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A STUDY ON CORRELATION BETWEEN MICROALBUMINURIA AND SOFA SCORE AND APACHE II SCORE AS A MARKER OF SEPSIS AND TREATMENT EFFICACY IN PATIENTS ADMITTED TO A MEDICAL INTENSIVE CARE UNIT OF A TERTIARY HEALTH CARE CENTRE

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Abstract

Background: Sepsis is a life-threatening medical condition characterized by a dysregulated response of the body to infection, leading to organ dysfunction. The study aimed to assess whether microalbuminuria can serve as a reliable marker of sepsis severity and treatment efficacy in critically ill patients using Sofa score and Apache II score. **Materials and Methods:** This prospective observational study was conducted at Rajiv Gandhi Government General Hospital, Chennai for 6 months on 96 patients admitted with sepsis in Intensive Care Unit. A patient's history includes age, sex, symptoms and SOFA score ≥2/3. Assessments include vital signs, Co- morbid conditions and organ failure complications. CBC, Renal Function Tests, Liver function test, S. Electrolytes, hsCRP, ESR, Urine routine, Urine Albumin Creatinine ratio (ACR) at 6 hours and 12 hours, S. Lactate, ABG, urine culture, blood culture was also performed. **Results:** The patient's average duration of ICU stay among survivors of sepsis is 5.93±1.69 compared to non-survivors (4.87±1.57) days. Respiratory source of infection is more prevalent (57.2%) than other sources, such as urosepsis (49%), CNS (14.3%) and GIT (10.2%). The patient's mean urine microalbumin ratio (ACR 2) and urine ACR difference are 94.03±55.36 and 40.02±31.64, which are the better predictors compared to the mean ACR 1 (64.43±28.72). The mean SOFA and APACHE II were 15.63±5 and 18.04 ± 5.92, respectively. Both SOFA and APACHE II scores were significant compared to the outcome, with the p-value being significant (<0.001). **Conclusion:** Using SOFA and APACHE II scores, the Urine microalbuminuria test (ACR) serves as a good predictor of morbidity and mortality of patients with sepsis.

INTRODUCTION

Sepsis is a common and deadly disease characterized by a life-threatening organ dysfunction caused by a dysregulated host response to infection. The incidence of severe sepsis is estimated to be 300 cases per 100 000 population.[1] Approximately half of these cases occur outside the ICU. A fourth of patients who develop severe sepsis will die during their hospitalization. Septic shock is associated with the highest mortality, approaching 50%.

Normally, as blood passes through healthy kidneys, it filters the waste products out and leaves in the things the body needs, like proteins in the blood is normally unable to pass through the glomerular capsule due to their large size. These proteins are screened by tubular epithelial cells. However, it may be mentioned that there are a number of conditions such as diabetes mellitus, hypertension, eclampsia, severe febrile illness, immune system disorders, abnormal swelling, malnutrition, cancer and many other systematic infections which can result in proteinuria.[2] Other causes include the presence of tumors, both of which may cause inflammation directly or be associated with a secondary bacterial infection. Patients who survive early sepsis but remain dependent on intensive care occasionally demonstrate evidence of a suppressed immune system. These patients may have ongoing infectious

1364

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foci despite antimicrobial therapy or may experience the reactivation of latent viruses.

Sepsis is commonly associated with coagulation disorders and frequently leads to disseminated intravascular coagulation. Abnormalities in coagulation are thought to isolate invading microorganisms and prevent the spread of infection and inflammation to other tissues and organs.

Recent studies have suggested that measuring the urine albumin-creatinine ratio (ACR) may have some predictive value for organ failure and mortality in ICU patients.[3-6] However, these studies involved various medical, surgical, and trauma patients, with urine albumin assessed between 6 and 120 hrs of ICU admission and outcome measures, including mortality, intensive care unit (ICU) stay, and physiologic and organ function scores.[7]

The acute physiology score and the chronic health evaluation (APACHE) were used in the first major attempts to quantify the severity of the illness in ICU patients. The major advantage of the APACHE II scoring system, as compared to the other systems, is that it can be used in monitoring the patient's response to therapy, and it takes into account 12 variables which include body temperature, mean arterial pressure (mm Hg), Heart rate, respiratory rate, Oxygenation (mm Hg), PH, Na (mmol/l), k (mmol/l), Creatinine (mg/100ml), Haematocrit, total leucocyte count and the Glasgow coma score.

