mean ± SD) in our study; it was significantly lower in severe illness with AKI group (group IIIB) than other groups (p-value=0.014). In addition severe illness with AKI group (group IIIB) displayed significantly higher levels of serum creatinine and blood urea. This is in agreement with Hodovanets J et al., as they stated that the groups of severely ill neonates had significantly higher levels of serum creatinine and blood urea than the group of infants with moderate disorders. The group with AKI appeared to have significantly higher levels of serum creatinine when compared to the non-AKI group [6].

The highest level of Albumin/creatinine ratio (ACR) in our study was shown in patients with severe neonatal disorders and AKI. In concordance with our results, Westhoff et al. reported a high level of urinary proteins in infants with AKI when compared to ill infants without AKI [15]. Marked albuminuria in infants with AKI indicates the occurrence of non-selective proteinuria with loss of glomerular barrier properties [15, 16].

Our results showed that not only infants with AKI but also infants in NICU with moderate neonatal disorders and critically sick infants without AKI had higher values of

ACR than healthy infants. Mean ± SD of ACR ratio was 233.90 ± 91.08 mg/g in AKI group, 130.07 ± 21.95 mg/g in critically ill neonates without AKI, 79.85 ± 14.38 mg/g in neonates with moderate illness and 29.22 ± 6.63 mg/g in control group. This is explained by different degrees of kidney dysfunction with or without signs of AKI, caused by different disorders during their first week after birth.

Beta-2 microglobulin is a low molecular weight protein that is freely filtered at the glomerulus. Almost all of the filtered β2-MG is reabsorbed and catabolized by proximal renal tubules. Only very small amounts of β2-MG are excreted. Increased serum level of β2-MG indicates glomerular dysfunction, while increased urinary Uβ2-MG predicts tubular dysfunction [7].

In this study, the highest level of urinary β2-MG was detected in infants with severe neonatal disorders and AKI. These findings were in agreement with Hodovanets J, et al., who found high values of Uβ2-MG in infants with AKI when compared to ill infants without AKI [6].

Our results revealed no significant difference in β2-MG between healthy infants and infants with moderate neonatal disorders (787.23 ± 208.42 ug/L vs 1611.57 ± 490.1 ug/L with P-value > 0.05) this can be due to glomerular membrane defects with very minute or without tubular affection.

ROC curve was plotted for urinary β2-MG to determine the best cutoff for diagnosis AKI. AUC^{ROC} was 0.994 and a cutoff value of >8961 ug/L showed a sensitivity of 100.0% and a specificity of 93.88%. In a large cohort study

included 637 patients reported that urinary β2-MG was associated with AKI and the severity of AKI with nearly similar value to our study with AUC^{ROC} was 0.74 [17].

AKI in critically ill pediatrics can be predicted by renal angina index [8]. The index can be calculated as the product of scores for early signs of kidney injury and AKI risk. The score ranges between 1 and 40 and score more than 8 is considered a cutoff value that predicts renal angina [9]. Renal angina index (RAI) ≥8 on hospitalization reliably recognizes development of severe AKI in critically ill infants with accuracy supersedes that of creatinine alone [18].

In this study, the mean ± SD of renal angina index was 11.82 ± 5.60 significantly higher in severely ill neonates with AKI (p-value=0.000). While Basu et al. and Kaur et al. found that higher value of RAI score (≥12 or ≥20) was significantly associated with increased severe AKI risk [9, 19].

ROC curve was plotted for renal angina index to determine the best cutoff for diagnosis of AKI. AUC^{ROC} was 0.911 and the cut off value of RAI was >9 with sensitivity 81.82%, specificity 87.76%, positive predictive value 60.0 and negative predictive value 95.6. Close to our study, Gauadia et al., reported that AUC^{ROC} was 0.90 and the cut off value of RAI was >8 with sensitivity 96.9%, specificity 75.4%, positive predictive value 72.0 and negative predictive value 97.4 [18].

