URINE ALBUMIN CREATININE RATIO AS A PREDI CTOR OF RENAL INJURY IN SEPTIC CHILDREN

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Abstract

Background: The pediatric intensive care unit (PICU) plays an important role in delivering demanding and required care to seriously ill children. In both developing and developed countries, PICU children have a considerably higher risk of morbidity and death**.** The aim of this study was to assess the urine albumin creatinine ratio as predictor of renal injury in septic children and it's role in predicting PICU outcomes.
Methods: This study was carried out in Pediatric Intensive Care Unit and clinical pathology department at Zagazig University Hospitals in the period from April 2022 to October 2022. It was approved by Institutional Review Board- Zagazig University (IRB 9482). Written informed consent was taken from all parents.
Results: Our study revealed that, blood culture was positive in 80.9% of patients and 44.1% had sepsis degree 3. In the current study, PRISM-III score ranged from 4 to 28 with median 14.5. p-SOFA on admission ranged from 3 to 19 with median 9. P-SOFA after 48 hours ranged from 3 to 20 with median 10. Glasgow coma scale ranged from 4 to 14 with mean 9.4. In the current study, median albumin/creatinine ratio on admission was 319 mg/g which significantly decreased to 253 mg/g after 24 hours. Thirty-five patients (51.5%) had increasing ACR and 33 patients had decreasing ACR. Concerning cause of admission, 39.7%, 20.6% and 11.8% of patients had respiratory, neurology and hepatic diseases respectively. In our study regarding outcome, thirty three patients survived till end of study (48.5%). In the present study, there is statistically significant very strong positive correlation between albumin/creatinine ratio on admission and after 24 hours and PRISM-III scores. In this study, there is statistically significant very strong positive correlation between albumin/creatinine ratio on admission and after 24 hours and p-SOFA scores on admission and after 48 hours. In this study, there is statistically significant negative correlation between albumin/creatinine ratio on admission and after 24 hours and Glasgow coma score. In the present study, there is statistically significant positive correlation between PICU stay and all of albumin/creatinine ratio on admission and after 24 hours, PRISM-III, p-SOFA on admission and after 48 hours.
Conclusion: In conclusion, elevated urinary ACR is associated with the severity of sepsis, morbidity, and mortality. ACR was found to have significant relation to the need for inotropes. In addition, ACR had a good correlation to the duration of the PICU stay. ACR is an easy, cost-effective, and reliable test for predicting morbidity and mortality in a PICU setting.

Keywords: Urine Albumin Creatinine Ratio - Predictor – Renal Injury - Septic Children

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1. Introduction

The pediatric intensive care unit (PICU) plays an important role in delivering demanding and required care to seriously ill children. In both developing and developed countries, PICU children have a considerably higher risk of morbidity and death (1).

Sepsis is the leading cause of death worldwide in the pediatric population resulting in an estimated 7.5 million deaths annually (2).

Predicting morbidity and mortality in pediatric intensive care units is of extreme importance and can be challenging. Appropriate prediction helps to make the right decisions and thereby improve outcomes (3).

An early feature of the acute inflammatory process is capillary endothelial cell activation accompanied by a rapid increase in capillary permeability to plasma proteins such as albumin. The extent of albuminuria is variable, and most instances are not measured by urine dipstick protein estimation, hence known as microalbuminuria (4)

The microalbuminuria can be measured by spot urine albumin creatinine ratio (ACR) (5). The ACR is a simple, easy, and non-invasive measure that can be a good predictor of PICU outcome (6).

AKIs are independently associated with increased morbidity and mortality (7). Current management guidelines for patients with AKI recommend that early recognition of AKI risks and augmentation of supportive care will limit AKI progression (8). According to the 2012 KDIGO criteria, the definition of AKI depends on serum creatinine and urine volume. The accuracy of any creatinine-based or urine volume-based classification is likely to be affected by age, pre-existing sarcopenia, catabolism and fluid intake and diuretic, respectively (8).

Due to the uncertainty of serum creatinine and urine volume, the diagnosis of AKI is often delayed, which creates great obstacles for effective early intervention.

One of the ways to solve this problem is to combine other clinical indicators to alleviate the uncertainty of creatinine and urine volume in judging renal function. According to reports, RAI can improve accuracy for prediction of AKIs in critically ill children and young adults (9).

