Comparative study between Microalbuminuria and Simplified Acute Physiology score as a marker of mortality in septic critically ill patients

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Abstract: Background: Sepsis remains a major global healthcare concern, owing to high morbidity and mortality, despite the advances in medical therapeutics. Microalbuminuria, is a common finding in critically ill patients, where it has shown promise not only as a predictor of organ failure and vasopressor requirement but of mortality, faring better than SAPS II and APACHE II score. **Aim of the Work:** to evaluate the relation between microalbuminuria (urine micro albumin / creatinine ratio) and SAPS II score in patients with sepsis and whether it could predict mortality in critically ill patients and to develop a simple, inexpensive and dynamic marker of critical illness. **Patients and Methods:** This study was conducted at Ain Shams University Hospitals and Port Said governorate Hospitals. After getting approval from ethical committee, 45 patients presented with features of SIRS and suspected infection were included after fulfilling the exclusion criteria. Urine for Albumin creatinine ratio was done at 6 hours (ACR1) and at 24 hours (ACR2) of admission and SAPS II Score was calculated in the first 24 hours of admission. **Results:** 27 patients (60%) had all the 4 criteria for SIRS, 16 patients (35.5%) had 3 criteria and 2 patients (4.5%) had 2 criteria. Mortality percentage in this study was 55.56%. Mortality was maximum among those aged >40 years. Age of non-survivors patients ranging from 49 to 86 years with Mean of 69.800 years. SAPS II score ranged from 18 to 107 with a mean score of about 39.200 among survivors and 69.680 among non survivors with statistically significant P value of <0.001. Mean Urine ACR 1 among survivors was 81.395 µg/mg and among non Survivors 670.680 and ACR 2 was 70.350 among survivors and 681.920 among non survivors. Both were statistically significant with p value of 0.0001. All of 25 non survived patients (100%) had SAPS II score more than 50 and both Urine ACR1 and Urine ACR2 more than 150 with statistically significant p-value of <0.001 of each of them. **Conclusion:** Presence of significant microalbuminuria at admission and persistence of microalbuminuria at 24 hrs of admission correlated well with mortality as comparable to SAPS II score. Microalbuminuria is an inexpensive rapid diagnostic as well as prognostic tool that can be used as dynamic marker of sepsis.

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Key words: Microalbuminuria, Simplified Acute Physiology score, Mortality Sepsis

1. Introduction

Sepsis is defined as SIRS (systemic inflammatory response syndrome) that has a proven or suspected microbial etiology. Invasive bacterial infections like Non-typhoidal salmonella species, Streptococcus pneumonia, Haemophilus influenza, and Escherichia coli were the most commonly isolated bacteria and the prominent causes of death around the world. **(Routray et al, 2016)**

Sepsis is marked by severe host defense response that releases a plethora of proinflammatory molecules into the circulation. The endothelium becomes dysfunctional due to the effect of inflammatory molecules and oxidative stress. Therefore increased capillary permeability is an early feature of Systemic Inflammatory Response Syndrome (SIRS). **(Routray et al, 2016)**

Numerous markers or methods have been utilized as prognostication tools for managing such patients thereby effectively and the mortality both short- and long-term. Acute Physiology and Chronic Health Evaluation (APACHE) II and Simplified Acute Physiology Score (SAPS) II scores are two of the most commonly used methods to predict mortality but have found to be of limited value for daily practical purposes due to their complex nature, though they have been efficient in evaluating the outcome. The measures used in ICU should ideally be sensitive, inexpensive, preferably detect short-term changes that can produce rapid and reliable results including the impact of therapeutic outcomes on the patients. **(Gagarin et al, 2012)**

In various studies microalbuminuria has been correlated with rapid changes in vascular integrity. Microalbuminuria, defined as 30–300 mg/day of albumin excretion in the urine, occurs rapidly after an acute inflammatory injury such as sepsis and persists in patients with complications. It is a common finding

in critically ill patients, where it has shown promise not only as a predictor of organ failure and vasopressor requirement but also of mortality. **(Routray et al, 2016)**

A more convenient method to detect microalbuminuria is the albumin /creatinine ratio (ACR) measured in a random urine specimen. Currently, the National Kidney Foundation recommends the use of spot urine ACR obtained under standardized conditions to detect microalbuminuria. The ACR is more convenient test for patients and may be less prone to errors due to improper collection methods and variations in 24-h protein excretion compared with a random urine specimen. **(MATTIX et al, 2002)**

Aim of the Study

The purpose of this study is to evaluate the relation between microalbuminuria (urine micro albumin / creatinine ratio) and SAPS II score in patients with sepsis and whether it could predict mortality in critically ill patients and to develop a simple, inexpensive and dynamic marker of critical illness.

