# Microalbuminuria as a Marker of sepsis - A Prospective Study in a Tertiary Care Hospital

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## Abstract

**Background**: There are various ICU scoring systems like APACHE and SAPS II to predict mortality which are done at 24 hours of admission during which precious time is lost in administering therapy. In various studies microalbuminuria has shown promise not only as a predictor of organ failure and vasopressor requirement but also of mortality.

**Aim:** 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 the risk of developing multiorgan failure.

**Methods**: In was a prospective, non-interventional study conducted on 64 patients admitted to ICU. Spot urine samples were collected at 6 and 24 hours of admission and were tested for urine microalbumin by immunoturbidometric method and for urine creatinine by Jaffe method and urine microalbumin: creatinine (Urine ACR) ratio was calculated. The urine ACR was co-related with SAPS II score and mortality of the patients.

**Results:** SAPS II score ranged from 13 to 87. Median SAPS II score among survivors were 42.0 and among non survivors were 63.5. Non survivors had a higher SAPS II score compared to survivors (P value=0.0001).Urine ACR 1(urine micro albumin creatinine ratio at 6 hour) was 66.4 µg/mg among survivors and 166.5 µg/mg among non survivors and ACR 2 (urine micro albumin creatinine ratio at 24 hour) was 34.6 among survivors and 151.4 among non survivors (p value = 0.0001). Urine ACR 1 and Urine ACR 2 were correlated with SAPS II score and found statistically significance.

**Conclusion:** The degree of microalbuminuria was more among patients with organ dysfunction than among patients with no organ dysfunction. Significant microalbuminuria is also predictive of organ dysfunction.

**Key words:** Microalbuminuria, Sepsis, SAPS II score

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## Introduction

SEPSIS is defined as SIRS (systemic inflammatory response syndrome) that has a proven or suspected microbial etiology.[1] Invasive bacterial infections like Non-typhoidal *salmonella* species, *Streptococcus pneumonia*, *Haemophilus influenza*, and *Escherichia coli* were the most commonly isolated bacteria[2] and the prominent causes of death around the world.

Sepsis is marked by severe host defense response that releases a plethora of pro-inflammatory molecules into the circulation[3]. 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).[4] In various studies microalbuminuria has been correlated with rapid changes in vascular integrity.[5] Microalbuminuria, defined as 30–300 mg/day of albumin excretion in the urine, occurs rapidly after an acute inflammatory insult 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.[6,7].

Various ICU scoring systems to predict mortality are in current use like the APACHE II and SAPS II score. These scoring systems have many variables and are cumbersome and are done at 24 hours of admission during which precious time is lost in administering therapy.

This study is an attempt to understand the usefulness of Urine Microalbumin and creatinine ratio in predicting the mortality of the patient and to compare it with validated ICU scoring systems such as SAPS II.[8]

## Material & Methods

The present study was a Prospective, non-interventional study conducted on patients admitted to Medicine ICU/ Central ICU, S.C.B Medical College& Hospital, Cuttack from Nov 2013 to Oct 2015. Patients of age 18-80 from both sexes with 2 or more features of SIRS (systemic inflammatory response syndrome) and

suspected infection were included in the study. Patients receiving nephrotoxic drugs, with preexisting urinary tract infection, with urologic trauma resulting in frank hematuria or urinary infection, with preexisting chronic kidney disease (serum creatinine level ≥ 2.0mg/dL), pregnancy, anuria were excluded from the study.

Spot urine samples were collected at 6 and 24 hours of admission to medical ICU. Samples were tested for urine microalbumin by immunoturbidometric method and for urine creatinine by Jaffe method and urine microalbumin: creatinine ratio was calculated. All the investigations like Haemoglobin, Serum Electrolytes, Blood urea and serum creatinine, RBS (Random Blood Sugar), LFT (Liver Function Test), White blood cell count, ABG (Arterial Blood Gas) if patient was on mechanical ventilator were sent and noted. Urine microalbumin: urine creatinine ratio was calculated at 6 hour( Urine $ACR_1$) and 24 hour ( Urine $ACR_2$) of admission to the ICU[7,8,9].