Quality and quantities of PICUs are improving in developing countries, but it is an uphill process, as the units need modern, expensive equipment and a large highly trained staff. So there is a need for time to employ methods, techniques, and scoring systems that are predictive of mortality and morbidity risk in these patients, thus allowing these systems to assist intimely and focused decisions regarding the deployment of different expertise and resources, to produce highly productive results (10).

The aim of this study was to assess the urine albumin creatinine ratio as predictor of renal injury in septic children and it's role in predicting PICU outcomes and compare it with other scores that predicting mortality.

Patients and Methods

This study was carried out in Pediatric Intensive Care Unit and clinical pathology department at Zagazig University Hospitals in the period from April 2022 to October 2022. It was approved by Institutional Review Board- Zagazig University (IRB 9482). Written informed consent was taken from all parents.

Patients:

From 200 patients admitted to Pediatric Intensive Care Unit, Children's Hospital Zagazig University. Sixty eight patients were included aged between1month and 14 years , critically ill patients , diagnosed as sepsis by Systemic inflammatory response syndrome (SIRS) criteria and documented infection. SIRS is an exaggerated defense response of the body to a noxious stressor (infection, trauma, surgery, acute inflammation, ischemia or reperfusion, or malignancy, to name a few) to localize and then eliminate the endogenous or exogenous source of the insult (11).

SIRS is defined by the satisfaction of any two of the criteria below:

-Body temperature over 38 or under 36 degrees Celsius.

-Heart rate greater than 90 beats/minute

-Respiratory rate greater than 20 breaths/minute or partial pressure ofCO_2 less than 32 mmHg

-Leukocyte count greater than 12000 or less than 4000 /microliters or over 10% immature forms or bands.

Sepsis was classified into:

-**SEPSIS**

SIRS+ infection (or suspected infection)

-**SEVERE SEPSIS**

Sepsis + CV dysfunction or ARDS or 2 other dysfunctional organs

-**SEPTIC SHOCK**

Sepsis+ CV dysfunction

Exclusion criteria:

- Patients with chronic renal disease
-Acute kidney injury
-Urinary tract infections
-Nephrotic syndrome
-Acute glomerulonephritis
- Nephrotoxic drugs.

2. Methods

Operational design

All participants were subjected to the followings:

1- Subjective global assessment (full history taking: name ,age ,sex)

2- Anthropometric measurements.

3- Clinical examination (General, Neurological, Respiratory, Cardiovascular,Gastrointestinal).

4- Routine laboratory testing including:

a -Complete Blood Count: done on automated cell counter, model XN 330(Sysmex, Japan)

b- Coagulation profile: done on automated blood coagulation analyzer, model CS 2100 (Sysmex, Japan)

c- Blood chemistrytesting including

-Liver and kidney function tests

Blood glucose

-Procalcitonin and C-reactive protein These tests performed on Roche Cobas as 8000 auto analyzer, using dedicated reagents supplied by the manufacturer (Roche diagnostics, Switzerland).

d-Arterial blood gases and electrolytes by Blood Gas Analysis ABG Radiometer ABL80 Flex Basic Device, Denmark. Bacteriological examination: Blood culture, Cultures done to the samples from different sites include: tracheal aspirate,CSF , urine and CVC according to every case Specific research test : (Measurement of albumin creatinine ratio). The test was performed on admission within 1 h and after 24 hrs.It was performed on Cobas 6000 auto analyzer, c 501 module ,using dedicated reagent according to manufacturer recommendation (Roche diagnostics, Switzerland).

-Test principle : immunoturbidemetric assay for urine albumin while kinetic colourmetric assay which is based on Jaffe method was used for urine creatinine estimation.

-Specimen collection and preparation: spot urine sample was used The sample was collected in a sterile urine cup. No preservative was added to the urine sample

The urine samples containing precipitates were centrifuged before the assay.

Sample stability: stable for 2 days at (15 - 25 °C), 6 days at (2 - 8°C) and for 3weeks at (-15) -(-20) °C.

-Calculation : Cobas c System automatically calculate the concentration of urine albumin and urine creatinine for each sample. The laboratory data manager of Zagazig University hospitals reports the results of the test in milligrams of albumin per gram of creatinine

-Expected values : < 30 mg albumin per gram of creatinine.

