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Original Article

Can Microalbuminuria Predict the Outcome (Mortality) in Critically ill Patients? A Hospital-based, Prospective, Observational Study

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Abstract

Background: Complex scores, such as Acute Physiology and Chronic Health Evaluation II (APACHE II) scores, are highly reliable methods of to predict the mortality in critically ill patients. However, due to their complex nature intense resource requirements, their utility is limited in resource-poor settings like India. Hence, low-cost reliable markers like microalbuminuria can be utilized in such situations. Hence, the present study intends to assess the role of microalbuminuria in predicting the mortality among critically ill patients.

Materials and Methods: The study was a prospective observational study, conducted in a medical-surgical intensive care unit (ICU) of a private tertiary care teaching hospital. A total of 50 adult patients (>18 years) with a stay in the ICU for more than 24 h were included. For disease severity scoring, urinary microalbumin will be measured using the immunoturbidimetric method with an albumin creatinine ratio cutoff of 30-300 mg/L.

Results: The mean microalbumin level was 25.39 g/dl higher in people who met with mortality, compared to people who survived (95% confidence interval [CI]: 43.57-94.37, $P < 0.463$), which was statistically not significant. The mean microalbumin level was 25.39 g/dl higher in people who met with mortality, compared to people who survived (95% CI: 43.57-94.37, $P = 0.463$), which was statistically not significant. The area under receiver operating characteristic curve for microalbumin in predicting mortality was 0.59 (95% CI: 0.41-0.772, $P = 0.398$) and was very close to the null value of 0.5% and 95% CI included the null value of 0.5.

Conclusions: To conclude, the findings reveal that microalbuminuria weakly correlated with the mortality of the ICU patients and that the APACHE II scores may be more reliable and accurate measure, though it employs cumbersome data collection methods and complex statistical analysis.

Key words: Micro albumin, Critically ill, Mortality, Prediction

INTRODUCTION

The systemic inflammatory response is usually widespread and severe in patients with critical illnesses, sometimes in advanced cases may result in multiple organ failures and eventually death.[1] Systemic inflammatory response syndrome (SIRS), as the name suggests, is a consequence to a variety of acute pathological conditions such as hemorrhagic shock, sepsis, multiple trauma, or pancreatitis.[2] Precise prediction of the outcome of critically ill patients and the best use of the intensive care unit (ICU) resources have been the objectives of studies since many years.[3] Such measures enable the intensivist to prepare for accurate and aggressive therapeutic interventions by early identification of patients most at risk of life-threatening outcomes and also suitable counseling of the family members and/or the patient.

Numerous markers or methods have been utilized as prognostication tools for managing such patients thereby effectively the mortality both short- and long-term. Acute Physiology and Chronic Health Evaluation (APACHE) II and Simplified Acute Physiology Score (SAP) II scores are two of the most commonly used methods to predict the

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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.[1,3,4] 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.

Considerable research has shown that various reliable short-term markers have been assessed among such patients, though to a variable degree. Red cell distribution width is one such measure, which has been found to be an inexpensive, robust predictor of patient mortality.[5] Similarly, elevated levels of blood urea nitrogen,[6] blood glucose amplitude variability,[7] extravascular lung water index,[8] CD8(+) T-cell counts,[9] sequential organ failure assessment (SOFA),[10] and microalbuminuria levels[11] are some of the commonly used markers having varying degree of applicability.

Microalbuminuria is a common consequence to numerous inflammatory conditions such as burns, meningitis, pancreatitis, myocardial infarction, and cerebral ischemia. Several studies have consistently shown that microalbuminuria is a simple, suitable, non-invasive, and inexpensive predictor of mortality, which can be used as a bedside tool in critically ill patients.[11-14] In fact, its utility and efficiency are found to be equal to APACHE II score, a standard but complex tool in predicting the ICU patient mortality.[12] In countries like India, where the sophisticated and cost demanding therapeutic interventions are scarce, effective determination, and monitoring of optimal treatment procedures and patient mortality is of utmost importance. Hence, low-cost reliable markers like microalbuminuria can be utilized in such situations; hence, the present study intends to assess the role of microalbuminuria in predicting the mortality among critically ill patients.

Objectives

The goal of our study is to evaluate whether microalbuminuria (albumin creatinine ratio [ACR]). Measured within 6 h of ICU admission is as effective as the APACHE II score to predict outcome in critically ill patients.