**Two or more of the following if present: SIRS[2]**

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

Data were collected using a pretested proforma meeting the objectives of the study. Detailed history, physical examination and necessary investigation was undertaken. The purpose of the study was explained to the patient and informed consent were obtained. Patients were followed up during the course of the hospital stay and the outcome of the patient (i.e. Death /Survival) were recorded.

**Data Analysis and Interpretation:**

Data was entered into Microsoft excel and analyses were done using the SPSS for Windows software (version 18.0; SPSS Inc, Chicago). Descriptive statistics such as mean and standard deviation (SD) for continuous variables, and frequency and percentage for categorical variables were determined. The chi-square test and fisher's exact test (when appropriate) was used to show the associations between predictor and outcome variables. The level of significance was set at 0.05.

## Observation

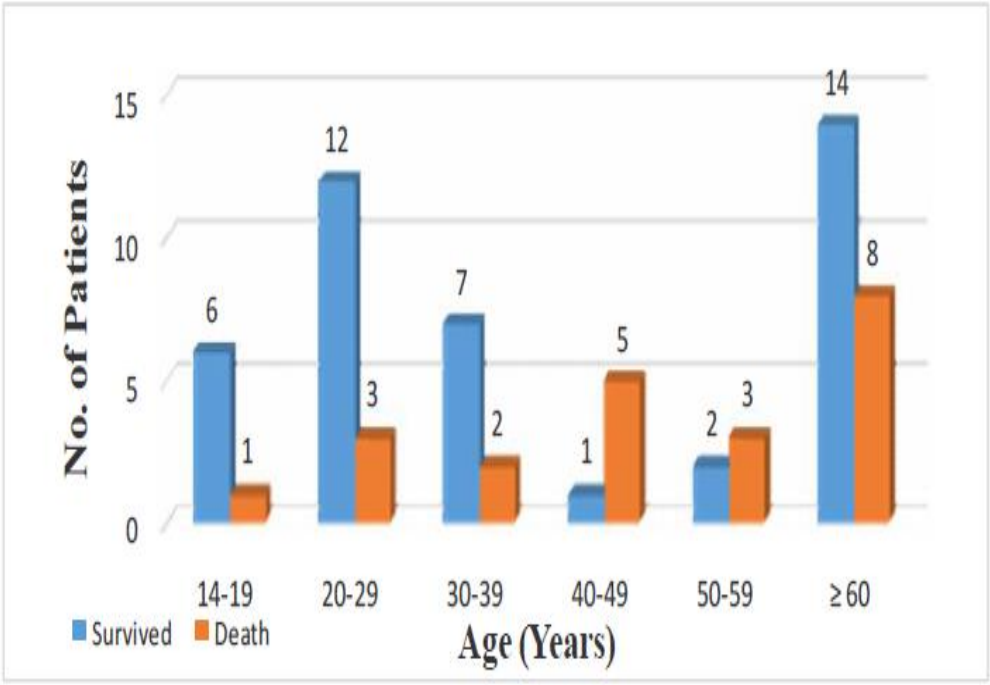


**Figure 1: Distribution of patients according to their age group**

In this study was conducted at SCB Hospital, a total of 64 patients were included in the study. Majority of the patients were more in the age group of 60-80 years (34.8%)

In this study out of 64 patients, 27 patients were females (42.18%) as compared to 37 males (57.81%).