5- Calculation of Pediatric Risk of Mortality score (PRISM III), pediatric Sequential Organ Failure Assessment (p-SOFA) score were done on admission and repeated p-SOFA after 48hrs was done.

6- Follow up patients as regard to PICU stay, need for inotropes ,developmentof multiple organ dysfunction syndrome (MODS),recovery or mortality was done.

Table 1: PRISM III score

Variables	Age restrictions and Range		Score
Systolic blood pressure in mm Hg	Infants 130-160 55-65 >160 40-54 < 40	Children 50-200 65-75 >200 50-64 <50	 2 6 7
Diastolic blood pressure in mm Hg	All ages >110		6
Heart rate in beats per minute	Infants > 160 <90	Children > 150 < 80	 4 4
Respiratory rate in breaths per minute	Infants 61-90 >90 apnea	Children 51-70 > 70 apnea	 1 5 5
PaO2/FiO2	All ages	200-300 <200	2 3
PaCO2 in torr (mm Hg)	All ages	51-65 >65	1 5
Glasgow coma score	All ages	<8	6
Pupillary reactions	All ages	Unequal or dilated Fixed and dilated	4 10
PT/PTT	All ages	1.5 times control	2
Total bilirubin mg/dL	>1 month	> 3.5	6
Potassium in mEq/L	All ages	3.0-3.5 6.5-7.5 < 3.0 > 7.5	1 1 5 5
Calcium in mg/dL	All ages	7.0-8.0 12.0-15.0 <7.0 >15.0	2 2 6 6
Glucose in mg/dL	all ages	40-60 250-400 <40 >400	4 4 8 8
Bicarbonate in mEq/L	all ages	<16 >32	3 3

Table (2):Pediatric Sequential Organ Failure Assessment (pSOFA)Score(El-Mashad et al.,2020).

Variables	Score				
	0	1	2	3	4
Respiratory					
PaO2:FiO2 or	≥400	300-399	200-299	100-199 With respiratory support	<100 With respiratory support
SpO2:FiO2	≥292	264-291	221-264	148-220 With respiratory support	<148 With respiratory support
Coagulation					
Platelet count, $\times 10^3$ /µL	≥150	100-149	50-99	20-49	<20
Hepatic					
Bilirubin, mg/dL	<1.2	1.2-1.9	2.0-5.9	6.0-11.9	>12.0
Cardiovascular					
MAP by age group or vasoactive infusion, mm Hg or µg/kg/min[d]					
<1 mo	≥46	<46	Dopamine hydrochloride ≤5 or dobutamine hydrochloride (any)	Dopamine hydrochloride >5 or epinephrine ≤0.1 or norepinephrine bitartrate ≤0.1	Dopamine hydrochloride >15 or epinephrine >0.1 or norepinephrine bitartrate >0.1
1-11 mo	≥55	<55			
12-23 mo	≥60	<60			
24-59 mo	≥62	<62			
60-143 mo	≥65	<65			
144-216 mo	≥67	<67			
>216 mo	≥70	<70			
Neurologic					
Glasgow Coma Score[f]	15	13-14	10-12	6-9	<6
Renal					
Creatinine by age group, mg/dL					
<1 mo	<0.8	0.8-0.9	1.0-1.1	1.2-1.5	≥1.6

1-11 mo	<0.3	0.3-0.4	0.5-0.7	0.8-1.1	≥1.2
12-23 mo	<0.4	0.4-0.5	0.6-1.0	1.1-1.4	≥1.5
24-59 mo	<0.6	0.6-0.8	0.9-1.5	1.6-2.2	≥2.3
60-143 mo	<0.7	0.7-1.0	1.1-1.7	1.8-2.5	≥2.6
144-216 mo	<1.0	1.0-1.6	1.7-2.8	2.9-4.1	≥4.2
>216 mo	<1.2	1.2-1.9	2.0-3.4	3.5-4.9	≥5

The pSOFA score was calculated on admission and repeated after 48 hrs PaO2 was measured in millimeters of mercury. Only SpO2 measurements of 97% or lower were used in the calculation. MAP (measured in millimeters of mercury) was used for scores 0 and 1; vasoactive infusion (measured in micrograms per kiligram per minute), for scores 2 to 4. Maximum continuous vasoactive infusion was administered for at least 1 hour. Cutoffs for patients older than 18 years (216 months) were identical to the original SOFA score. Glasgow Coma Scale was calculated using the pediatric scale.

