Section: Biochemistry

Original Research Article

STUDY OF MICROALBUMINURIA IN SEPSIS WITH SPECIAL REFERENCE TO SAPS II SCORE

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Abstract

Background: Invasive bacterial infections are one of the leading causes of death around the globe, especially among young children. Sepsis is connected with a severe host defence response that involves the launching of robust inflammatory cascades that release a multitude of proinflammatory molecules into the circulation. This reaction occurs as part of the host's attempt to protect itself from the harmful effects of the infection. It is not uncommon to observe microalbuminuria in critically sick patients, and recent research suggests that it may be useful not just as a prediction of organ failure and the requirement for vasopressors, but also as a predictor of mortality. The purpose of this study is to determine the utility of the Urine Microalbumin and Albumin creatinine ratio in predicting patient mortality and to compare it to validated ICU scoring systems such as SAPS II. **Materials and Methods:** A prospective non-interventional study was conducted on fifty patients for a period of one year. Patients admitted in the Medical Emergency ward with features of SIRS (systemic inflammatory response syndrome), QSOFA and suspected infection, Immunocompromised patients, Hypertensive patients were included in the study. **Results:** Outcome in the present study was 76% patients have survived and 24% died. There was no statistically significant difference observed with relation to number of SIRS Criteria and outcome. The mean SAPS II score in Survived group was 36.50 ±14.95 and in non-survived group was 65.25 ±7.11. This finding was statistically significant. The mean Albumin creatinine ratio-1 in the present study was 91.55 ± 48.20. in the survived group It was 68.14 ±18.29 and in non-survivor group it was 165.68 ± 36.58, this observation was statistically significant. The mean Albumin creatinine ratio-2 in the present study was 61.93 ± 54.00. in the survived group It was 33.49 ± 9.85and in non-survivor group it was 151.98 ± 32.01; this observation was statistically significant. **Conclusion:** Significant microalbuminuria is predictive of mortality which is equivalent to the time tested SAPS II score. Microalbuminuria is an inexpensive and rapid diagnostic tool. Serial measurements may help in the clinical assessment of critically ill patients at risk of worse prognosis, even in resource poor areas.

INTRODUCTION

Sepsis is a life threatening complication of a infection. SIRS (systemic inflammatory response syndrome) that has a proven or suspected microbial etiology.[1] Invasive bacterial infections are the prominent causes of death around the world, particularly among young children. Non-typhoidal salmonella species, Streptococcus pneumonia, Haemophilus influenza, and Escherichia coli were the most commonly isolated bacteria.[2]

Sepsis is associated with severe host defense response that involves triggering of potent inflammatory cascades which release a plethora of proinflammatory molecules into the circulation. The endothelium becomes dysfunctional as a result of the continuous onslaught of inflammatory molecules and the accompanying oxidative stress. The loss of barrier integrity, which results in a systemic capillary leak, is an initial event. Systemic Inflammatory Response Syndrome is characterized by increased capillary permeability (SIRS). The glomerular manifestation of capillary permeability is increased albumin excretion in the urine. Microalbuminuria has

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been linked to rapid changes in vascular integrity in several studies. Early mortality prediction in critically ill sepsis patients, as well as early initiation of intensive therapy, is critical, with significant implications for the patient's survival. Various ICU scoring systems, such as the APACHE II and SAPS II scores, are currently in use to predict mortality. These scoring systems are time consuming and are completed within 24 hours of admission, during which valuable time is lost administering therapy.[2]
Microalbuminuria, defined as 30–300 mg/day of albumin excretion in the urine, develops quickly after an acute inflammatory insult such as sepsis and persists in patients who develop complications. It is a common finding in critically ill patients, and it has shown promise not only as a predictor of organ failure and the need for vasopressors, but also as a predictor of mortality.[2]
The purpose of this study is to determine the utility of the Urine Microalbumin and Albumin creatinine ratio in predicting patient mortality and to compare it to validated ICU scoring systems such as SAPS II.