The Sequential Organ Failure Assessment (SOFA) is an objective scoring model to offer an improved mortality risk stratification in the ICU. This model uses the severity of organ dysfunction in terms of the number of six organ systems of the body, including the Liver, lungs, coagulatory, CVS, renal, and neurologic (each 1–4) to offer a final score [6–24 (maximum)]. It computes individual or cumulative organ dysfunction. This score is calculated at the time of admission and subsequently every 24 hours till discharge. The study aimed to assess whether microalbuminuria can serve as a reliable marker of sepsis severity and treatment efficacy in critically ill patients using the Sofa and Apache II scores.

MATERIALS AND METHODS

This prospective observational study was conducted at Rajiv Gandhi Government General Hospital, Chennai for 6 months on 96 patients admitted with sepsis on ICU. All the patients were explained about the study design at the time of enrollment, and detailed consent regarding their willingness to participate was obtained. Ethical committee approval was obtained before the study started.

Inclusion Criteria

Age > 12 years, male and female sex, admitted in ICU with Sepsis and critically ill patients defined as qSOFA score ≥2/3.

Exclusion Criteria

Patients admitted for hanging, drowning and poisoning, patients with anuria, microscopic haematuria, and pre-existing chronic kidney disease. Females with menstruation and pregnancy and female patients with malignancy were excluded.

A thorough history and physical examination were done. Patients also underwent routine investigations such as CBC, Renal Function Tests, Liver function tests, S. Electrolytes, hs CRP, ESR, Urine routine, Urine Albumin Creatinine ratio (ACR) at 6 hours and 12 hours, S. Lactate, ABG, urine culture, blood culture were sent. Patients 'course at IMCU/ Emergency department was followed up regarding various outcomes. The change in ACR over 24 hours was compared with the SOFA and APACHE II scores and the correlation was analyzed using software to ascertain the statistical significance.

Statistical Analysis

Statistical analysis was done using SPSS software. Mean and standard deviations were calculated for linear dimensions and correlation using the Chi-square test, and p-values were calculated. Variables were considered significant if the p-value was less than 0.05.

RESULTS

Among 96 study subjects, 6.3% were <40 years, 29.2% were 41-50 years, 27.1% were between 51-60 years, 28.1% were between 61-70 years, and 9.4% were more than 70 years of age (Table 1).

Table 1: Age distribution of the study population

Age group	Frequency (N)	Percentage (%)
<40	6	6.3%
41-50	28	29.2%
51-60	26	27.1%
61-70	27	28.1%
>70	9	9.4%
Total	96	100%

32.3% of the patients had diabetes and hypertension, 28.1% had only diabetes, 25% had only hypertension and 14.6% had without any co-morbidities. The most common organ failure in patients with sepsis is renal failure, about 26%. The incidence of both Multi Organ Dysfunction Syndrome and septic shock was (18.8%). 15.6% of ARDS, 13.5% of septic encephalopathy and 6.3% of Disseminated Intravascular Coagulation were found. The source of sepsis was undifferentiated at 20.8%. The various sources of sepsis identified are as shown.
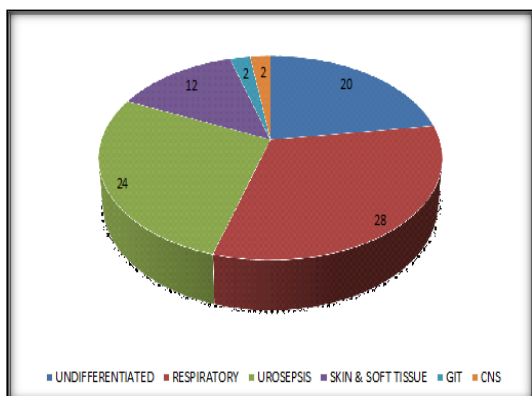
Figure 1: Sources of Sepsis in our study