Statistical analysis:

The data were coded, entered and processed on computer using Statistical package for social science (SPSS) (version24).The results were represented in tabular and diagrammatic forms then interpreted.

Mean, standard deviation, range, frequency, and percentage were use as descriptive statistics.

The following test was done:

- **Chi-Square testX²** was used to test the association variables for categorical data.
- **Student's t-test** was used to assess the statistical significance of the difference between two population means in a study involving independent samples.
- **ANOVA (F test)** For normally quantitative variables, to compare between more than two groups, and Post Hoc test (LSD) for pairwise comparisons
- **. r→Pearson's Product correlation coefficient:** it evaluates the linear association between 2 quantitative variables (one is the independent var.X, and the other is the dependent var., Y). value of "r" ranges from -1 to 1

0= no linear correlation

1= perfect positive correlation

-1 = perfect negative correlation

Positive= increase in the independent variable leads to increase in the dependent variable

Negative = increase in the independent variable leads to decrease in the dependent variable.

- **ROC curve** = receiver operator characteristic curve,

Sensitivity = ability of the test to detect the true +ve cases with minimal false negatives

Specificity = ability of the test to detect the true –ve cases with minimal false positives

PPV= positive predictive value= probability that an individual with +ve test result (≥cut off value) has the condition.

NPV=negative predictive value = probability that an individual with –ve test result **don't have** the condition.

The accepted level of significance in this work was stated at 0.05 (P <0.05 was considered significant),.P value >0.05 is non-significant (N-S)

2. Results:

Table (1) Distribution of studied patients according to their charactaristics:

	N=68	%
Gender:		
Female	32	47.1%
Male	36	52.9%
	Median (IQR)	**Range**
Age (months):	1 (6 months – 6 years and 9 months)	One month – 14 years
MV:		
No	28	41.2%
Yes	40	58.8%
Inotropes		

Yes	43	63.2%
No	25	36.8%

	Mean ± SD	Range
Systolic blood pressure (mmHg)	82.63 ± 16.09	50 – 120
Diastolic blood pressure (mmHg)	49.6 ± 11.9	30 – 80
Heart rate (beat/minute)	141.07 ± 26.04	40 – 185
Respiratory rate (/minute)	39.1 ± 9.28	20 – 65
GCS	9.4 ± 2.35	4 – 14
	Median (IQR)	**Range**
PRISM III	14.5 (11 – 20)	4 – 28
P-SOFA on admission	9 (5.25 – 15)	3 – 19
P-SOFA after 48 hours	10 (5 – 17)	3 – 20
Pupillary reaction		
Irreactive	1	1.5%
Dilated fixed	1	1.5%
RRR	62	91.2%
Unequal	4	5.9%
GCS	9.4 ± 2.35	4 – 14
Sepsis degree		
sepsis	22	32.4%
sever sepsis	16	23.5%
septic shock	30	44.1%
Length of PICU stay	15.5 (8 – 19)	5 – 28
Outcome		
Survivors	33	48.5%
Non-survivors	35	51.5%

Table (2) Distribution of studied patients according to vital data and scores:

MV mechanical ventillation GCS glassco coma scale RRR round, regular, reactive This study included 68 patients with age range from one month to 14 years and females represented 47.1%. Larger percentage of patients (91.2%) had round regular reactive pupil. Forty patients (58.8%) underwent mechanical ventilation and forty three patients received inotropes and 44.1% had sepsis degree 3. Regarding outcome, thirty three patients survived till discharge (48.5%). Length of PICU stay ranged from 5 to 28 days with median 15.5 days

Mean systolic and diastolic blood pressure were 82.63 and 49.6 mmHg respectively. mean heart rate was 141.07 beat/minute while mean respiratory rate was 39.1 per minute. Glasgow coma scale ranged from 4 to 14 with mean 9.4.

PRISM-III score ranged from 4 to 28 with median 14.5. p-SOFA on admission ranged from 3 to 19 with median 9. P-SOFA after 48 hours ranged from 3 to 20 with median 10.