There are some limitations that faced this study; one of these is financial limitation that restricted the number of participants to 100 infants. Also indwelling urinary catheters in neonates were not available sufficiently for urine sampling.

Conclusions

Renal angina index with cut off value of more than 9 can predict the development of AKI in full term infants that is accompanied with complex disorders affecting all structural elements of the nephron, identified by increased levels of urinary protein markers of glomerular (albumin-creatinine ratio) and tubular (β2-microglobulin) malfunction.

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Author's contributions

Authors contributed equally in the study concept, design, supervision, methodology, statistical analysis and data collection.

Conflict of interest

The authors have no conflict of interests to declare.

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References

1- Chaturvedi S, Ng KH, Mammen C. The path to chronic kidney disease following acute kidney injury: a neonatal perspective. Pediatr Nephrol. 2017; 32:227–241.

2- Agras PI, Tarcan A, Baskin E, Cengiz N, Gurakan B, Saatci U. Acute renal failure in the neonatal period. Renal Failure. 2004; 26:305–309.

3- Abitbol CL, Bauer CR, Montane B, Chandar J, Duara S, Zilleruelo G. Long-term follow-up of extremely low birth weight infants with neonatal renal failure. Pediatr Nephrol. 2003; 18:887–893.

4- Jetton JG, Askenazi DJ. Update on acute kidney injury in the neonate. Curr Opin Pediatr. 2012; 24:191–196.

5- Selewski DT, Charlton JR, Jetton JG, Guillet R, Mhanna MJ, Askenazi DJ, et al. Neonatal acute kidney injury. Pediatrics. 2015; 136(2):463-473.

6- Hodovanets J, Babintseva A, Longford N T, Agafonova L. Urinary protein markers of renal dysfunction in full-term newborns with disorders of early neonatal period. Journal of Pediatric and Neonatal Individualized Medicine (JPNIM) 2018; 7(1): 70-109.

7- Guder WG, Hofman W. Markers for the diagnosis and monitoring of renal tubular lesions. Clin Nephrol. 2010; 152:178–184.

8- Goldstein SL, Chawla LS. Renal angina. Clin J Am Soc Nephrol. 2010; 5:943–949.

9- Menon S, Goldstein SL, Mottes T, Fei L, Kaddourah A, Terrell T, *et al.* Urinary biomarker incorporation into the Renal Angina Index early in intensive care unit admission optimizes acute kidney injury prediction in critically ill children. Nephrol DialTransplant 2016; 31:586-94.

10- Basu RK, Wang Y, Wong HR, Chawla LS, Wheeler DS, Goldstein SL et al. Incorporation of biomarkers with the renal angina index for prediction of severe AKI in critically ill children. Clin J Am Soc Nephrol. 2014; 9: 654–662.

11- Gray JE, Richardson DK, Mccormick MC, Workman-Daniels K, Goldmann DA. Neonatal Therapeutic Intervention Scoring System: a therapy-based severity-of-illness index. Pediatrics. 1992; 90:561–567.

12- Jetton JG, Guillet R, Askenazi DJ, Dill L, Jacobs J, Kent AL, et al. Neonatal Kidney Collaborative. Assessment of Worldwide Acute Kidney Injury Epidemiology in Neonates: Design of a Retrospective Cohort Study. Front Pediatr. 2016; 4:68.

13- Papile LA. The Apgar score in the 21st century. N Engl J Med 2001;344:519–520

14- Askenazi DJ, Koralkar R, Hundley HE, Montesanti A, Patil N, Ambalavanan N. Fluid overload and mortality are associated with acute kidney injury in sick near-term/term neonate. Pediatr Nephrol. 2013; 28(4):661–666.

15- Westhoff JH, Tönshoff B, Waldherr S, Pöschl J, Teufel U, Westhoff TH, et al. Urinary tissue inhibitor of Metalloproteinase-2 (TIMP-2) • Insulin-Like Growth Factor-Binding Protein 7 (IGFBP7) predicts adverse outcome in pediatric acute kidney injury. PLoS ONE. 2015; 10(11):e0143628.