2. Patients and Methods

Patients

This study was conducted in Ain Shams University Hospitals and portsaid governorate hospitals for one year. After obtained approval of research ethical committee and patients' informed consents. A sample size of 45 achieves 81% power to detect a difference of -0.3 between the null hypothesis correlation of 0.4 and the alternative hypothesis correlation of 0.7 using two-sided hypothesis test with significance level of 0.05. Forty Five (45) patients of both genders, aging between 18- 80 years old, with 2 or more features of SIRS (systemic inflammatory response syndrome) were included in the study.

Two or more of the following if present: SIRS

1. Fever (>38 C)/Hypothermia (<36)
2. Tachypnea (Respiratory rate >24/min)
3. Tachycardia (Heart rate >90/min)
4. Leukocytosis (>12000/microL) or Leucopenia (<4000/microL) or >10% bands.

Infection is defined by the presence of clinical signs of SIRS along with identified source of infection and/or positive blood cultures.

Exclusion criteria:

1) Patients receiving nephrotoxic drugs e.g. Aminoglycosides, Amphotericin B.

2) Patients with urologic injury resulting in frank hematuria or urinary infection.

3) Patients with preexisting chronic kidney disease (serum creatinine level ≥ 2.0mg/dL).

4) Female patient during pregnancy.

5) Patients with anuria (septic shock).

Methods

On admission, demographic data was collected for each patient such as age, gender, date of admission, patient's clinical classification (medical or surgical), provisional diagnosis, co-morbid conditions such as diabetes, hypertension. Detailed history, physical examination and necessary investigation were undertaken.

For disease severity scoring, SAPS II score was calculated from data collected during the first 24 h following ICU admission. Parameters include Age, Heart Rate, Systolic Blood Pressure, Temperature, Glasgow Coma Scale, Mechanical Ventilation or CPAP, PaO2, FiO2, Urine Output, Blood Urea Nitrogen, Sodium, Potassium, Bicarbonate, Bilirubin, White Blood Cell, Chronic diseases and Type of admission.

Spot urine samples were collected within 6 and 24 hours of admission to medical-surgical ICU. Sample was tested for urine microalbumin and for urine creatinine and urine microalbumin: creatinine ratio will be calculated. Urine microalbumin: urine creatinine ratio is calculated at 6 hour (Urine ACR1) and 24 hour (Urine ACR2) of admission to the ICU.

Patients were followed up during the course of the hospital stay and the outcome of the patient (i.e. Death /Survival) will be recorded.

Statistical Analysis

- All collected data was cleaned and filtered.
- Each variable was coded to facilitate the transfer of data.
- These codes were entered into computer through Statistical Package for Social Science (SPSS) version 20 where all statistical analyses were performed.
- The process of data analysis which consists of:

- Descriptive statistics were applied in numerical form; mean (standard deviation) for quantitative data and number (%) for qualitative data, or whatever suitable.
- Associations between the outcome measures and different components of the program was tested for significance by using Chi-square test for categorical variables and the paired student t- test for continuous variables with normally distributed data, and Mann-Whitney Rank sum test for non-parametric data, or whatever suitable.
- Statistical significance is pre-determined at 95% level of confidence (i.e. differences was considered significant if $P < 0.05$).

3. Results

In this study out of 25 patients who did not survive 21 were diagnosed with generalized undefined sepsis (84%), 3 patients were diagnosed with chest

infection (12%) and 1 patient was diagnosed with leg gangrene (4%) and out of 20 patients who survived 7 patients were diagnosed with generalized undefined sepsis (35%), 7 patients were diagnosed with chest infection (35%), 2 patients were diagnosed with surgical site infection (10%), 1 patient was diagnosed with gluteal abscess (5%), 1 patient was diagnosed with diabetic foot (5%), 1 patient was diagnosed with bilateral leg cellulites (5%) and 1 patient was diagnosed with pancreatitis (5%).

Table 2: Distribution of patients according to their diagnosis

Diagnosis	Outcome				
	Survival		Mortality		
	N	%	N	%	P-value
Sepsis	7	35.00	21	84.00	0.033*
Chest Inf	7	35.00	3	12.00	
Sur. Inf	2	10.00	0	0.00	
Gluteal abscess	1	5.00	0	0.00	
Diab. foot	1	5.00	0	0.00	
Leg gang	0	0.00	1	4.00	
Cellulitis	1	5.00	0	0.00	
Pancreatitis	1	5.00	0	0.00	
Total	20	100.00	25	100.00	

Table 3: Distribution of patients according to their outcome

Outcome		
	N	%
Survival	20	44.44
Mortality	25	55.56
Total	45	100.00

In this study out of 45 patients, 25 patients (55.56 %) did not survive and 20 patients (44.44%) survived.

