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A STUDY OF MICROALBUMINURIA IN SEPSIS AND ITS PROGNOSTIC SIGNIFICANCE IN CRITICALLY ILL PATIENTS

General Medicine

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ABSTRACT

a) Background : Microalbuminuria occurs due to changes in glomerular permeability within few hours of inflammation in sepsis. It reflects generalised endothelial damage throughout the vasculature. So, microalbumiuria serve as marker of sepsis. The measurement of microalbuminuria at the time of admission and after 24 hour of admission can be taken as prognostic indicator of mortality in critically ill patients.
b) Materials and Methods : This is a prospective study of 100 patients admitted to emergency ward and ICU. The microalbumiuria was assessed to evaluate as marker of sepsis and to predict ICU mortality. Albumin creatinine ratio 1 (ACR 1) is considered as marker in sepsis and albumin creatinine ratio (ACR 2) is considered as the prediction of ICU mortality.
c) Results - In our study, Microalbuminuria occurred in 68.3% of the patient. Mortality rate was 70.38%. Median ACR1 was 140.05 among survivors and ACR 1 among non-survivors was 262.77, p value was <0.001 which was statistically significant. Median ACR2 among survivors was 220.62 and median ACR2 among non survivors was 412.36, p value was < 0.001 which was statistically significant, indicating ACR2 can be taken as prognostic marker in ICU mortality.
d) Conclusion - Microalbuminuria is a common in critically ill patients and reliable marker of sepsis. At 24hours of admission, ACR 2 indicates its prognostic significance among survivors and non survivors in critically ill patients.

KEYWORDS

Sepsis, Microalbumiuria, Albumin-Creatnine ratio.

2. INTRODUCTION

Sepsis remains a major global health care concern, owing to high morbidity and mortality, despite the advances in medical therapeutics.[1] Sepsis is characterized by SIRS (systemic inflammatory syndrome) and the presence of known or suspected infection.[2]

The endothelium is recognized as an endocrine/paracrine structure which secretes several vasoactive mediators or autocoids that decisively affect vascular tone and platelet function. Endothelium lining circulatory system serves as a important target to endotoxin. The secretion of excess of endothelium derived substances - nitric oxide (NO), endothelin in response to endotoxin and pro inflammatory substances. Nitric oxide causes persistent vasodilatation and may contribute to hypotension and MODS and on the other hand endothelin evokes profound vasoconstriction within vital organs and inturn lead to dysfunction.[3]

The effects of disruption of the integrity of the endothelial barrier is manifested as altered glomerular endothelial permeability in the kidneys, allowing increased amounts of albumin to escape into the glomerular ultra filtrate. The tubular reabsorptive mechanism for albumin from the ultrafiltrate is exceeded beyond its threshold capacity, leading to increased excretion of albumin in the urine. The degree of albuminuria is dependent on the intensity of the inflammatory responses, and therefore microalbuminuria reflects disease severity found to be prevalent in a broad spectrum of critically ill patients.

The development of microalbuminuria include the malfunction and depletion of podocytes (cells that form an essential part of the glomerular filtration barrier), resulting in a leaky endothelial barrier.[4] So, there is the potential for glomerular capillaries to be affected by acute endothelial injury.[5]

Levels of microalbuminuria increases within hours of inflammatory insult. Albumin creatinine ratio 1 is considered as better discriminator, in diagnosing sepsis and Albumin creatinine ratio 2 is considered in the prediction of ICU mortality.[6]

Microalbuminuria defined as 30-300mg/day occurs rapidly after an acute insult and persists in patients with complications.[7] Diagnosing sepsis early is vital for patient management and outcome.[8] The incidence of polymicrobial infection has progressively increased in recent years.[9,10] Hence this, current study has been undertaken to evaluate a microalbuminuria as a marker of sepsis and its ability to predict mortality in the Intensive Care Unit.

3. Aims and objectives of the study:

- To evaluate microalbuminuria as marker of sepsis.
- To evaluate the ability of microalbuminuria to predict ICU mortality

4. MATERIALS AND METHODS

Data for the study was collected from patients during 2018-2019 admitted to emergency ward and ICU – ESI PGIMSR Rajajinagar, Bangalore. We conducted a prospective study of sample size of 100 patients.

a) Inclusion criteria:

Adults patients >18years
patient fulfilling SIRS criteria (two or more of the following)

a) Temperature less than or equal to 36deg Celsius OR more than or equal to 38deg Celsius
b) Heart rate more than or equal to 90bpm
c) Respiratory rate more than or equal to 20 breaths/min
d) White blood cell count more than or equal to 12,000 OR less than or equal to 4,000 cells/mm3 OR > 10%bands.

b) Exclusion criteria:

- Patients with anuria, haematuria.
- Patients with pre-existing chronic kidney disease (Patients on long term renal replacement therapy/sonological features of chronic kidney disease).
- Patients with Diabetes and Hypertension
- Patients with proteinuria due to renal and post renal causes.
- Patients with urinary tract infection.
- Female patients with menstruation or pregnancy.

