



**ORIGINAL RESEARCH PAPER**

**Medicine**

**“A STUDY ON ASSOCIATION BETWEEN MODERATELY INCREASED ALBUMINURIA AND HOSPITAL OUTCOME IN PATIENTS OF SEPSIS ADMITTED IN INTENSIVE CARE UNIT OF A TERTIARY CARE HOSPITAL”**

**KEY WORDS:** MIA (moderately increased albuminuria), ACR, Sepsis, APACHEII,

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**ABSTRACT**

**BACKGROUND:** There is a great need for sensitive, inexpensive and dynamic prognostic markers which generate rapid and reliable results as prognostication tools in the setting of treatment of sepsis in critically ill in the ICU. We surmised that degree of albuminuria measured within 24 hours of ICU can serve as a cost effective tool to predict the outcome in critically ill sepsis patients.  
**AIM:** This study is directed towards finding out whether moderately increased albuminuria can serve the purpose of being a prognostic marker for severe sepsis.  
**MATERIAL AND METHODS:** A Hospital-based, Short term, Prospective (non-interventional) Cohort study of 100 adult patients of both gender and presenting with sepsis to I.C.U. with stay of more than 24hours  
**RESULTS:** ACR measured within 24 hours of admission was found to be as good as APACHE II score in predicting mortality in sepsis patients.  
**CONCLUSION:** ACR is a much simpler and rapid test as compared to APACHEII scoring this prognostic marker is an effective tool for identifying patients who are likely to survive in the ICU.

**INTRODUCTION**

Sepsis and related syndromes are complex disease states affecting a diverse group of patients. They are the most common cause of ICU admission throughout the world. They can originate from multiple sites and be triggered as a result of infection by a variety of microorganisms. Patients with sepsis and related syndromes present with a wide spectrum of symptoms and signs. Sepsis is a systemic, deleterious host response to infection leading to severe sepsis (acute organ dysfunction secondary to documented or suspected infection) and septic shock (severe sepsis plus hypotension not reversed with fluid resuscitation). Severe sepsis and septic shock are major healthcare problems, affecting millions of people around the world each year, killing one in four (and often more), and increasing in incidence. Similar to poly-trauma, acute myocardial infarction, or stroke, the speed and appropriateness of therapy administered in the initial hours after severe sepsis develops are likely to influence outcome.

In critical care units, prediction of outcome of patients is of vital importance to the intensivist. It allows planning of early aggressive therapeutic interventions, optimising resource allocation and appropriate counseling of the family and/or patient. A number of prognostication tools have been developed for the above purpose. The two widely adopted systems to predict mortality are the Acute Physiology and Chronic Health Evaluation (APACHE) II and the Simplified Acute Physiology Score (SAP) II scores. Though useful to evaluate outcome, these cumbersome tools are of limited use in day to day practice. Prognostication measures employed in the intensive care unit (ICU) should ideally detect short term changes in critical illnesses and also reflect the impact of early therapeutic interventions on the outcome of a patient. Sensitive, inexpensive and dynamic prognostic markers which generate rapid and reliable results are therefore desirable in the ICU setting.

Critical illnesses are more than often characterized by the systemic inflammatory response syndrome (SIRS) - the host response to an acute insult. SIRS is a common finding in the ICU patient which, when severe, can lead to multiple organ failure and finally death. A severe and sustained inflammatory reaction induces rapid and profound changes in the endothelium resulting in loss of 2 barrier

integrity leading to systemic capillary leak. In the kidneys this manifests as altered glomerular permeability culminating in increased renal albumin excretion in the urine. Moderately increased albuminuria (the new terminology for what was once termed "microalbuminuria") which is defined as 30–300 mg/day of albumin excretion in the urine, occurs rapidly after acute inflammatory insult such as sepsis and persists in patients with complications.

We surmised that degree of albuminuria measured within 24 hours of ICU admission would reflect the degree of ongoing endothelial dysfunction and it can serve as a cost effective tool to predict the outcome in critically ill sepsis patients.

**MATERIALS AND METHODS:**

The study was performed after ethical approval on the consenting patients admitted in the ICU of Patna Medical College and Hospital, Bihar who fulfilled the criteria.