16- Josep C and Gattineni J. Proteinuria and Hematuria in the Neonate. Curr Opin Pediatr. 2016; 28(2): 202–208.

17- Barton K, Kakajiwala A, Dietzen DJ, Goss CW, GU H and Dharnidharka VR. Using the newer Kidney Disease: Improving Global Disease: Improving Global Outcomes criteria beta-2-microglobulin levels, associate with severity of acute kidney injury. Kidney Journal. 2018; 11(6): 797–802.

18- Gawadia J, Mishra k, Kumar M, Saikia D. Prediction of Severe Acute Kidney Injury using Renal Angina Index in a Pediatric Intensive Care Unit. Indian Pediatr 2019; 56: 647–652

19- Kaur R, Dhooria Gs, Pooni PA, Bhat D, Bhargava S, Kakkar S, et al. Utilization of the renal angina index in PICU of a developing country for prediction of subsequent severe acute kidney injury. Pediatr Nephrol. 2018; 33(11):2185-2191.

Table 1: The renal angina index (RAI). Patients are stratified depending on the risk for developing acute kidney injury (AKI) and signs of injury [9, 10].

Table 1: Renal Angina Index (RIA)	**Score**
Acute kidney injury risk strata	
Moderate risk: PICU admission	1
High risk: History of bone marrow or solid organ transplantation	3
Very high risk: Ventilation and inotrope use	5
Clinical injury signs	
<5% fluid overload or no change in eCrCl	1
5% to <10% fluid overload or decrease in eCrCl by 0%‑24%	2
10% to <15% fluid overload or decrease in eCrCl by 25%‑49%	4
≥15% fluid overload or decrease in eCrCl by ≥50%	8

eCrCl: Estimated creatinine clearance, PICU: Pediatric intensive care unit

Table 2: Demographic and clinical data of the studied groups

Parameter		**Control group (I)**	**Moderate illness (II)**	**Severe illness (III)**		**P-value**
				Without AKI (IIIA)	**With AKI (IIIB)**	
		No. (%)	**No. (%)**	**No. (%)**	**No. (%)**	
Sex	Female	17 (42.5%)	13 (43.3%)	8 (42.1%)	3 (27.3%)	0.808
	Male	23 (57.5%)	17 (56.7%)	11 (57.9%)	8 (72.7%)	
Weight (Kg)	Mean ± SD	3.23 ± 0.63	3.17 ± 0.45	3.05 ± 0.60	3.17 ± 0.18	0.703
	Range	2.1 – 4.4	2.5 – 4.2	2.1 – 4.2	2.9 – 3.4	
Length (cm)	Mean ± SD	52.88 ± 4.85	51.67 ± 2.14	50.89 ± 4.42	51.18 ± 1.33	0.234
	Range	44 – 60	49 – 58	44 – 58	49 – 53	
Body mass index(BMI)	Mean ± SD	11.43 ± 0.36	11.84 ± 1.00	11.69 ± 0.64	11.71 ± 0.50	0.096
	Range	10.82 – 12.23	10.6 – 14.7	10.8 – 13.88	11.00 – 12.80	
Apgar score at 1 min.	Mean ± SD	4.68 ± 0.47	4.03 ± 0.85	3.16 ± 0.69	2.00 ± 1.26	0.000
	Range	4 – 5	2 – 5	2 – 4	1 – 4	
Apgar score at 5 min.	Mean ± SD	9.38 ± 0.81	8.30 ± 1.32	6.74 ± 1.15	4.64 ± 2.16	0.000
	Range	8 – 10	6 – 10	5 – 9	3 – 8	
Gestational age by weeks	Mean ± SD	39.00 ± 1.21	38.72 ± 1.00	38.37 ± 1.12	38.64 ± 1.12	0.243
	Range	37 – 41	37 – 41	37 – 41	37 – 41	