The association of source of sepsis and outcome in patients with urosepsis, skin and soft tissue infection, CNS, GIT causes had a higher mortality than other causes.
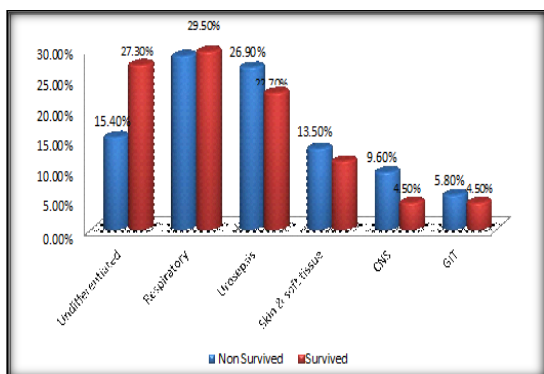

Figure 2: Association of source of sepsis and outcome

53.1% out of 96 patients needed supportive treatment of vasopressors or inotropes in continuous infusions with either noradrenaline, dopamine, or vasopressin at any time during their hospital stay. 63.7% out of 51 patients on inotropes did not survive. 43.2% of patients who were given RRT had a better outcome compared to the ones who were not given RRT 59.6%, and the outcome was found to be 45.8% of patients survived and 54.2% did not survive.

The mean value of ACR1 was 64.43±28.72, while the mean ACR 2 was 94.03±55.36, and the mean urine ACR difference was 40.02±31.64. On comparing with the outcome of patients in the study, ACR 2 and urine ACR difference are better predictors compared to ACR 1. The mean SOFA and APACHE II were 15.63±5 and 18.04 ± 5.92, respectively. Both SOFA and APACHE II scores were significant when compared to the outcome, with the p-value being significant (<0.001). (Table 2).

Table 2: Comparison of ACR1, ACR2, ACR difference, SOFA score, APACHE II and outcome

	Outcome		Unpaired t-test P value
	Non-Survived	**Survived**	
ACR 1	67 ± 32.21	61.39 ± 23.97	0.343
ACR 2	116.10 ± 55.83	67.95 ± 42.30	<0.001
Urine ACR difference	-49.10 ± 37.19	-6.57 ± 34.46	<0.001
SOFA	18.44 ± 4.22	12.82 ± 5.75	<0.001
APACHE II	20.71 ± 4.43	14.89 ± 5.95	<0.001

There is a strong negative correlation between urine ACR difference, SOFA and APACHE II score, and ICU stay duration. It means that urine ACR difference will be low when SOFA and APACHE II scores are high. (Table 3).

Table3: Correlation between SOFA, APACHE II and URINE ACR DIFFERENCE and also with DURATION OF STAY IN ICU

	Correlation 1	**P value 1**	**Correlation 2 (duration of stay in ICU)**	**P value 2 (duration of stay in ICU)**
SOFA	-0.742	<0.001	-0.142	0.169
APACHE II	-0.723	<0.001	-0.119	0.247
Urine ACR difference	-	-	-0.217	0.034

The mortality rate is predicted for ACR 1, ACR 2 and Urine ACR difference indicated by the area under the curve of 0.523 (95% CI 0.406 to 0.641, p-value 0.694) with specificity 52% for ACR 1, which denotes poor predictor, 0.767 (95% CI 0.673 to 0.862, p-value <0.001) for ACR 2 which means its better predictor of mortality with a sensitivity of 77% and 0.724 (95% CI 0.620 to 0.828, p-value <0.001) for urine ACR difference which means its better predictor of mortality with a sensitivity of 72%. (Table 4).

Table 4: Predictive validity of ACR in predictive Mortality

Test Result Variable(s)	Area Under the Curve	Std. Error	Asymptotic Sig	95% CI	
				Lower	Upper
ACR 1	0.523	0.060	0.694	0.406	0.641
ACR 2	0.767	0.048	0.000	0.673	0.862
Urine ACR difference	0.724	0.053	0.000	0.620	0.828

DISCUSSION

Sepsis is a life-threatening condition represented by an abnormal response of the body to infection, leading to organ dysfunction. This study was conducted in the ICU of a tertiary care hospital among 96 patients and mainly focused on comparing three different scores. In our study, the maximum incidence was in the same age group, 41-50, in both males and females. The survival rate was higher among patients < 50 years, probably owing to the co-morbidities with increasing age (40.9%) and higher mortality rates were seen in patients of the age group of 61-70 years (32.7%).