1. **STUDY AREA** –Intensive care unit, Patna Medical College and Hospital
2. **STUDY POPULATION** - Adult patients of both gender (aged>18years and <60yrs), presenting with sepsis to I.C.U. with I.C.U. stay of more than 24hours.
3. **SAMPLE SIZE** - 100 Adult Patients of Sepsis with I.C.U. stay>24hrs
4. **SAMPLE DESIGN** - Simple random selection.
5. **STUDY DESIGN**- A Hospital-based, Short-term, Prospective (non- interventional) Cohort study.
6. **STUDY TOOLS:**
  - Clinical Examination
  - Blood Examination (7ml)
    1. WBC Count
    2. Hematocrit
    3. Blood culture
    4. Serum Sodium
    5. Serum Potassium
    6. SerumCreatinine
    7. Arterial Blood gas analysis
    8. SerumProcalcitonin (quantitative)

- Urine Examination(5ml)
  - a. Routine and Microscopic examination
  - b. Culture and sensitivity
  - c. Albumin-creatinine Ratio

Sputum microscopy and culture (if needed), other Body fluid study (e.g. CSF, Ascitic fluid etc.-if needed)

- **Radiology:**
  - a) Chest X ray (PA view)
  - b) Ultrasonography (whole abdomen)

**8. STUDY TECHNIQUE:** Meeting the inclusion and exclusion criteria, 100 adult patients were selected, whose I.C.U. stay period was more than 24hrs. Thorough history, clinical and routine laboratory parameters were obtained of them and their Acute Physiology and Chronic Health Evaluation( APACHE II) scores were calculated within first 24hrs of their I.C.U. admission.

A spot urine sample (5ml) was collected and sent for Urinary albumin measurement by the auto-analyser (immunoturbidometric method) and urinary creatinine by auto-analyser (modified kinetic Jaffe reaction -Dimension RxL Max, Dade Behring Inc., U.S.A). The methods covered an analytical range of 30-300 mg for moderately increased albumin and 0-20 mg/dl for creatinine. Moderately increased albuminuria was defined by ACR (albumin-creatinine ratio) values between 30and 299 mg/dl. ACR of > 300 mg/dl is considered as severely increased proteinuria. ACR <30 mg/g is normal for a healthy population. These threshold values are well accepted for clinical use and have been predefined on the basis of published literature.

These patients were followed up on 3rd, 7<sup>th</sup> and 14<sup>th</sup> day in I.C.U. to assess treatment outcome in terms of mortality and length of I.C.U. stay.

The data was analysed by a standard statistical method, using SPSS (version 20.0) software

**9. INCLUSION CRITERIA :**

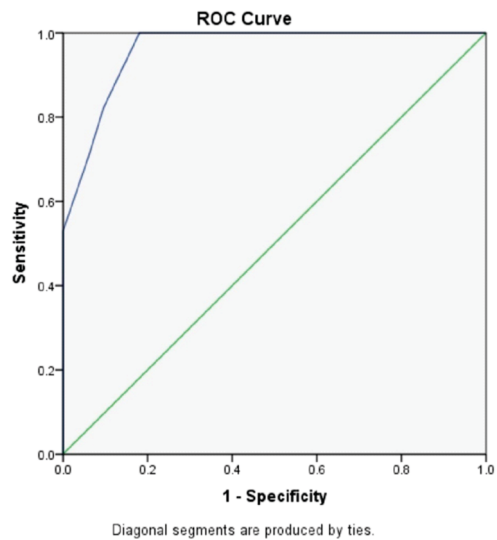
1. Adult patients of any sex
2. Sepsis- A proven or suspected microbial etiology PLUS 2 or, more of the following
  - A Core temperature >38oC or, <36oC
  - Heart rate >90/min
  - Respiratory rate >20/min
  - WBC count >12000/mm<sup>3</sup> or, <4000/mm<sup>3</sup>.
3. Duration of I.C.U. stay >24 hours