Table 4: Distribution of patients according to their sex

Sex	Outcome				
	Survival		Mortality		
	N	%	N	%	P-value
Male	11	55.00	15	60.00	0.736
Female	9	45.00	10	40.00	
Total	20	100.00	25	100.00	

In this study out of 20 patients who survived 11 were males (55%) and 9 were females (45%) and out of 25 patients who did not survive 15 were males (60%) and 10 were females (40%). The P value is >0.001, which is statistically not significant.

Table 5: Distribution of patients according to their age

Age	Outcome						
	Survival			Mortality			P-value
Range	24	-	82	49	-	86	0.124
Mean ±SD	63.050	±	18.741	69.800	±	9.552	

In this study survived patients range from 24 to 82 years and patients who did not survive range from 49 to 86 years. Patients with age > 60 years constituted 80% of the study population The P value is >0.001, which is statistically not significant.

Table 6: Distribution of patients according to the number of SIRS criteria

Sirs variables	Outcome				
	Survival		Mortality		
	N	%	N	%	P-value
Two Criteria	2	10.00	0	0.00	0.030*
Three Criteria	10	50.00	6	24.00	
Four Criteria	8	40.00	19	76.00	
Total	20	100.00	25	100.00	

In this study out of 20 survived patients, 8 patients had four Sirs criteria (40%) 10 patients had three criteria (50%) and 2 had two criteria (10%) and out of 25 patients who did not survived 19 patients had four Sirs criteria (76%) and 6 had three criteria (24%). There is good correlation between number of SIRS criteria and mortality. The P value is 0.030, which is statistically significant. Increased number of SIRS criteria caused increased mortality rate.

Table 7: Distribution of patients according to their SAPS II Score

SAPS II Score	Outcome				
	Survival		Mortality		
	N	%	N	%	P-value
<50 Score	17	85.00	0	0.00	<0.001*
50-107 Score	3	15.00	25	100.00	
Range	18 - 58		57 - 107		<0.001*
Mean ±SD	39.200 ± 9.322		69.680 ± 11.257		

In this study out of 20 survived patients 17 patients had SAPS II score less than 50 (85%) and 3 patients had score more than 50 (15%). And all of 25 patients who did not survive had score more than 50 (100%). There is good co-relation between SAPS II score total points and mortality. The P value is 0.001, which is statistically significant.

Table 8: Distribution of patients according to their Urine ACR1

Urine ACR1 (ug/mg)	Outcome				
	Survival		Mortality		
	N	%	N	%	P-value
<150 (ug/mg)	16	80.00	0	0.00	<0.001*
>150 (ug/mg)	4	20.00	25	100.00	
Range	4.8 - 178		157 - 3262		0.002*
Mean ±SD	81.395 ± 56.378		670.680 ± 794.170		

In this study out of 20 survived patients, 16 patients had albumin creatinine ration within 1st 6 hours of admission (ACR1) less than 150 (80%) and 4 had ratio more than 150 (20%) And all of 25 patients who did not survive had ratio more than 150 (100%). There is good correlation between number of Urine ACR1 and mortality. The P value is <0.001, which is statistically significant.

Table 9: Distribution of patients according to their Urine ACR2

Urine ACR2 (ug/mg)	Outcome				
	Survival		Mortality		
	N	%	N	%	P-value
<150 (ug/mg)	18	90.00	0	0.00	<0.001*
>150 (ug/mg)	2	10.00	25	100.00	
Range	4.1 - 166		181 - 3248		0.001*
Mean ±SD	70.350 ± 48.767		681.920 ± 771.110		

In this study out of 20 survived patients 18 had albumin creatinine ratio within 24 hours of admission (ACR2) less than 150 (90%) and 2 had ratio more than 150 (10%) and all patients who did not survive had ratio more than 150 (100%). There is good correlation between number of Urine ACR2 and mortality. The P value is <0.001, which is statistically significant.

Table 10: Correlations between age and SAPS II Score, Urine ACR1 and Urine ACR2

Correlations		
	Age	
	r	P-value
SAPS II Score	0.351	0.018*
Urine ACR1 (ug/mg)	0.018	0.907
Urine ACR2 (ug/mg)	0.020	0.894

There is good correlation between SAPS II Score and Age. The P value is 0.018, which is statistically significant.

Table 11: Correlations between SAPS II Score, Urine ACR1 and Urine ACR2

Correlations				
	SAPS II Score		Urine ACR1 (ug/mg)	
	R	P-value	r	P-value
Urine ACR1 (ug/mg)	0.444	0.002*		
Urine ACR2 (ug/mg)	0.462	0.001*	0.995	<0.001*

There is good correlation between SAPS II Score and Urine ACR1. The P value is 0.002, which is statistically significant.