Methodology:

Patients admitted to Emergency ward and ICU during fulfilling the inclusion and exclusion criteria was taken into study after obtaining

written informed consent. Demographic data, history, clinical examination was recorded in the study proforma. A thorough clinical evaluation was carried out and recorded in the protocol. Temperature, Heart rate, Respiratory rate, Blood pressure was recorded. Relevant laboratory investigations - complete haemogram, blood culture and sensitivity, C reactive protein, Blood urea, Serum creatinine, Serum electrolytes, Random blood sugar, Erythrocyte sedimentation Rate, was sent. Routine urine analysis, urine culture and sensitivity, Sputum culture and sensitivity, chest x ray was done in required patients. Urine – urine spot samples was collected at the time of ICU admission for Albumin Creatinine Ratio 1 and Albumin Creatinine Ratio 2 at 24hrs of ICU admission and samples were received in bio chemistry lab stored at -20 degree celcius till analysis. Urinary microalbumin is measured by immunoturbidimetric method and urinary creatinine by modified kinetic jaffe reaction. The methods covers an analytical range of 1.3-100mg/L for microalbumin and 0-20mg/dl for creatinine. Microalbuminuria was defined by Albumin Creatinine Ratio values between 30 and 300mg/g. Trend of Microalbuminuria is assessed from change of Albumin Creatinine Ratio 1 to Albumin Creatinine Ratio 2. The difference between those values delta Albumin creatinine ratio is calculated.

5. RESULTS AND OBSERVATIONS

Table 1 : Distribution of Microalbuminuria (ACR1) in patients

Microalbuminuria	No. of patients	%
PRESENT	82	82%
ABSENT	18	18%
TOTAL	100	100%

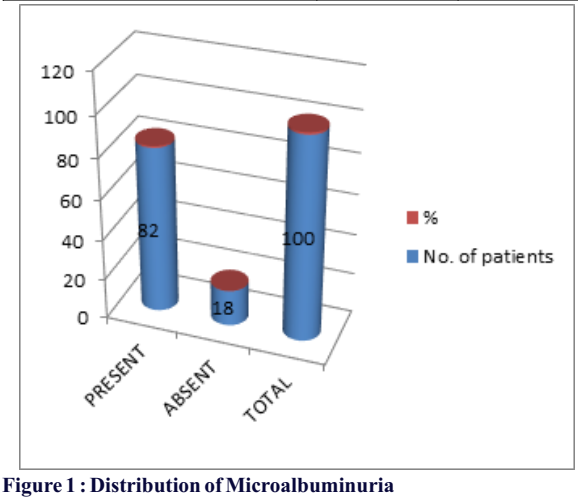

Figure 1 : Distribution of Microalbuminuria

In our study, microalbuminuria was found in 82 patients (82%).

Table 2 : Need for ventilation in microalbuminuria and non - microalbuminuria patients

Need for ventilation in patients	No. of patients	%
Microalbuminuria	68	93.15%
Non-microabluminuria	5	6.85%
TOTAL	73	100%

In this study, 93.15% of the patient required ventilation in microalbuminuria group, 6.85% of the patient required ventilation in non microalbuminuria group

Table 3 : Percentage of culture positive, culture negative in ventilated patients

Need for ventilation in patients	Culture positive	Culture negative
Microalbuminuria	93.9%	91.7%
Non-microalbuminuria	6.1%	8.3%
TOTAL	100%	100%

In our study, 93.9% of the patient required ventilation in culture positive, microalbuminuria patients and 6.1% of the patient required ventilation in culture positive non microalbuminuria patients.

In our study, 91.7% required ventilation in culture negative microalbuminuria patients, 8.3% in culture negative non microalbuminuria patients.

Table 4 : Distribution of mortality in microalbuminuria patients (culture positive and culture negative patients)

Death	Mortality in Microalbuminuria patients	No. of patients	%
YES	Culture positive	38	70.38%
NO	Culture negative	16	29.62%
	Total	54	100%

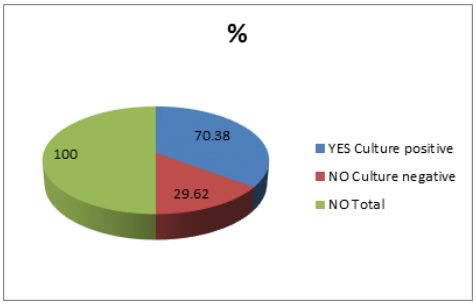

Figure 2 : Distribution of mortality in microalbuminuria patients

In our study, mortality was 70.38% in culture positive microalbuminuria patients.