P-value <0.05: Significant

Table 3: Admission diagnosis of cases of the study

Admission diagnosis	Moderate illness (II)		Severe illness (III)			
			Without AKI (IIIA)		With AKI (IIIB)	
	No.	%	No.	%	No.	%
Congenital pneumonia	12	40.0%	4	21.1%	2	18.2%
Infant of diabetic(IDM)	4	13.3%	0	0.0%	0	0.0%
Congenital heart disease (CHD)	5	16.7%	3	15.8%	2	18.2%
Meconium aspiration syndrome (MAS)	3	10.0%	4	21.1%	2	18.2%
Mild hypoxic ischemic-encephalopathy (HIE)	6	20.0%	0	0.0%	0	0.0%
Moderate hypoxic ischemic-encephalopathy (HIE)	0	0.0%	8	42.1%	0	0.0%
Severe hypoxic ischemic- encephalopathy (HIE)	0	0.0%	0	0.0%	5	45.5%

P-value <0.05: Significant

Table 4: Renal functions tests and urine chemistry among study groups

Day 3 Renal functions		Control group (I)	Moderate illness (II)	Severe illness (III)		P-value
				Without AKI (IIIA)	With AKI (IIIB)	
		No. = 40	No. = 30	No. = 19	No. = 11	
Urine output (ml/kg/hr)	Mean ± SD	2.29 ± 0.39	2.47 ± 0.54	2.19 ± 0.67	1.89 ± 0.48	0.014
Serum Creatinine (mg/dL)	Median (IQR) Range	0.7 (0.5–0.9) 0.3– 1	0.95 (0.8–1.1) 0.5–1.4	0.9 (0.7–1.1) 0.5–1.3	1.3 (1.1–1.5) 0.9–1.7	0.000
Blood Urea (mg/dL)	Median(IQR) Range	25 (17.5–31.5) 11–61	31.5 (25–44) 4–51	33 (30–44) 22–55	60 (43–70) 39–117	0.000
Serum Na (mmol/L)	Mean ± SD Range	138.63 ± 5.25 130–148	138.97 ± 7.33 125–155	139.16 ± 7.51 125–155	136.00 ± 7.55 122–148	0.593
Serum Ca (mg/dL)	Mean ± SD Range	9.16 ± 0.45 8–9.9	8.82 ± 0.62 7.5–10.1	9.13 ± 0.45 8.5–9.9	8.59 ± 0.54 7.8–9.3	0.002
Serum K (mmol/L)	Mean ± SD Range	4.95 – 0.22 3.9– 5.5	4.69 ± 0.72 3.4–6	4.70 ± 0.67 3.8–6	5.05 ± 0.59 4.3–5.8	0.185
CRP (mg/dL)	Negative Positive(>6)	40 (100.0%) 0 (0.0%)	25 (83.3%) 5 (16.7%)	14 (73.7%) 5 (26.3%)	5 (45.5%) 6 (51.5%)	0.000
Albumin-creatinine ratio (ACR) mg/g	Mean ± SD Range	29.22 ± 6.63 19.7–49	79.85 ± 14.38 40.45–110.5	130.07 ± 21. 9 59.45–165.52	233.9± 91.0 124.5–400	0.000
Beta2 microglobulin (Uβ2-MG) ug/L	Mean ± SD Range	787.2± 208.4 368.6–1096.5	1611.5±490.1 602.4–2236.5	6466.8±3157.6 609.8–9746.2	5079.9±3207.6 9150–19425.64	0.000

P-value <0.05: Significant

Table 5: urine chemistry and renal angina index among patient groups

Day 3 Urine chemistry		Moderate illness +Severe illness Without AKI	Severe illness With AKI	P-value
		No. = 49	**No. = 11**	
Albumin-creatinine ratio mg/g	Mean ± SD	99.32 ± 30.28	233.90 ± 91.08	0.000
	Range	40.45 – 165.52	124.5–400	
Urinary beta2 microglobulin ug/L	Mean ± SD	3494.22 ± 3097.94	15079.93±3207.6	0.000
	Range	602.48 – 9746.2	9150–19425.64	
Renal angina index	Mean ± SD	3.67 ± 3.46	11.82 ± 5.60	0.000
	Range	1 – 10	5 – 20	