**12. STUDY DURATION :** June 2017-December 2018

**RESULTS**

1. Of total 100 patients studied, 91 had medical etiology of sepsis and 9 had surgical etiology
2. Of 100 patients, 60 fell into Sepsis group, 26 had severe sepsis and 14 were in septic shock group. Overall 83 patients survived and rest i.e. 17 died when followed up for 14 days period.
3. Acute Physiology Score (APS) was also significantly more in more severe form of sepsis, as well as in Non survivors (Mean 11.06, SD 2.44). Among different parameters studied under APS, the Mean BP and serum creatinine level showed similar trends
4. Mean APACHE II score was significantly worse in Severe sepsis (Mean 17.08 , SD 2.43) and Septic shock (Mean 19.36, SD 2.59) patients and also in Non survivors (Mean 19.82, SD 2.04)
5. Mean ACR (within 24 hours of ICU admission) was found to be significantly higher in more severe forms of sepsis as well as in those patients who couldn't survive (Mean 198.41 ,SD 37.68)
6. ACR measured within 24 hours of admission was found to be as good as APACHE II score in predicting mortality in sepsis patients (AUC of APACHE II – 0.961 & AUC of ACR – 0.95 on ROC curve)

**AUC of APACHE II**



**Area Under the Curve**

Test Result Variable(s): APACHE II SCORE

| Area  | Std. Error <sup>a</sup> | Asymptotic Sig. <sup>b</sup> | Asymptotic 95% Confidence Interval |             |
|-------|-------------------------|------------------------------|------------------------------------|-------------|
|       |                         |                              | Lower Bound                        | Upper Bound |
| 0.961 | 0.018                   | <0.001                       | 0.926                              | 0.996       |

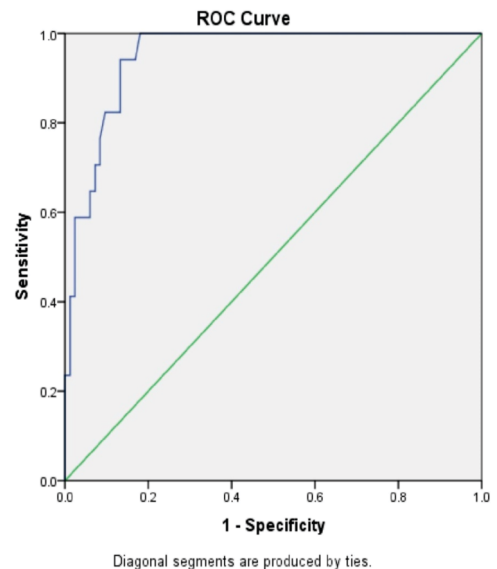
The test result variable(s): APACHE II SCORE has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.

- A. Under the nonparametric assumption
- B. Null hypothesis: true area = 0.5

**Cut-off – 18, Sensitivity – 0.824 and Specificity - 0.904**

So, to conclude, an APACHE II score of 18 and above had 82% sensitivity and 90% specificity in predicting mortality in critically ill sepsis patients.

**AUC OF ACR CURVE:**



**Area Under the Curve**

Test Result Variable(s): ACR (mg/gm of Cr)

| Area  | Std. Error <sup>a</sup> | Asymptotic Sig. <sup>b</sup> | Asymptotic 95% Confidence Interval |             |
|-------|-------------------------|------------------------------|------------------------------------|-------------|
|       |                         |                              | Lower Bound                        | Upper Bound |
| 0.950 | 0.020                   | <0.001                       | 0.910                              | 0.990       |

The test result variable(s): ACR (mg/gm of Cr) has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.

**Cut off-162.50, Sensitivity-0.941, Specificity-0.831**

So, to conclude, an ACR value of 162.5 mg/gm of Cr and above was found to be having a 94% sensitivity and 83 % specificity in predicting mortality in critically ill sepsis patients.

The Area under curve for both APACHE II (AUC 0.961) and ACR (AUC 0.950) are almost same.

**CONCLUSION:**

So, to conclude MIA within 24 hours of ICU admission is as good a predictor of mortality as the time-tested APACHE II score, in critically ill sepsis patients. The study indicated that MIA, a simple noninvasive and inexpensive bedside tool could be effectively utilized to identify patients of sepsis who are likely to survive in the CCU.

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