MATERIALS AND METHODS

A prospective non-interventional study was conducted on fifty patients for a period of one year. Patients admitted in the Medical Emergency ward with features of SIRS (systemic inflammatory response syndrome), QSOFA and suspected infection, Immunocompromised patients, Hypertensive patients were included in the study. Patients with preexisting urinary tract infection, chronic kidney disease (serum creatinine level ≥ 2.0 mg/dL), diabetes mellitus were excluded.
SIRS was defined if two or more of the following were present: Fever (>38 C)/Hypothermia(24/min); Tachypnea (respiratory rate > 24/min); Tachycardia (Heart rate >90/min); Leucocytosis(>12000/microL) or Leucopenia(10% bands).
Following Investigations were done

- Haemogram
- Urine microalbumin and urine albumin - creatinine ratio (Urine ACR) done at 6 hour and 48 hour of admission to Medical emergency ward
- Serum Electrolytes
- Blood urea and serum creatinine
- RBS
- LFT
- ABG (Arterial Blood Gas) if patient is on mechanical ventilator

Data was collected using a pretested proforma that met the study's objectives. A thorough history was taken, as well as a physical examination and any necessary investigations. The study's purpose was explained to the patient, and informed consent was obtained. The patient was monitored throughout his or her hospital stay, and the outcome (death or survival) was recorded.
Data was entered into Microsoft Excel and analysed with the Statistical Package for Social Sciences (SPSS) for Windows software (version 18.0; SPSS Inc, Chicago). For continuous variables, descriptive statistics such as mean and standard deviation (SD) were calculated, and for categorical variables, frequency and percentage were calculated. The chi-square test and the Fisher's exact test (when appropriate) were used to demonstrate the relationships between predictor and outcome variables. The significance level was set at 0.05.

RESULTS

In the present study, 76% patients have survived and 24% died [Table 1].

- The mean age of the study population in the survived group was 37.76 ± 19.46 and in the non-survivor group was 48.33 ± 19.74. Majority in the non-survivor group belong to >45 years age group where as in the survivor group it was <50%.
- Male were 60% and female were 40%. Out the 30 male participated in the study, 24 survived and 6 didn‘t survive. Out of the 20 female participated in the study, 14 have survived and 6 have not survived.
- Based on number of SIRS criteria, in 6% it was 2, 3 in 32% and 4 in 62%. There was no statistically significant difference observed with relation to number of SIRS Criteria and outcome as the p value calculated to be >0.05.
- The mean Albumin creatinine ration-1 in the present study was 91.55 ± 48.20. in the survived group It was 68.14 ±18.29 and in non-survivor group it was 165.68 ± 36.58. this observation was statistically significant as the p value calculated to be <0.05.
- The mean Albumin creatinine ration-2 in the present study was 61.93 ± 54.00. in the survived group It was 33.49 ± 9.85and in non-survivor group it was 151.98 ± 32.01. this observation was statistically significant as the p value calculated to be <0.05 [Table 2].

The mean SAPS II score in Survived group was 36.50 ±14.95 and in non-survived group was 65.25 ±7.11. This finding was statistically significant as the p value calculated to be <0.05 [Table 3].
The mean predicted mortality in the survived group was 26.46 ±20.99 and in the dead group was 75.58 ±10.18. this observation was statistically significant as the p value calculated to be <0.05 [Table 4].
In the present study, a significant positive correlation (r=0.82; p=<0.0001) was observed between urine ACR-1 and SAPS-II Score as the p value calculated to be <0.05.
Significant positive correlation (r=0.78; p=<0.0001) was observed between urine ACR-2 and SAPS-II Score as the p value calculated to be <0.05 [Table 5].

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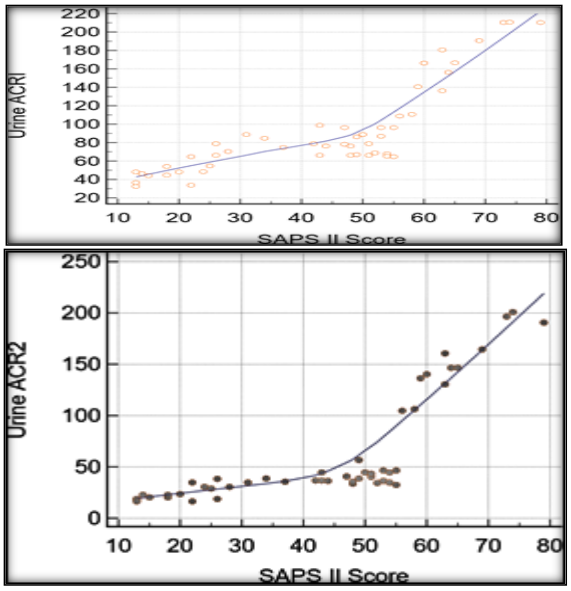
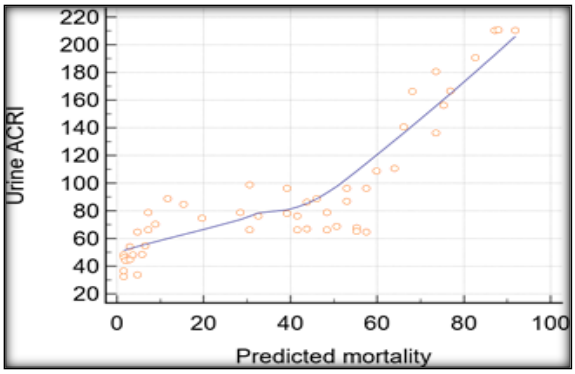
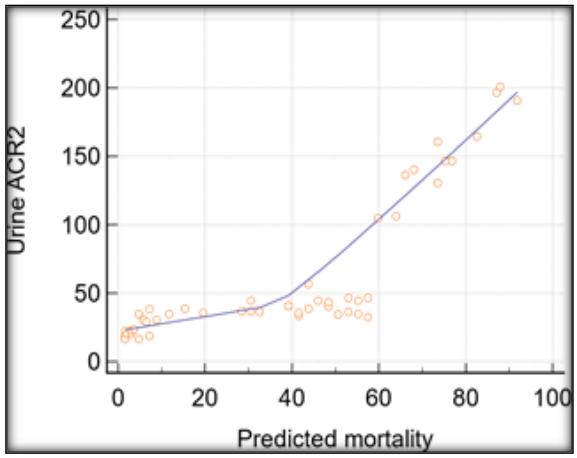