Table (3) Distribution of studied patients according to cause of admission:

	N=68	%
Cause of admission		
Cardiac	6	8.8%
GIT	2	2.9%
Endocrine	2	2.9%
Hematology	2	2.9%
Hepatic	8	11.8%
Metabolic	2	2.9%
Neurology	14	20.6%

Oncology	2	2.9%
Respiratory	30	44.1%

Most common cause of admission is respiratory 44.1% .

Table (4) Distribution of studied patients according to ACR on admission and after 24 hours:

	Median (IQR)	Range	p
On admission	319 (119.75 – 766.25)	32 – 9212	<0.001**
After 24 hours	253 (94.25 – 897.5)	6.6 – 5340	
% change in ACR	35.1 (-59.33, 132.75)		
	N=68	**%**	
Increasing ACR	35	51.5%	
Decreasing ACR	33	48.5%	

p for Wilcoxon signed rank test **p≤0.001 is statistically highly significant

Median albumin/creatinine ratio on admission was 319 mg/g which significantly decreased to 253 mg/g after 24 hours. Thirty-five patients (51.5%) had increasing ACR and 33 patients had decreasing ACR.

Table (5) Correlation between ACR on admission and on 24th hour later and laboratory data:

	ACR on admission		ACR at 24th	
	r	p	r	p
Age (months)	-0.363	0.002*	-0.305	0.011*
Gender	0.102	0.408	-0.021	0.865
Weight (kg)	-0.345	0.004*	-0.3	0.013*
Hemoglobin (g/dl)	-0.405	0.001**	-0.373	0.002*
WBCS(10^3/mm^3)	0.031	0.802	0.046	0.709
Platelet count (10^3/mm^3)	-0.475	<0.001**	-0.44	<0.001**
CRP	0.551	<0.001**	0.544	<0.001**
Procalcitonin	0.533	<0.001**	0.458	<0.001**
Systolic blood pressure(mmHg)	-0.709	<0.001**	-0.692	<0.001**
Diastolic blood pressure (mmHg)	-0.641	<0.001**	-0.608	<0.001**
Heart rate (beat/minute)	0.538	<0.001**	0.524	<0.001**
Respiratory rate (/minute)	0.468	<0.001**	0.498	<0.001**
Bilirubin (mg/dl)	0.601	<0.001**	0.594	<0.001**
Serum potassium (mg/dl)	-0.673	<0.001**	-0.465	<0.001**
Serum calcium (mg/dl)	-0.556	<0.001**	-0.462	<0.001**
Blood glucose (mg/dl)	-0.536	<0.001**	-0.445	<0.001**
Serum bicarbonate (mEq/L)	-0.114	0.357	-0.096	0.438
PaO_2/FiO_2	-0.513	<0.001**	-0.489	<0.001**
$PaCO_2$ (mmHg)	0.341	<0.001**	0.47	<0.001**
PT	0.431	<0.001**	0.48	<0.001**
PTT	0.374	0.002*	0.356	0.003*
Sepsis degree	0.812	<0.001**	0.736	<0.001**

r Spearman rank correlation coefficient *p<0.05 is statistically significant **p≤0.001 is statistically highly significant There is statistically significant positive correlation between albumin/creatinine ratio on admission and each of heart rate, respiratory rate, total bilirubin, CRP, procalcitonin, PaCO2, PT, PTT and sepsis degree but significant negative correlation as regard the others .There is statistically significant positive correlation between albumin/creatinine ratio after 24 hours and each of diastolic blood pressure, heart rate, respiratory rate, total bilirubin, CRP, procalcitonin, PaCO2, PT, PTT and sepsis degree but significant negative correlationas regard the others

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Table (6) Correlation between ACR on admission and on 24th hour later and PRISM -III score:

	r	p
ACR on admission	0.977	<0.001**
ACR at 24th hour	0.806	<0.001**

r Spearman rank correlation coefficient *p<0.05 is statistically significant **p≤0.001 is statistically highly significant There is statistically significant strong positive correlation between albumin/creatinine ratio on admission and after 24 hours and PRISM-III score.