**Table 1: Distribution of patients according to the number of SIRS criteria**

| Number of SIRS Criteria | Death | | Survived | | Total | |
|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % |
| **2** | 1 | 1.56 | 3 | 4.68 | 4 | 6.3 |
| **3** | 6 | 9.37 | 14 | 21.87 | 20 | 31.3 |
| **4** | 15 | 23.43 | 25 | 39.06 | 40 | 62.5 |

In this study out of 64 patients, 40 patients (62.5%) had all the 4 criteria of SIRS and 20 patients (31.3%) had 3 criteria of SIRS and 4 patients (6.3%) had 2 criteria of SIRS. Out of the study patients 22 patients (34.4%) did not survive and 42 patients (65.6%) survived.

**Table 2: Distribution of patients according to their SAPS II Score**

| SAPS II Score | Death | | Survived | | Total | |
|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % |
| **13-25** | 0 | 0 | 12 | 18.75 | 12 | 18.8 |
| **26-50** | 0 | 0 | 21 | 32.81 | 21 | 32.8 |
| **51-87** | 22 | 34.37 | 9 | 14.06 | 31 | 48.4 |
| **Mean ± SD** | **46.95 ± 19.11** | | | | | |
| **Range** | **13-87** | | | | | |
| **P Value** | **<0.0001** | | | | | |

In this study SAPS II score ranged from 13 to 87, majority of patients had SAPS II score above 51 (48.4%) and 29 patients (45.3%) had predicted mortality according to SAPS II Score of >50 %.

**Table 3: Distribution of patients according to their Urine ACR1**

| Urine ACR1(µg/mg) | Death | | Survived | | Total | |
|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % |
| **30-90** | 0 | 0 | 38 | 59.37 | 38 | 59.37 |
| **90-150** | 8 | 12.50 | 4 | 6.25 | 12 | 18.75 |
| **>150** | 14 | 21.87 | 0 | 0 | 14 | 21.87 |
| **Mean ± SD** | **102.44 ± 57.8** | | | | | |
| **Range** | **32.6-266.4** | | | | | |
| **P Value** | **<0.0001** | | | | | |

**Table 4: Distribution of patients according to their Urine ACR2**

| Urine ACR2(µg/mg) | Death | | Survived | | Total | |
|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % |
| **0-90** | 0 | 0 | 42 | 65.62 | 42 | 65.62 |
| **90-150** | 11 | 17.81 | 0 | 0 | 11 | 17.81 |
| **>150** | 11 | 17.81 | 0 | 0 | 11 | 17.81 |
| **Mean ± SD** | **75.8 ± 64.7** | | | | | |
| **Range** | **16.4-230.4** | | | | | |
| **P Value** | **<0.0001** | | | | | |