Graph 1: Correlation between Urine ACR 1 & 2 with SAPS-II Score





Graph 2: Correlation between ACR 1 & 2 with predicted mortality

In the present study, a significant positive corealtion (r=0.84; p=<0.0001) was observed between urine ACR-1 and predicted mortality as the p value calculated to be <0.05.

In the present study, a significant positive corealtion (r=0.82; p=<0.0001) was observed between urine ACR-2 and predicted mortality as the p value calculated to be <0.05 [Table 6].

Table 1: Distribution of patients based on the Diagnosis

	Frequency	Percentage
Acute cholecystitis with sepsis	1	2.00%
Acute kidney injury with sepsis	1	2.00%
Acute decompensated liver disease with sepsis	1	2.00%
Acute gastro enteritis with sepsis	1	2.00%
Acute gastroenteritis with sepsis	2	4.00%
Meningitis with sepsis	1	2.00%
Acute liver failure with sepsis	1	2.00%
Acute pancreatitis with sepsis	2	4.00%
Acute pulmonary edema with cardiogenic shock	1	2.00%
Acute pyelonephritis	1	2.00%
AKI with sepsis	1	2.00%
ARDS	1	2.00%
B/L pneumonia with tpe 2 respiratory failure with septic shock	1	2.00%
Cardiogenic shock with aspiration pneumonia with sepsis	1	2.00%
Chronic pancreatitis with chronic liver disease	1	2.00%
COPD	1	2.00%
COPD with secondary infection	1	2.00%
COPD with septic shock	1	2.00%
CVA with right hemiparesis with aspiration pneumonitis	1	2.00%
Right lobar pneumonia with sepsis	2	4.00%
Bilateral pyelonephritis with sepsis	1	2.00%
Fever with altered sensorium with sepsis	1	2.00%
Fever with sepsis	1	2.00%
HSV encephalitis with mods with sepsis	1	2.00%
LRTI with pulmonary TB with type 2 DM	1	2.00%
LRTI with sepsis	1	2.00%
LRTI with sepsis with AKI	1	2.00%
Recurrent hypoglycemia secondary to sepsis	1	2.00%
Respiratory failure with septic shock	1	2.00%

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Right pleural effusion	1	2.00%
Right lower lobe pneumonia with type 2 DM	1	2.00%
Right pleural effusion	1	2.00%
Sepsis	1	2.00%
Sepsis with AKI	1	2.00%
Acute pancreatitis	2	4.00%
Right lower limb cellulitis with sepsis	1	2.00%
Sepsis with right lower lobe pneumonia	1	2.00%
AKI with septic shock	1	2.00%
Septic arthritis	1	2.00%
Septic shock with AKI	1	2.00%
Acute myocardial infarction with septic shock	1	2.00%
TB abdomen with DKA with bacterial peritonitis	1	2.00%
Meningoencephalitis with sepsis	1	2.00%
Urosepsis	1	2.00%
Bilateral pleural effusion	1	2.00%
Viral fever with pneumonia	1	2.00%
Total	50	100.00%