MATERIALS AND METHODS

- Study design: The study was a prospective observational study
- Study setting: The study was conducted in a medical-surgical ICU of a private tertiary care teaching hospital
- Study population: The study was conducted on adult patients admitted to ICU
- Sample size: A total of 50 study participants were included in the study
- Sampling method: All the eligible subjects were included sequentially into the study, hence no sampling was done.

Inclusion and Exclusion Criteria

All adult patients (>18 years) with a stay in the ICU for more than 24 h were considered for inclusion into the study. Exclusion criteria - Patients with anuria, macroscopic hematuria, preexisting chronic kidney disease, female patients with menstruation, pregnancy. Retrospectively, patients with marked proteinuria due to renal and post-renal causes, for example, urinary tract infection and previously undiagnosed chronic renal failure will be excluded.

Study Procedure

On admission, demographic data were collected for each patient such as age, gender, date and time of admission, patient's clinical classification (medical or surgical), provisional diagnosis, co-morbid conditions such as diabetes, hypertension, and chronic kidney disease. For disease severity scoring, APACHE II score was calculated from data collected during the first 24 h following ICU admission. ABG analysis is done using i-STAT system (Sandor Medicaids Pvt., Ltd.) Each patient will be followed up throughout their ICU stay and the following outcome data obtained; ICU length of stay and mortality. At the time of admission, patients were examined for vital signs and symptoms of SIRS, organ failure, and/or infection. Culture samples sent and antibiotics received within 24 h of admission to be noted. Infection is defined by the presence of clinical signs of SIRS along with an identified source of infection and/or positive blood cultures. The American College of Chest Physicians/ Society of Critical Care Medicine Consensus Conference definitions is used to identify patients with SIRS, sepsis (SIRS with infection), septic shock (sepsis with hypotension on vasopressor support), and multiorgan dysfunction syndrome. Glomerular filtration rate is estimated using Cockcroft-Gault formula. Spot urine samples were collected within 6 h of admission for quantification of ACR. The ACR test had already been in general use in the lab before the study started. Urinary microalbumin will be measured using the immunoturbidimetric method (Turbilyte Ma-Tulip Diagnostics (P) Ltd. Goa, India). Microalbuminuria is defined as ACR of 30-300 mg/L. The ratio has a conventional cutoff value of 20 mg/L in the healthy reference population. The reference range for mortality prediction in critically ill population is yet to be determined. Statistical analysis of results will be done to assess the sensitivity and specificity of the study. The

clinical outcomes were compared with the APACHE II Scores and microalbuminuria levels statistically.

Ethical Considerations

The study was approved by Institutional Human Ethics Committee. Informed written consent was obtained from the legal guardian of the study participants after explaining the purpose of the study, risks, and benefits involved. The personal data of the participants were kept confidential throughout the study period.

Statistical Analysis

Mortality was the primary outcome variable in the study. Urine albumin levels and APACHE II score were considered as primary explanatory variables. Various sociodemographic, clinical, and laboratory parameters were considered as other explanatory variables. Descriptive analysis of the explanatory and outcome variables was done using mean and standard deviation for quantitative variables, frequency, and percentages for categorical variables. The correlation between microalbumin levels and APACHE II score was assessed by Spearman rank correlation and its *P* value. Receiver operating characteristic (ROC) analysis was done to assess the validity of microalbumin predicting mortality. The sensitivity, specificity, and predictive values for various cutoff levels of microalbumin were calculated. IBM SPSS version 21 was used for statistical analysis.

RESULTS

A total of 50 participants were included in the final analysis.

The mean age of study participants was 53.14 years. Males and females constituted 52% and 48% of the study participants, respectively. The incidence of mortality in the study population was 18% (Table 1 and Figure 1).

The mean microalbumin level was 25.39 g/dl higher in people who met with mortality, compared to people who survived (95% confidence interval [CI]: 43.57-94.37, $P < 0.463$), which was statistically not significant. The mean APACHE II score was 14.56 in people with mortality, compared to 10.80 in people who survived (mean difference - 3.75, 95% CI: 0.15-7.34, $P = 0.041$), which was statistically significant (Table 2).

There was very weak positive correlation between urine microalbumin and APCHE-II score in the study population (correlation coefficient $r = 0.199$, $P = 0.166$).

The area under ROC curve for microalbumin in predicting mortality was 0.59 (95% CI: 0.41-0.772, $P = 0.398$) and was very close to null value of 0.5 and 95% CI included the null value of 0.5 (Figure 2).