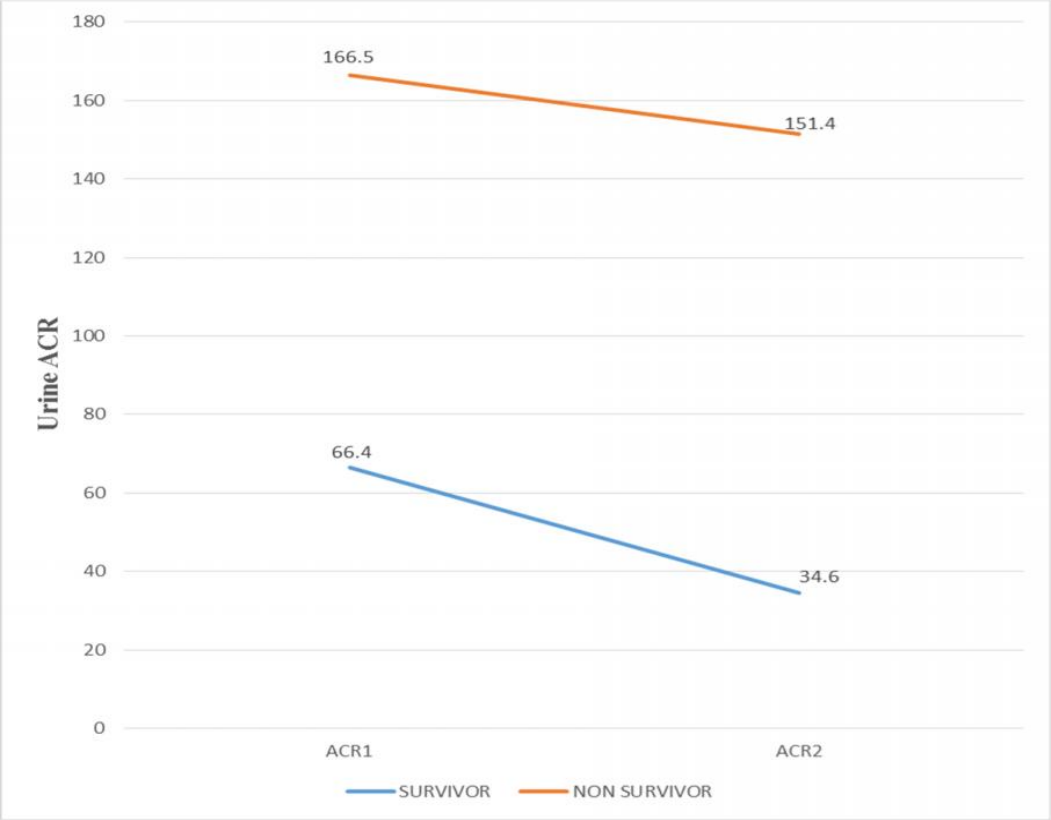


**Figure 2: Comparison of urine ACR 1 & 2 among survivors and non-survivors**

Urine ACR 1(albumin creatinine ratio) were 66.4 µg/mg among survivors and 166.5µg/mg among non survivors and Urine ACR 2 were 34.6 among survivors and 151.4 among non survivors. Both were statistically significant with p value of 0.0001.

In this study out of 64 patients, 59 patients (92.2%) had no chronic disease and 2 patients (3.1%) had metastatic malignancy and 3 patients (4.7%) had AIDS.

**Table 5: Co-relation between UACR and SAPS II Score**

| | Co-relation Co-efficient | P Value |
|---|---|---|
| Urine ACR 1 and SAPS II Score | 0.858 | <0.0001 |
| Urine ACR 2 and SAPS II Score | 0.841 | <0.0001 |
| Urine ACR 1 and Urine ACR 2 | 0.976 | <0.0001 |

**Table 6: Prediction of mortality by using SAPS II Score and micro-albuminuria**

| | | SAPS II Score | Urine ACR1 | Urine ACR2 |
|---|---|---|---|---|
| Survived (n=42) | **Mean** | 36.71 | 67.07 | 32.96 |
| | **SD** | 14.28 | 17.81 | 9.77 |
| | **SE of mean** | 2.20 | 2.74 | 1.50 |
| Died (n=22) | **Mean** | 66.5 | 169.97 | 157.59 |
| | **SD** | 9.38 | 46.08 | 41.18 |
| | **SE of mean** | 2.00 | 9.82 | 8.78 |
| **Mean difference** | | -29.78 | -102.90 | -124.62 |
| **SE Difference** | | 3.37 | 8.02 | 6.64 |
| **P value** | | <0.0001 | <0.0001 | <0.0001 |

## Discussion

In the present study we found sepsis is more common among the elderly age group (34.8%) which is also found by the study of S Todi et al [10] and Angus DC et al [11].

In this study done out of 64 patients, 7 patients (10.93%) had COPD and 11patients (17.18%) had type 2 Diabetes mellitus, 12 patients (18.75%) had local infection as a source of infection and 3 patients (4.7%) were Immunocompromised (HIV). A study done by Angus DC et al[11] showed that COPD was the most common underlying co-morbidity which was present in 12.3% of the patients. This shows that lung is the most common source of infection leading to sepsis. In the present study 40 patients (62.5%) had all the 4 criteria for SIRS, 20 patients (31.3%) had 3 criteria and 4 patients (6.3%) had 2 criteria.