Table 2: Distribution of patients based on the outcome with different variables

	Survived		Dead		Total		P Value
	N	%	N	%	N	%	
AGE							
<20	7	18.4%	1	8.3%	8	16%	0.96
21 – 30	5	13.2%	2	16.7%	17	34%	
31 – 40	3	7.9%	1	8.3%	4	8%	
41 – 50	1	2.6%	2	16.7%	3	6%	
51 – 60	4	10.5%	2	16.7%	6	12%	
61 – 70	7	18.4%	3	25.0%	10	20%	
71 – 80	1	2.6%	1	8.3%	2	4%	
GENDER							
Male	24	63.2%	6	50.0%	30	60%	0.42
Female	14	36.8%	6	50.0%	20	40%	
SIRS CRITERIA							
2	3	7.9%	0	0.0%	3	6%	0.19
3	14	36.8%	2	16.7%	16	32%	
4	21	55.3%	10	83.3%	31	62%	
Urine ACR 1							
<109.5	38	100.0%	1	8.3%	39	78%	0.001
>109.5	0	0.0%	11	91.7%	11	22%	
Urine ACR 2							
<118.5	38	100%	2	16.7%	40	80%	0.001
>118.5	0	0%	10	83.3%	10	20%	

Table 3: SAPS -II Score and Outcome

	Survived	Dead	T value	P value	95% CI
SAPS-II	36.50 ±14.95	65.25 ±7.11	6.40	<0.0001*	19.72 to 37.78

Table 4: Predicted mortality and Outcome

	Survived	Dead	T value	P value	95% CI
Predicted mortality	26.46 ±20.99	75.58 ±10.18	7.77	<0.0001*	36.42 to 61.81

Table 5: Correlation between Urine ACR 1 & 2 with SAPS-II Score

	Variable	R value	P value	95% CI
Urine ACR-1	SAPS-II score	0.82	<0.0001*	0.70 to 0.89
Urine ACR-2	SAPS-II score	0.78	<0.0001*	0.64 to 0.87

Table 6: Correlation between Urine ACR 1 & 2 with predicted mortality

	Variable	R value	P value	95% CI
Urine ACR-1	Predicted mortality	0.84	<0.0001*	0.73 to 0.90
Urine ACR-2	Predicted mortality	0.82	<0.0001*	0.71 to 0.89

DISCUSSION

Early diagnosis of sepsis is critical for patient management and outcome, as appropriate therapy can be life-saving for the patient. The gold standard for diagnosing sepsis is the isolation of the causative organism in a culture of appropriate body fluids or tissue, which usually takes more than 24 hours, resulting in a delay in the initiation of targeted therapy, which in turn affects outcome.[3] For this reason, the search for early marker of sepsis continues. Various ICU scoring systems, such as the APACHE II and SAPS II scores, are currently in use

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to predict mortality. These scoring systems are time consuming and are completed within 24 hours of admission, during which valuable time is lost administering therapy. The purpose of this study is to determine the utility of the Urine Microalbumin and Albumin creatinine ratio in predicting patient mortality and to compare it to validated ICU scoring systems such as SAPS II.

In the present study, 76% patients have survived and 24% died. Bhadade et al.[4] conducted a study in which 37 patients died out of 125. The higher mortality rate in our study could be attributed to a large population of patients suffering from severe sepsis and MODS. Because age is a factor, lower scores in our study population could be due to a younger study population. Basu et al., on the other hand, discovered higher scores.[5,6]

In the present study, the mean Albumin creatinine ration-1 was 91.55 ± 48.20. in the survived group It was 68.14 ±18.29 and in non-survivor group it was 165.68 ± 36.58. this observation was statistically significant as the p value calculated to be <0.05. Sharmila et al,[7] reported that On admission, the urine microalbumin creatinine ratio ranged from 33 to 245 micrograms/mg. All 16 patients (32 percent) who had an ACR 1 value greater than 109.5 died. Three patients died out of 34 (68%) who had an ACR 1 value less than 109.5. (8.82 percent). The P value is statistically significant at 0.0001. In Sharmila et al,[7] study Urine ACR 1 was 74.06 gm/ mg among survivors and 164g/ mg among nonsurvivors, while ACR 2 was 45.81 gm/ mg among survivors and 157 g/ mg among nonsurvivors. Both had a statistically significant p value of 0.0001.

The mean Albumin creatinine ration-2 was 61.93 ± 54.00. in the survived group It was 33.49 ± 9.85 and in non-survivor group it was 151.98 ± 32.01. this observation was statistically significant as the p value calculated to be <0.05. Sharmila et al,[7] reported that the Urine Micro Albumin Creatinine Ratio done at 24 hours of admission ranged 15 to 221microgram/mg. All 16 patients (32 percent) who had an ACR 2 value greater than 118,[5] died. Three patients died out of 34 (68%) who had an ACR 2 value less than 118.5. (8.82 percent). There is a P value that is statistically significant. Sharmila et al,[7] reported that Urine microalbumin levels were significantly higher in those with organ dysfunction than in those without, and the degree of elevation was greater in those with multiorgan dysfunction than in those with single organ dysfunction. The absence of significant microalbuminuria at admission is predictive of survival in sepsis patients, and significant microalbuminuria is predictive of death. The time of admission predicts mortality, which is equivalent to the time of death. SAPS II score was tested.