There is good correlation between SAPS II Score and Urine ACR2. The P value is 0.001, which is statistically significant.

There is good correlation between Urine ACR1 and Urine ACR2. The P value is <0.001, which is statistically significant.

4. Discussion

In the present study, Patients who were admitted to medical-surgical ICU with features of SIRS and suspected infection were included in the study after inclusion and exclusion criteria. Spot urine samples were collected within 6 and 24 hours of admission to medical-surgical ICU. Sample was tested for urine microalbumin and for urine creatinine and urine microalbumin: creatinine ratio will be calculated. Urine microalbumin: urine creatinine ratio is calculated at 6 hour (Urine ACR1) and 24 hour (Urine ACR2) of admission to the ICU. Patients were followed up and the outcome of the patient was recorded.

Patients were distributed from age 24 to 86 years. Mean age of the study population was 63.050 years among survivors and 69.800 years among non survivors. Patients with age > 60 years constituted 80% of the study population. A study done by **Angus DC et al,** showed mean age of 57.0 and a study done by **Routray et al,** showed that the majority of patients were among age group of 60-80. This is in consistence with the fact that sepsis is more common among the elderly age group.

Mortality percentage in this study was 55.56% compared to the study done by **Routray et al** which shows mortality percentage of 34.4%. Mortality was maximum among those aged >40 years. Age of non-survivors patients ranging from 49 to 86 years with Mean of 69.800 years.

In the present study 26 patients (57.77%) were males and 19 patients were females (42.22%). This is consistent with study conducted by **Angus DC et al** showed male patients constituted 51.9% and study conducted by **Routray et al,** showed male patients constituted 57.81%. This study shows that sepsis is more common among males compared to females.

Mortality was higher among male patients (57.69%) than among female patients (52.63%). A study done by **Angus DC et al** showed that women had less age specific incidence and mortality rates compared to men.

In the present study 27 patients (60%) had all the 4 criteria of SIRS, 16 patients (35.5%) had 3 criteria and 2 patients (4.5%) had 2 criteria.

Mortality was highly correlated with number of SIRS criteria. Out of 25 patients who did not survive 16 patients has four SIRS criteria (76%) and 9 had three SIRS criteria (24%) with p-value 0.030, which is statistically significant.

Among the patients who died 21 (84%) patients out of 25 had bacteremia from an unidentified source. Other causes included respiratory source of infection and leg gangrene. Urinary tract infections were excluded from the study as it was an exclusion criteria

of the study. Study done by **Angus DC et al** showed that 44% of the cause of mortality had a respiratory source of infection, 17.3 % had bacteremia from an unidentified source and 8.6 % had an abdominal source and 6.6 % had local wound as a source of infection.

SAPS II score ranged from 18 to 107 with a mean score of about 39.200 among survivors and 69.680 among non survivors with statistically significant P value of <0.001. This constituted with study conducted by **Routray et al,** which showed that Median SAPS II score among survivors were 42.0 and among non survivors were 63.5 (P value =0.0001).

Urine for ACR (Urine Albumin Creatinine Ratio) collected within 6 hours (Urine ACR1) and within 48 hour of admission (Urine ACR2).

Urine ACR1 ranged from 4.8 microgram/mg to 3262 µg/mg. Patients who survived had mean ACR1 of 81.395µg/mgand patients who died had mean ACR1 of 670.680µg/mgwith statistically significant p-value of 0.002. A study done by **Routray et al,** showed that patients who survived had median ACR1 of 66.4 µg/mg and patients who died had ACR1 of 166.5 µg/mg (P value=0.0001).

Urine ACR2 ranged from 4.1 microgram/mg to 3248 µg/mg. Patients who survived had mean ACR2 of 70.350 µg/mg and patients who died had ACR1 of 681.920 µg/mg with statistically significant p-value of 0.001. A study done by **Routray et al** showed that Median ACR2 among survivors was 34.6 µg/mg and among non survivors were 151.4µg/mg. P value was statistically significant with p 0.0001.

All of 25 non survived patients (100%) had:

* SAPS II score more than 50 compared to 3 survived patients (15%) out of 20

* Urine ACR1 more than 150 compared to 4 survived patients (20%)

* Urine ACR2 more than 150 compared to 2 survived patients (10%)

With statistically significant p-value of <0.001 of each of them.

Conclusion

• Presence of significant microalbuminuria at admission and persistence of microalbuminuria at 24 hrs. of admission correlated well with mortality as comparable to SAPS II score.

• Microalbuminuria is an inexpensive rapid diagnostic as well as prognostic tool.

• Hence microalbuminuria can be used as dynamic marker of sepsis.

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