**Cardiovascular system:** 24 Patients (37.5 %) had cardiovascular system dysfunction in the form of SBP < 90 mmHg, median ACR1 and ACR2 were 143.80µg/mg and 121.68 µg/mg among patients with cardiovascular dysfunction and 77.62 and 48.28 among patients with no cardiovascular dysfunction respectively. P value was statistically significant.

**Renal system:** 26 patients had renal dysfunction in the form of urine output <0.5L/24 hr. Median ACR1 and ACR2 were 140.19 µg/mg and 118.05 µg/mg among patients with renal dysfunction and 76.61 µg/mg and 46.90 µg/mg among patients with no renal dysfunction respectively. P value was statistically significant.

**Haemotologic system:** 20 patients (31.25 %) had haematologic dysfunction in the form of platelet count <80000/cumm. The degree of microalbuminuria was more among patients with organ dysfunction than among patients with no organ dysfunction.

Urine microalbumin was significantly elevated among those with organ dysfunction than those without organ dysfunction and the degree of elevation was more in those with multiorgan dysfunction than those with single organ dysfunction. Hence urine microalbumin might be used as a marker of multiorgan organ dysfunction.

Mortality percentage in this study was 34.4%.This is consistent with various studies including study done by Rangel-Frausto MS et al [12] which showed mortality ranging from 20-35% .Study done by Angus DC et al[11] 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. Similar study done by Mandell G et al[13] showed that most common primary sources of infection resulting in sepsis are the lungs, the abdomen, and the urinary tract. Of the 22 patients who died 5 patients were diabetic and 2 patients were immune-compromised.

SAPS II score ranged from 13 to 87 with a mean score of about 46.95(SD 19.11). Majority of patients (31 patients-48.4%) had SAPS II score of 51 to 87. The predicted mortality with the above SAPS II Score ranged from 1.5 to 95.7 % with a predicted mean mortality of 43.36(SD 29.79).Median SAPS II score among survivors were 42.0 and among non survivors were 63.5 (P value =0.0001).

Urine ACR1 ranged from 32.6 microgram/mg to 266.4 µg/mg with a mean of 102.44 (SD 57.8). Urine ACR1 differed significantly among survivors and non survivors. 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)(Mann whitney test applied). A study done by S basu et al[14] and Gosling et al[15] showed that Urine ACR at 6 hours was 70.4 µg/mg and 108µg/mg among survivors, 168.6 µg/mg and 156.6 µg/mg among non- surviver respectively.

Urine ACR2 ranged from 16.4-230.4 µg/mg with a mean of 75.8 (SD 64.7). Urine ACR2 differed significantly among survivors and non survivors. 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. A study done by gosling et al[15] showed that Urine ACR at 24 hours was 36.96 µg/mg among survivors and 156.64 µg/mg among non-survivors with significant p value of 0.0002(Mann Whitney). A study done by S basu et al[14] showed that Urine ACR at 24 hours was 50.8 µg/mg among survivors and 154.0 µg/mg among non-survivors with significant p value of 0.0004 .

## Conclusion

Urine microalbumin was significantly elevated among those with organ dysfunction than those without organ dysfunction and the degree of elevation was more in those with multiorgan dysfunction than those with single organ dysfunction. Absence of significant microalbuminuria among sepsis patients at admission is predictive of survival and significant microalbuminuria at admission is predictive of mortality which is equivalent to the time tested SAPS II score. Early institution of intensive therapy to these patients can improve survival rates. Microalbuminuria is an inexpensive and rapid diagnostic tool, serial measurements may prove a useful aid in the clinical assessment of critically ill patients at risk of worse prognosis, even in resource poor areas. Hence microalbuminuria can be used as a dynamic marker of critical illness.

**Conflict of Interest: None**

**Source of Support: Nil**

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