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Internal Medicine

AN OBSERVATIONAL STUDY OF ASSOCIATION BETWEEN MICROALBUMINURIA AND HOSPITAL OUTCOME IN PATIENTS OF SEPSIS IN JLNMCH, BHAGALPUR

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ABSTRACT **OBJECTIVE** To assess the change in microalbuminuria levels as a predictor of mortality and morbidity relative to the APACHE II and SOFA scores and to find out the association between Microalbuminuria and hospital outcome in critically ill sepsis patients. **METHODS** The study was undertaken in Intensive Care Unit (I.C.U.) of JLNMCH , Bhagalpur, Bihar and patients of both gender in age groups of 18-60yrs admitted in ICU for more than 24 hours with confirmed diagnosis of sepsis. The study period was 1st December 2021 – 30TH December2022 and the study population included 100 patients selected by simple random sampling and the study done was a prospective observational (non-interventional) study. **RESULTS** Microalbuminuria was found to be very much prevalent in all these critically ill patients studied, with a range of 30 mg/gm of Cr (min)- 304 mg/gm of Cr(max),with a mean ACR level of 137.74 and SD of 46.85. **CONCLUSION** Microalbuminuria is of common occurrence in a heterogeneous critically ill population. Patients without significant microalbuminuria during first six hours of ICU admission are less likely to have sepsis. At 24 hours, absence of elevated levels of microalbuminuria is strongly predictive of ICU survival, equivalent to the time-tested APACHE II scores. 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.

KEYWORDS :

INTRODUCTION

Sepsis remains a major global healthcare concern, owing to high morbidity and mortality, despite the advances in medical therapeutics. Targeted therapies probably lose their efficacy due to late administration. Till date, there is no reliable method of diagnosing sepsis early in the critically ill. In critical care units, prediction of outcome of patients is of vital importance to the intensivist. 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 [1, 2]. 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 of mortality, fairing better than Acute Physiological and Chronic Health Evaluation (APACHE) II score and Sequential Organ Function Assessment (SOFA) scores 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. Microalbuminuria, 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. Microalbuminuria is found to occur in several acute inflammatory states such as burns, pancreatitis, meningitis, ischemia reperfusion injury, acute myocardial infarction, and cerebral ischemia [8-13]. Increased levels of microalbuminuria on admission have been shown to be associated with indicators of organ dysfunction such as hypoxia index (PaO2/FiO2 ratio), serum creatinine, duration of mechanical ventilation and vasopressor use and also with physiological scoring systems. [14, 19-21]. Microalbuminuria has been found to be a sensitive predictor of outcome in critically ill patients early after ICU admission in several clinical situations [15-23].

We summarized that degree of microalbuminuria measured within 24 hrs 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.

METHODOLOGY

1. STUDY SITE– Intensive Care Unit (I.C.U.) of JLNMCH , Bhagalapur, Bihar

2. STUDY POPULATION - Patients of both gender in age groups of 18-60yrs admitted in ICU for more than 24 hours with confirmed diagnosis of sepsis.

3. STUDY PERIOD- 1st DECEMBER 2021 – 30TH DECEMBER 2022

4. SAMPLE SIZE – 100 Patients

5. SAMPLE DESIGN - Simple random sampling.

6. STUDY DESIGN- Prospective observational (non-interventional) study.

7. INCLUSION CRITERIA:

A. Adult patients of both sex admitted in I.C.U. for >24hrs
B. Patient of sepsis with a proven or suspected microbial etiology along with 2 or, more of the following-:

a. Core temperature >38*C or, <36*C
b. Heart rate >90/min
c. Respiratory rate >20/min
d. WBC count >12000/mm3 or, <4000/mm3.

8. EXCLUSION CRITERIA

a. Patients getting discharged/discharged against medical advice/ death/ transferred out within 24 hours of admission from I.C.U.
b. Patient with anuria or macroscopic hematuria
b. History of CKD with eCrcl < 60ml/min
c. Comorbid condition such as diabetes mellitus, hypertension
d. Menstruating or pregnant females
e. Patients with significant proteinuria due to renal and post renal causes.

STUDY TOOLS:

A. Clinical Examination
a. Sphygmomanometer
b. Stethoscope
c. Pulse-oximeter

B. Blood Examination
a. 7ml blood is taken for CBC and serum CREATININE examination through SYSMEX XT 2000i automated hematology analyzer and fully autoanalizer Erba Manheim EM 360 respectably installed in clinical pathology.

b. 2ml arterial blood in heparinized syringe was taken and measurement was done by SIEMENS RAPIDLab 384EX ABG machine installed in ICU. Analysis was done through "rkdas Indian 2017 method of ABG interpretation".

C. Urine Examination
a. 10ml of urine is taken for routine and microscopic examination and culture and sensitivity

b. Spot urinary albumin-creatinine ratio was done by collected 5ml urine in separate bottle

c. Deep stick test

13. STUDY TECHNIQUE:
Meeting the inclusion and exclusion criteria 100 adult patients are selected. Thorough History, clinical and routine laboratory parameters are obtained. Acute Physiology and Chronic Health Evaluation (APACHE II) scores are calculated within first 24hrs of their I.C.U. admission.