Table (7) Correlation between ACR on admission and on 24th hour later and P-SOFA score:

	p-SOFA on admission		p-SOFA at 24th	
	r	p	r	p
ACR on admission	0.953	<0.001**	0.814	<0.001**
ACR at 24th hour	0.798	<0.001**	0.935	<0.001**

r Spearman rank correlation coefficient **p≤0.001 is statistically highly significant
There is statistically significant very strong positive correlation between albumin/creatinine ratio on admission and after 24 hours and p-SOFA scores on admission and after 48 hours

Table (8) Correlation between ACR on admission and on 24th hour later and GCS:

	r	p
ACR on admission	-0.599	<0.001**
ACR at 24th hour	-0.597	<0.001**

r Spearman rank correlation coefficient **p≤0.001 is statistically highly significant

There is statistically significant negative correlation between albumin/creatinine ratio on admission and after 24 hours and Glasgow coma score.

Table (9) Linear stepwise regression analysis of factors significantly associated with ACR on admission:

	Unstandardized Coefficients		Standardized Coefficients	t	p	95.0% Confidence Interval	
	β	Std. Error	Beta			Lower	Upper
(Constant)	-1235.985	338.718		-3.649	0.001**	-1912.256	-559.713
Prism III	128.994	20.457	.613	6.306	0.001**	88.151	169.837

**p≤0.001 is statistically highly significant **p≤0.001 is statistically highly significant On doing linear stepwise regression analysis with ACR on admission, only PRISM III significantly independently associated with it.

Table (10) Linear stepwise regression analysis of factors significantly associated with ACR after 24 hours:

	Unstandardized Coefficients		Standardized Coefficients	t	p	95.0% Confidence Interval	
	β	Std. Error	Beta			Lower Bound	Upper Bound
(Constant)	-625.757	156.662		-3.994	0.001**	-938.726	-312.789
P-SOFA after 48 hours	76.193	15.996	.401	4.763	0.001**	44.237	108.149
ACR on admission	.291	.064	.350	4.572	0.001**	.164	.418
CRP	4.052	.996	.313	4.066	0.001**	2.061	6.042

**p≤0.001 is statistically highly significant **p≤0.001 is statistically highly significant
On doing linear stepwise regression analysis with ACR after 24 hours, P-SOFA after 48 hours (unstandardized β=76.193), ACR on admission (unstandardized β=0.291) and CRP (unstandardized β=4.052) significantly independently associated with it.

Table (11) Correlation between Length of PICU stay and ACR and scores:

	r	p
ACR on admission	0.476	<0.001**
ACR at 24th hour	0.782	<0.001**

PRISM-III	0.489	<0.001**
p-SOFA on admission	0.501	<0.001**
p-SOFA after 48 hours	0.793	<0.001**

r Spearman rank correlation coefficient **p≤0.001 is statistically highly significant
There is statistically significant positive correlation between PICU stay and all of albumin/creatinine ratio on admission and after 24 hours, PRISM-III, p-SOFA on admission and after 48 hours.

Table (12) Relation between outcome and ACR on admission and after 24 hours:

Parameter	Outcome		Test	
	Non-survivors N=35 (%)	Survivors N=33(%)	χ^2	p
Change in ACR Increasing Decreasing	 34 (97.1%) 1 (2.9%)	 1 (3%) 32 (97%)	Fisher	<0.001**
ACR on admission Median IQR	 703 255 – 1030	 149.6 92.05 – 350.5	-3.755	<0.001**
ACR after 24 hours Median IQR	 852 323 – 2134	 94 52.05 – 144.5	-6.301	<0.001**
P (Wx)	<0.001**	<0.001**		

Z Mann Whitney test IQR interquartile range χ^2 Chi square for trend test **p≤0.001 is statistically highly significant Wx Wilcoxon signed rank test

There is statistically significant relation between mortality and ACR on admission and after 24 hours (significantly higher in those with non-survivors).

In non-survivors, there is significant increase in ACR while there is significant decrease in ACR in survivors after 24 hours.
Concerning trend for p-SOFA, 97.1% of non-survivors had increasing ACR after 24 hours versus one patient of survivors

Table (13) Survival analysis of ACR trend among studied patients:

	Total	Events	n	%	mean	Std error	95 CI		p
Increasing	35	34	1	2.9%	19.32	18.27	18.27	20.37	0.444
Decreasing	33	1	32	97%	20	0	20	20	
Overall	68	35	33	48.5%	19.43	0.52	18.41	20.45	

P for Mantel cox test
There is non-significant relation between ACR trend and time till death among studied patients (non-significantly higher in those with decreasing ACR).