In our study, symptoms with high mortality rates include cough (21.2%), breathlessness (15.4%), loose stools (13.5%) and vomiting (13.5%). Patients presenting with the symptom of fever (29.5%) had the best chance of recovery among the various clinical presentations. The mean duration of hospital ICU stay is 5.35±1.70. The average ICU stay duration among sepsis survivors is 5.93±1.69, while among non-survivors, it is 4.87±1.57 days in the study.

In our study, out of 96, 14(14.6%) subjects did not have any co-morbidities, 31 (32.3%) had both diabetes and hypertension, 27(28.1%) had diabetes alone, and 24 (25%) had hypertension alone. Therefore, patients with hypertension alone had the highest mortality of 17 (32.7%). The source of sepsis in our study showed that Respiratory cause is the most common (28, 29.2%) followed by urosepsis (24, 25%), undifferentiated in 20 patients (20.8%). Other rarer causes include GIT (5, 5.2%), CNS (7, 7.3%), and it shows that respiratory cause is the most common source of sepsis. In our study, 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 was reported in a study by Angus DC et al. The most common primary sources of infection resulting in sepsis are the lungs, the abdomen, and the urinary tract- A similar association was reported in a study by Dolin et al.

The most common organ failure noted in our study is renal insufficiency (26%), and the patients needed renal replacement therapy. Other complications include (18.8%) having septic shock and patients (18.8%) having multi-organ dysfunction syndrome. ARDS was seen in patients with (15.6%), and septic encephalopathy was seen in (13.5%). Among patients with various organ failures, it was seen that MODS (21.2%) and septic shock (19.2%) had the highest fatalities.

In our study, The mean value of ACR1 was 64.43±28.72, the mean ACR 2 was 94.03±55.36, and the mean urine ACR difference was 40.02±31.64. On comparing with the outcome of patients in the study, ACR 2 and urine ACR difference are better predictors compared to ACR 1. The mean SOFA and APACHE II were 15.63±5 and 18.04 ± 5.92, respectively. Both SOFA and APACHE II scores were significant when compared to the outcome, with the p-value being significant (<0.001).[8,9]

According to Surupa Basu et al., at 24 hours, the absence of elevated levels of microalbuminuria is strongly predictive of ICU survival, equivalent to the time-tested APACHE II scores.[10] In our study, The ROC curve analysis revealed that ACR2 at a cut-off of 99.6 mg/g could predict ICU mortality with an sensitivity of 85%, specificity of 68% with an NPV of 97% and PPV of 30%, showing that ACR 2 is a fair predictor of mortality among the study population, as indicated by area under the curve of 0.767 (95% CI 0.673 to 0.862, p-value <0.001) which means its better predictor of mortality with a sensitivity of 77%.[11]

The Mortality Prediction of Microalbuminuria in Septic patients in our study concluded that ACR is a simple prognostic marker in septic patients and could be used as a mortality predictor, particularly in early (within 6 hours) septic patients, unlike our study, which resulted that ACR 2 done after 24 hours of admission had a better predictor capacity compared to the ACR1 done at admission or within 6 hours – Report done by Walid Omar.[12,13]

CONCLUSION

The result of the study was that urine albumin creatinine ratio done after 24 hours of admission was a single good predictor of morbidity and mortality of patients with sepsis and so was the difference between urine ACR on admission and 24 hours (urine ACR difference) which predicted the outcome of patients admitted with sepsis as compared to the time tested prevalent and elaborate SOFA and APACHE II scores. A simple urine microalbuminuria test can give us an idea about a septic patient's progression of the disease and help us on timely intervention in order to improve patient care and reduce mortality rates prevalent.

Limitations

The main limitations were that this being a single-centre study and exclusion of children and patients with known microalbuminuria (nephropathies) due to any cause were excluded, and the long-term follow-up was not done.

1367

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1368

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