P-value <0.05: Significant
AKI: acute kidney injury

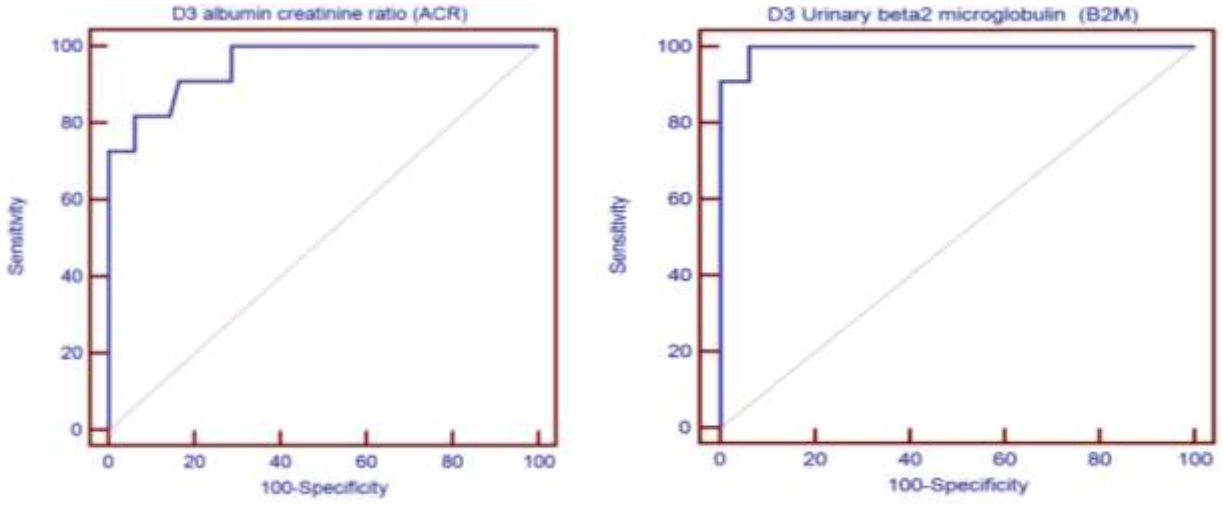

Fig. 1: Receiver operator characteristic (ROC) curve for diagnostic accuracy of Albumin-creatinine ratio and urinary beta2 microglobulin (Uβ2-MG) in discriminating patients with AKI and patients without AKI

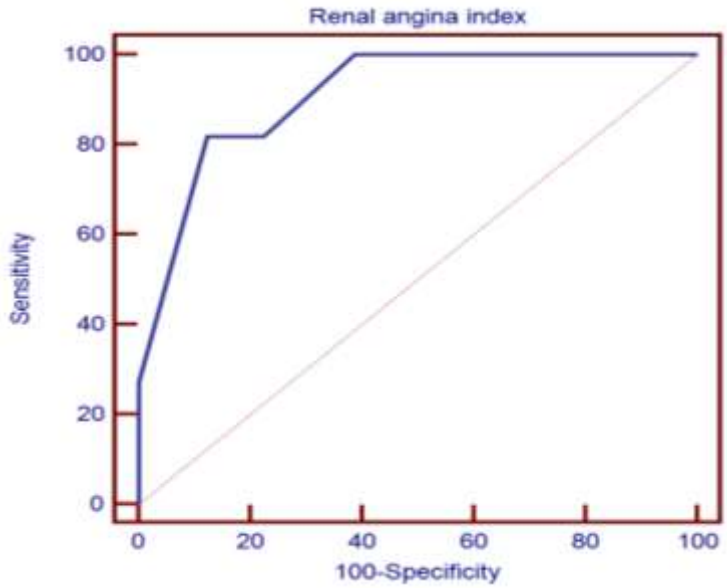

Fig 2: Receiver operator characteristic (ROC) curve for diagnostic accuracy of RAI score in discriminating patients with AKI and patients without AKI

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