In Sharmila et al,[7] study early institution of intensive therapy to these patients can Improve survival rates. One of the study's limitations was its small sample size, which may explain why microalbuminuria is a poor predictor of mortality. There is some evidence that suggests a significant role for microalbuminuria as a simple, quick, and low-cost biochemical tool. Microalbuminuria may be caused by both smoking and hypertension. Patients with urological causes of sepsis were excluded from the study. Sepsis with preexisting chronic kidney disease could not be included in the study. In systematic review on the ability of urinary micro albumin in predicting the severity of illness among critically ill patients ACR was significantly related to prognostic scores. Gosling et al,[8] suggests that ACR is an early marker of the systemic inflammatory response to an acute insult, and the effect of an acute event on a pre-existing medical condition that leads to ICU admission will be variable. The ACR in medical and diabetes patients on admission is higher than in surgical a non-diabetic patient. Many of the causes of critical illness are associated with intense inflammatory responses.

In the present study, a significant positive correlation was observed between urine ACR-1,2 and SAPS-II Score. Basu et al,[6] in his study of 238 critically ill patients, they discovered that on ICU admission, 76 percent of patients had ACR > 30 mcg/mg, and it persisted in 67 percent at 24 hours. At 24 hours, 43% of patients had ACR levels greater than 101 mcg/mg. Patel et al,[9]; On ICU admission, 71 percent of patients had ACR greater than 30 mcg/mg, and 68 percent had it after 24 hours. At 24 hours, 34% of patients had ACR levels greater than 101 mcg/mg. On admission, nonsurvivors had significantly higher microalbuminuria than survivors: 141 mcg/mg (31–1014) and 51.5 mcg/mg (5–272), respectively, with 0.001. After 24 hours, ACR2 levels in nonsurvivors were significantly higher (175 mcg/mg versus 49 mcg/mg in survivors) (0.001). Patel et al,[9] had similar results; Nonsurvivors had a significantly higher median ACR1 (161.5 (IQR 105.3–180.8) mcg/mg) than survivors (89.8 (IQR 28.7–101.3 mcg/mg) (0.001). Patients who died in the ICU had a significantly higher median ACR2 (164.5 (IQR 104.9–172.1 mcg/mg) than those who survived (46.0 (IQR 25.6–89.4) mcg/mg) (0.0001). Bhadade et al,[4] found similar results; The median ACR1 levels in the sepsis and nonsepsis groups were 152.70 mcg/mg (IQR 108.71 to 194.92) and 44.48 mcg/mg (IQR 26.80 to 108.41), respectively. Microalbuminuria levels were significantly higher in patients with sepsis at admission compared to those without sepsis. These levels remained significantly higher among nonsurvivors, whereas they had decreased among survivors. Bhadade et al,[4] found that those who died (37 patients) had a median ACR1 of 172.98 mcg/mg which increased to 246.22 mcg/mg after 24 hours. Similar findings were echoed in a study done by Basu et al,[6]

Nour et al,[3] study reported that a reduction in ACR after 24 hours in survivors, which was in accordance with previous studies of Abid et al,[10] and Gosling et al.8 indicating that failure of ACR to decline is associated with increased ICU mortality. Nour et al3 study found that nonsurvivors had higher levels of albumin excretion in urine on ICU admission

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compared to survivors. Also, there was a significant increase in microalbuminuria in nonsurvivors at 24 hrs which is similar to the present study.

The mean SAPS-II score in the present study was 43.4 ± 18.27. The mean SAPS II score in Survived group was 36.50 ±14.95 and in non-survived group was 65.25 ±7.11. This finding was statistically significant as the p value calculated to be <0.05. Godinjak A et al,[11] reported that Out of 174 patients, 70 patients (40.2%) died. Mean SAPS II score in all patients was 48.4±17.0, and they were significantly different between survivors and non-survivors. SAPS II >50.5 can predict the risk of mortality in these patients.

CONCLUSION

Significant microalbuminuria is predictive of mortality which is equivalent to the time tested SAPS II score. Microalbuminuria is an inexpensive and rapid diagnostic tool. Serial measurements may help in the clinical assessment of critically ill patients at risk of worse prognosis, even in resource poor areas.

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