Table (14) Performance of PRISM-III in prediction of mortality among studied patients:

	Cutoff	AUC	Sensitivity	Specificity	PPV	NPV	Accuracy	p
PRISM-III	≥14.5	0.762	71.4%	72.7%	73.5%	70.6%	72.1%	<0.001**

AUC area under curve PPV positive predictive value NPV negative predictive value **p≤0.001 is statistically highly significant The best cutoff of PRISM-III is ≥14.5 with area under curve 0.762, sensitivity 71.4%, specificity 72.7%, positive predictive value 73.5%, negative predictive value 70.6% and overall accuracy 72.1% (p<0.001)

Table (15) Performance of p-SOFA on admission and after 48 hour in prediction of mortality among studied patients:

	Cutoff	AUC	Sensitivity	Specificity	PPV	NPV	Accuracy	p
On admission	≥8.5	0.774	77.1%	66.7%	71.1%	73.3%	72.1%	<0.001**

After 48 hour	≥9.5	0.959	91.4%	84.8%	86.5%	90.3%	88.2%	<0.001**

AUC area under curve PPV positive predictive value NPV negative predictive value **p≤0.001 is statistically highly significant The best cutoff of p-SOFA on admission is ≥8.5 with area under curve 0.774, sensitivity 77.1%, specificity 66.7%, positive predictive value 71.1%, negative predictive value 73.3% and overall accuracy 72.1% (p<0.001) The best cutoff of p-SOFA after 48 hours is ≥9.5 with area under curve 0.959, sensitivity 91.4%, specificity 84.8%, positive predictive value 86.5 %, negative predictive value 90.3% and overall accuracy 88.2% (p<0.001).

Table (16) Performance of ACR on admission and on 24th hour in in prediction of mortality:

	Cutoff	AUC	Sensitivity	Specificity	PPV	NPV	Accuracy	p
On admission	≥350.5	0.765	71.4%	75.8%	75.8%	71.4%	73.5%	<0.001**
After 24th hour	≥223.5	0.945	94.3%	84.8%	86.8%	93.3%	89.7%	<0.001**

AUC area under curve PPV positive predictive value NPV negative predictive value **p≤0.001 is statistically highly significant The best cutoff of ACR on admission is 330.5 mg/g with area under curve 0.765, sensitivity 71.4%, specificity 75.8%, positive predictive value 75.8%, negative predictive value 71.4% and overall accuracy 73.5% (p<0.001) The best cutoff of ACR after 24 hours is 223.5 mg/g with area under curve 0.945, sensitivity 94.3%, specificity 84.8%, positive predictive value 86.8%, negative predictive value 93.3% and overall accuracy 89.7% (p<0.001).

3. Discussion

Concerning cause of admission, 39.7%, 20.6% and 11.8% of patients had respiratory, neurology and hepatic diseases respectively, most common cause of admission is respiratory 44.1% . Our study agreed with Rady et al., (12) in Cairo where children with pneumonias and foreign body (FB) inhalation represented the highest admission etiology, followed by encephalopathy.