A spot urine sample (5ml) is to be collected and sent for Urinary microalbumin and measured by the auto-analyser (immunoturbidometric method) and urinary creatinine by auto-analyser-modified kinetic Jaffe reaction -method. The methods covered an analytical range of 1.3-100 mg for microalbumin and 0-20 mg/dl for creatinine. Microalbuminuria was defined by ACR values between 30-299 mg/g. ACR of > 300 mg/g is considered as clinical 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 are followed up on 3rd, 7th and 14th day in I.C.U. to assess treatment outcome in terms of mortality and length of I.C.U. stay.

14. PLAN FOR ANALYSIS OF DATA: The data was analyzed by a standard statistical method, using SPSS (version 20.0) software

RESULTS
1. In our study, age of patients was below 60 yrs and age and sex were equitably distributed among various study groups (e.g. sepsis/severe sepsis/septic shock or, survivor/non survivor)

2. Among 100 patients studied, 91 had medical etiology of sepsis and 9 had surgical etiology

3. 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.

4. Chronic Health Condition score was significantly higher in Septic shock group(Mean 0.86, SD 0.77) as well as in Non-survivors (Mean 0.94, SD 0.83)

5. 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.

6. 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)

7. ABG analysis shows non significant value of oxygenation, ph and electrolyte, it needs further study

8. Mean ACR (within 24 hrs of CCU 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)

9. ACR measured within 24 hrs 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)

DISCUSSION
Our study was conducted in the Intensive Care Unit of JLNMCH, Bhagalpur, over a span of 1 yr 3 months periods. It was a short term prospective cohort study (non-interventional).Overall 100 patients of sepsis who got admitted in our ICU during this said period and fitted into our inclusion criteria, were studied. Their APACHE II score were calculated during first 24 hours of ICU admission and also their urine sample were sent for measurement of urinary spot Albumin Creatinine Ratio (ACR).These patients were then followed up for 14 days or till their discharge from ICU or death, whichever earlier. APACHE II score is an already established tool for prediction of mortality or outcome in sepsis patients. In our study, we tried to look into whether Microalbuminuria can also predict outcome in sepsis patients like APACHE II does and whether ACR (measured within 24 hrs of ICU admission) can be used as a cost effective indicator of prognosis in these patients.

In our study among all parameters studied for APACHE II score, the Chronic Health Condition score, Mean Blood Pressure and Serum Creatinine level were found to be varying significantly in various severity groups of sepsis (sepsis, severe sepsis and septic shock).These parameters were also worse in patients who expired, as compared to those who survived during follow up. Mean APACHE II score was progressively higher in patients of Severe sepsis and Septic shock, as compared to patients of sepsis alone(p value <0.001) and it was also found to be significantly higher in non survivors as compared to survivors. Whereas mean ACR value (measured once during first 24 hrs of ICU admission) also similarly were significantly worse in severe sepsis and septic shock patients, compared to sepsis patients & ACR value was worse in non survivors. And finally the ROC (Receiver Operator Characteristic) curve analysis showed that the Mean ACR value (area under curve 0.950) was as good as the APACHE II score (area under curve 0.961),in predicting mortality in sepsis patients. Just like an APACHE II cut-off of 18 showed 82% sensitivity and 90% specificity in predicting mortality in sepsis patients, with mean ACR cut off of 162.5 mg/gm of creatinine also showed 94% sensitivity and 83% specificity in prediction of mortality.

Assay of the amount of albumin excreted in urine, expressed as ACR [29], is a simple, validated, reliable and inexpensive test that adjusts for variable urine concentrations among patients and obviates the need for a timed urine collection. Moreover it can be performed if intended at the patient's bedside using a point-of-care device and results can be obtained as early as 15 min [21]. Microalbuminuria would be an ideal tool for the early and accurate identification of patients with high risk of morbidity and mortality. This would allow the intensivist to triage and optimize aggressive and sometimes expensive therapeutic interventions in patients most likely to benefit and to curb use in those who are unlikely to do so, especially in situations of financial constraints. Measurement of ACR can guide optimum allocation of resources, counseling of family and/or patient and opportune triaging to the wards, too. The study of Thorevska et al [20] showed that medical patients with an ACR value of more than 100 mg/g on ICU admission were 2.7 times more likely to die compared with those with ACR < 100 mg/g. A much lower cut-off value of 2.9 mg/mmol (25.6 mg/g) at 6 hrs of ICU admission was decided as optimum by Gosling et al [21] to predict mortality in a mixed medical surgical ICU population.

CONCLUSION
Microalbuminuria is of common occurrence in a heterogeneous critically ill population. Patients without significant microalbuminuria during first six hours of ICU admission are less likely to have sepsis. At 24 hours, absence of elevated levels of microalbuminuria is strongly predictive of ICU survival, equivalent to the time-tested APACHE II scores. 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.

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