Table 5 : Comparison of clinical variables with incidence of Micro albuminuria levels

Variables	Mirco albuminuria	
	No Micro albumin urea	Micro albumin urea
Age in years	36.45±12.74	42.73±18.64
HR(bpm)	108.95±10.60	109.10±12.01
RR per min	33.64±6.46	30.44±5.98
Hemoglobin %	12.64±7.97	11.52±2.51
WBC	19955.91±8012.12	17644.46±5666.93
Platelet count	1.81±0.77	1976.21±12427.13
RBS (mg/dl)	155.77±86.79	147.37±92.32
B. urea (mg/dl)	34.66±12.16	37.37±11.82
Serum Creatinine(mg/dl)	0.93±0.36	0.99±0.38
Total Bilirubin(mg/dl)	1.46±2.22	1.16±0.86
Direct bilirubin(mg/dl)	0.53±1.21	0.57±0.90
SGOT(IU/l)	52.32±23.93	65.18±48.4
SGPT(IU/L)	56.27±42.56	60.73±50.52
ALP	84.32±52.59	83.97±43.78
Serum albumin (mg/dl)	3.68±0.94	3.76±0.64
ICU stay in days	9.14±5.46	8.14±5.60

Mean age in no microalbuminuria and microalbuminuria patients was 36.45 and 42.73 years respectively. Mean Heart Rate in no microalbuminuria and microalbuminuria patients was 108.95 and 109.10 respectively. Mean respiratory rate in no microalbuminuria and microalbuminuria patients was 33.64 and 30.44. Mean WBC count in no microalbuminuria and no microalbuminuria patients was 19,955 and 17,644 respectively. Mean duration of ICU stay in no microalbuminuria and microalbuminuria patients was 9.14 and 8.14 days.

Table 6 : Correlation of ACR at admission and at 24 hours of admission

	Mortality	
	Survived	Death
ACR 1	140.05±133.77	262.77±185.95
ACR 2	220.62±165.04	412.36±278.02

ACR has been significantly been increased in non-survivors patients

Table 7 : Correlation of Incidence of microalbuminuria with mortality

Micro-albuminuria	Mortality	
	Survived	Death
No	18(39.13%)	0(0%)
Yes	28(60.87%)	54(100%)
Total	46(100%)	54(100%)

Incidence of Micro-albuminuria is statistically associated with Mortality with P<0.001

6. DISCUSSION

Diagnosing sepsis early is vital for patient management and outcome. Culture of body fluids, the gold standard are not always positive and yield results not earlier than 24hours, which may be too late for administering targeted therapies.

Microalbuminuria was the reason for increased incidence of mortality in critically ill patients. It is probably the result of widespread endothelial dysfunction arising from the effects of cytokines, and other inflammatory mediators, released during the intense inflammatory responses that are associated with critical illnesses.

In our study, Microalbuminuria occurred in 68.3% of the patient. In study done by Murugesan et al microalbuminuria occured in 78% of patients.[11] In our study mortality rate was 70.38%. In a study done by Bhadade et al mortality rate was 29.6%.[12]

In our study median ACR1 was 140.05 among survivors and ACR 1 among non-survivors was 262.77, p value was <0.001 which was statistically significant. In a study conducted by Groin et al median ACR1 among survivors was 61.88 and ACR1 among non-survivors was 137.02.[13] In a study done by Gosling et al median ACR1 among survivors was 37.2 and ACR1 among non-survivors was 161.8, p value was <.0002 which was statistically significant.[14]

In our study median ACR2 among survivors was 220.62 and median ACR2 among non survivors was 412.36, p value was < 0.001 which was statistically significant, indicating ACR2 can be taken as prognostic significance in ICU mortality. In a study done by Bhavita et al, median ACR2 at 24 hours of admission was 46 among survivors and median ACR2 at 24hours of admission was 164.5, p value was <0.0001 which was statistically significant, indicating its prognostic significance.[15] In a study conducted by Mackinnon et al, concluded ACR measured 6hour after admission to ICU demonstrated a significant difference (p =0.01) between survivors and non survivors, allowing identification of patients at increase risk of developing organ failure and death.[16]

7. CONCLUSION

Microalbuminuria is common in critically ill patients. It is a reliable marker of sepsis. At 24hours of admission, increased levels of microalbuminuria compared to microalbuminuria levels at admission, indicates its prognostic significance among survivors and non survivors in critically ill patients. It could be effectively utilised to identify patients likely to survive in the ICU. Serial measurements of microalbuminuria may prove a useful aid in the clinical assessment of critically ill patients.

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