Similarly in the recent Indian study by Gadappa et al., (13), the chief primary diagnosis were respiratory disease (25%). There is statistically significant relation between mortality and blood culture. Negative blood culture significantly associated with mortality. The most important factor associated with negative cultures is receipt of antibiotics during the preceding 48 hours, diagnostic workup may be insufficient or incomplete or sepsis caused by unusual organisms that are difficult to identify in routine practice. Negative cultures should not give the clinician a false sense of reassurance - patients are still at risk of death, with the risks being dependent on severity of the physiologic derangements before and on the day of sepsis (14). In our study there is statistically significant positive correlation between albumin/creatinine ratio on admission , after 24 hours and sepsis degree. A study conducted by Basu et al.,(6) the degree of microalbuminuria within 6 hours of admission was significantly higher in patients with sepsis at a median ACR of 206.5 mg/g. In our study ,There is statistically significant relation between mortality and sepsis degree. Sepsis degree 1 significantly prevailed in survivors and degree 3 significantly prevailed in non-survivors The stage at which sepsis is diagnosed also influences survival chances, as those initially clinically diagnosed with septic shock have an increased chance of dying within 28 days. Progression to severe sepsis and/or septic shock during the first week also increases chances of mortality_(15) In our study regarding outcome, thirty three patients survived till end of study (48.5%). The mortality rate was 33.1% reported from Abo El-Reesh hospital in Egypt by Rady et al., (12), Saudi Arabia (37.4%) by Alsuheel et al., (16) and India (24.3%) by Taori et al., (17). Our mortality rates were similar to Indonesian study performed by Sari et al., (18) where the mortality was (40.58%), Honna et al., (19) (45.7%) and the Indian study by Gandi et al., (20) (46.2%). In the present study, there is statistically significant very strong positive correlation between albumin/creatinine ratio on admission and after 24 hours and PRISM-III scores. This came in agreement with Sachdev et al. (21) who reported that, the ACR levels were correlated with PRISM 12 and 24 score. In this study, there is statistically significant strong positive correlation between albumin/creatinine ratio on admission and after 24 hours and p-SOFA scores on admission and after 48 hours. In this study, there is statistically significant negative correlation between albumin/creatinine ratio on admission and after 24 hours and Glasgow coma score. In the trauma patients, ACR has been correlated with trauma-related scores (22). ACR was predicted onset of postoperative sepsis and was correlated significantly with sequential organ failure assessment (SOFA) score (23). Our study showed that, there is statistically significant relation between mortality and ACR on admission and after 24 hours (significantly higher in those with non-

survivors). In non-survivors, there is significant increase in ACR while there is significant decrease in ACR in survivors after 24 hours. Concerning trend for ACR, 97.1% of non-survivors had increasing ACR after 24 hours versus one patient of survivors. Similarly, Sachdev et al. (21) reported that, serial levels of ACR were consistently higher in nonsurvivors and there was a significant drop in ACR in survivors in the first 24 hours of admission. We identified the level of ACR >102 mg/g at the time of admission, 12 hours, and 24 hours of admission significantly associated with morbidity and mortality. Research in 2010 found elevated levels of microalbuminuria within the first 24 hours in patients who died of sepsis (6). In the current study, there is statistically significant relation between mortality and P-SOFA on admission and after 48 hours (significantly higher in those with non-survivors). In non-survivors, there is significant increase in p-SOFA while there is significant decrease in p-SOFA in survivors after 48 hours. Concerning trend for p-SOFA, 94.2% of non-survivors had increasing p-SOFA versus one patient of survivors while 63.6% of survivors had decreasing p-SOFA after 48 hours. This was in accordance with Efat et al. (24) who showed that SOFA score was significantly higher among the non-survivor group than the survivor one. The best cutoff of ACR on admission is 330.5 mg/g with area under curve 0.765, sensitivity 71.4%, specificity 75.8%, positive predictive value 75.8%, negative predictive value 71.4% and overall accuracy 73.5% ($p<0.001$). The best cutoff of ACR after 24 hours is 223.5 mg/g with area under curve 0.945, sensitivity 94.3%, specificity 84.8%, positive predictive value 86.8%, negative predictive value 93.3% and overall accuracy 89.7% ($p<0.001$). There are very few pediatric studies on the outcome prediction values of ACR. The presence of urinary albumin excretion value ≥15 µg/minute at 25 to 48 hours had 42% sensitivity, 85% specificity, 79% PPV, and 53% NPV to indicate a more severe course of bacterial meningitis (25). In a study on children with admission diagnoses of sepsis, noninfectious SIRS and diseases without SIRS reported the predictive value of ACR obtained at the time of admission and at 24 hours similar to that of Pediatric Index of Mortality II, PRISM score, PELOD score, and inotrope scores (5). MacKinnon et al. (26) presented similar curves using multiple regression model and observed significance of urine ACR measured at 6 hours after the admission in adults (26).

4. Conclusion

In conclusion, elevated urinary ACR is associated with the severity of sepsis, morbidity, and mortality. ACR was found to have significant relation to the need for inotropes. In addition, ACR had a good correlation to the duration of the PICU stay. ACR is an easy, cost-effective, and reliable test for predicting morbidity and mortality in a PICU setting.

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