Table 1: Descriptive analysis of socio-demographic, clinical, and laboratory parameters (*n*=50)

Parameter	Mean/frequency
Age (mean±SD)	53.14 (±17.0)
Gender (%)	
Male	26 (52)
Female	24 (48)
Mortality (%)	
Yes	9 (18)
No	41 (82)

SD: Standard deviation

Table 2: Association between mean urine microalbumin, APACHE II scores, and mortality

Morality	Mean	Mean difference	*P* value	95% CI	
				Lower	Higher
Urine microalbumin					
Morality	90.16	25.39	0.463	−43.57	94.37
No mortality	64.76				
APACHE II score					
Morality	14.56	3.75	0.041	0.15	7.34
No mortality	10.80				

APACHE: Acute Physiology and Chronic Health Evaluation II, CI: Confidence interval

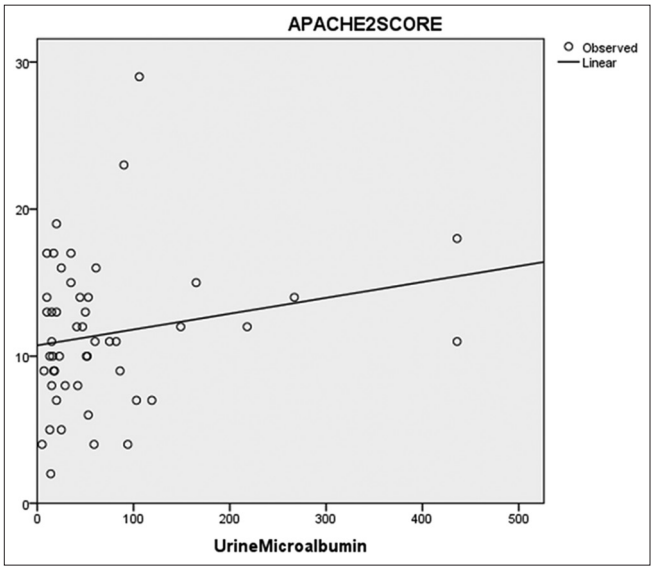

Figure 1: Correlation between urine microalbumin and Acute Physiology and chronic Health Evaluation II score in study population (*n*=50)

The area under ROC curve for APACHE II levels in predicting mortality was 0.678 (95% CI: 0.48-0.87, $P = 0.098$) (Figure 3).

DISCUSSION

The inflammatory reaction initiated in response to SIRS is usually severe and sustained that can induce rapid and profound changes in endothelial dysfunction in the form

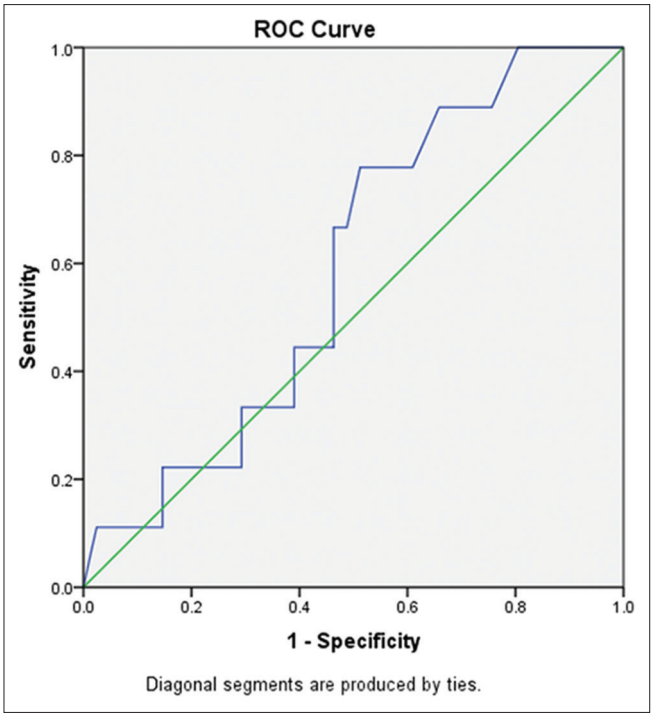

Figure 2: Receiver operating characteristic analysis of ability of microalbumin levels to predict mortality

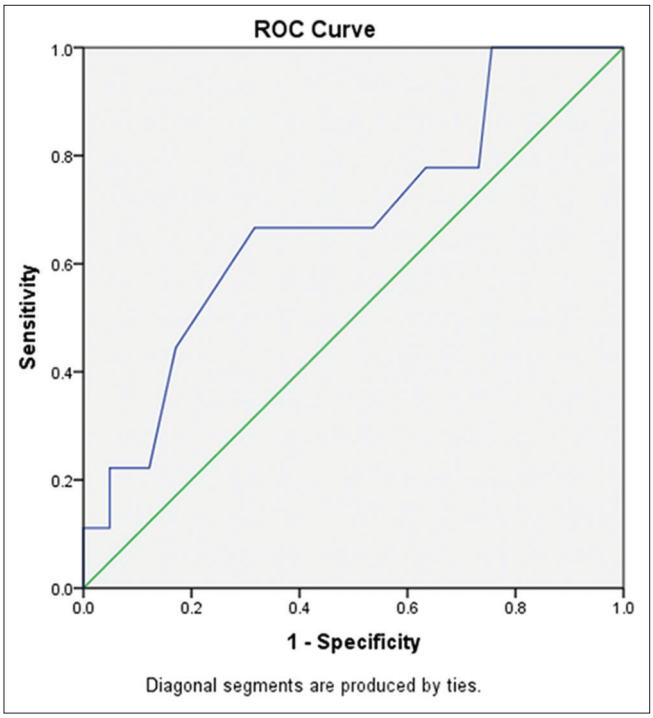

Figure 3: Receiver operating characteristic analysis of ability of Acute Physiology and chronic Health Evaluation II levels predicting mortality

of loss of barrier integrity causing capillary leak due to the effects of cytokines and other inflammatory mediators. Consequently, the glomerular permeability is altered in the kidneys resulting in enhanced albumin excretion, which seems to be quantitatively proportional to the degree of multiple of organ failure.[13,15]

There was very week positive correlation between urine microalbumin and APCHE-II score in the study population (correlation coefficient $r = 0.199$, $P = 0.166$). However, in a study by Basu *et al.*,[12] among 525 consecutively admitted ICU patients, the urine microalbumin was highly correlated with APACHE II illness severity score reflecting the acute physiologic response to the severe inflammation. The urinary microalbumin was highest among the patients with maximum APACHE II values in a pilot study done on 50 critically ill patients by Mac MacKinnon *et al.*[13]

The ROC curves showed that the area under the curve for microalbumin in predicting patient mortality was 0.59 (95% CI: 0.41-0.772, $P = 0.398$) and was very close to the null value of 0.5. However, for APACHE II levels, the area under ROC curve in predicting mortality was 0.678 (95% CI: 0.48-0.87, $P = 0.098$). Likewise, APACHE II had the highest area under the curve (0.78) than ACR2 (0.71) and ACR1 (0.58) in predicting the mortality in a study by Basu *et al.*[12]

The mean microalbumin level was 25.39 g/dl higher in people who met with mortality, compared to people who survived (95% CI: 43.57-94.37, $P < 0.463$), which was statistically not significant; however, the mean APACHE II score was 14.56 in people with mortality, compared to 10.80 in people who survived (mean difference - 3.75, 95% CI: 0.15-7.34, $P = 0.041$), which was statistically significant. A study by Abid *et al.*,[16] in their analysis of 40 ICU patients reported that the increasing urine ACR in patients had significantly higher mortality rates and correspondingly higher APACHE II and SOFA scores.

One of the limitations of the study was its smaller sample size, which may explain the weaker mortality predictivity of microalbuminuria. There is some evidence suggesting the appreciable role of using microalbuminuria as a simple, rapid, inexpensive biochemical tool.[12,13] A systematic review by Gopal *et al.*, on the ability of urinary microalbumin in predicting the severity of illness among critically ill patients concluded that currently, there was no evidence to suggest use of the test in ICUs and that there was a need to assess the optimal timing and threshold reference value for the urine ACR in diverse, heterogeneous ICU patients.[15]

Implications

The ICU prognostic scores such as APACHE II and the SAP II scores, though useful are very cumbersome tools in day to day practice. Whereas microalbuminuria expressed as ACR is a simple, validated, reliable, inexpensive test that obviates the need for a timed urine collection and

can be performed at the patient's bedside and results can be obtained within 15 min. Microalbuminuria could be an ideal tool for the early and accurate identification of patients with high risk of morbidity and mortality in ICU thereby guiding the intensivist to optimize triage, judicial allocation of resources and finance, counseling the family, early aggressive life support, and better patient outcome.

CONCLUSION

To conclude, the findings reveal that microalbuminuria weakly correlated with the mortality of the ICU patients and that the APACHE II scores may be more reliable and accurate measure, though it employs cumbersome data collection methods and complex statistical analysis. However, further studies among larger groups of diverse patient categories may help us to confirm the validity gap between urine microalbumin and APACHE II score.

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