ORIGINAL RESEARCH PAPER
Volume - 12 | Issue - 09 | September - 2023 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

ASSOCIATION OF MICROALBUMINURIA WITH SEPSIS

Medicine

Dr. Jaya Pathak Associate Professor, Department of Medicine, Medical College Baroda
Dr. Dipen Rajpura Senior Resident, Department of Medicine, Medical College Baroda
Dr. Karan Pandya 3rd year Resident, Department of Medicine, Medical College Baroda
Dr. Radhay Parikh 3rd year Resident, Department of Medicine, Medical College Baroda
Arushi Patel 3rd year MBBS Student, GMERS Medical College, Gotri

ABSTRACT

Sepsis is a life-threatening organ dysfunction, quantified using the SOFA score. A dysregulated host immune response in sepsis and related conditions produces excess cytokines that cause increase in systemic capillary permeability and endothelial dysfunction. The consequence of this on the renal system causes microalbuminuria. We conducted a comparative study on 60 adult patients who were clinically suspected of having sepsis, in order to learn the association between microalbuminuria and sepsis. Chi square test revealed a significant correlation between the two and hence, microalbuminuria can be used as a rapid, easily available and inexpensive test to diagnose sepsis.

KEYWORDS

Microalbuminuria, Sepsis, UACR (urine albumin-creatinine ratio), SOFA score (sequential organ failure assessment)

INTRODUCTION

Sepsis is defined as life threatening organ dysfunction that is caused by a dysregulated host response to infection (Evans et al., 2021) [1]. A recent global study reported 49 million cases and 11 million sepsis related deaths in 2017, accounting for approximately 20% of all annual deaths globally (Rudd et al., 2020) [2,3]. The sepsis cases in India alone were estimated to be 11.3 million, with 2.9 million deaths (297.7 per 100,000 population) in 2017 (Hammond et al., 2022) [4]. Early diagnosis and early initiation of the right treatment is key for the positive outcome of patients.

Sequential organ failure assessment (SOFA) is a scale widely used in emergency, internal medicine, surgery, and the ICU to evaluate the disease condition and prognosis of patients with multiple organ failure, which can dynamically reflect the changes of organ function. Quick SOFA (qSOFA) is a scale that can quickly analyze the changes of patients' condition by analyzing consciousness, systolic blood pressure, and heart rate (Liu et al., 2022) [5].

A definitive diagnosis of sepsis can be established only by cultures, which not only takes a long time but are also positive in only less than half of the cases. There is thus, a need for a marker for early detection of sepsis and thereby allowing timely intervention.

The host defense in sepsis involves potent inflammatory cascades which release a plethora of pro inflammatory molecules into the circulation (Bhadade et al., 2014) [6]. This leads to endothelial dysfunction and increase in systemic capillary permeability. The endothelial injury and capillary leak in the glomerulus results in increased excretion of albumin in the urine. This leads to the presence of microalbumin in the urine, i.e.30- 299mg/g creatinine. This study was done with the aim to look for presence of microalbuminuria in patients with sepsis. Also the presence of microalbuminuria was compared between blood culture positive versus negative patients.

MATERIALS AND METHODS

The present study, a prospective observational study, was conducted at Shri Sayaji General Hospital, Vadodara, a tertiary health care institute, from August 2020 to July 2021. Following the approval from the Institutional Ethics Committee, the study was conducted on 60 adult patients, admitted to the Medical Intensive Care Unit under the Department of Medicine, with the clinical suspicion of sepsis. Inclusion criteria included patients having clinical features of infection and 2 or more of the following:

1) Fever (Temperature >38°c) or hypothermia (Temperature <34°c)
2) Tachycardia (HR >90/min)
3) Tachypnea (RR>20/min)
4) Total WBC count (>12000 /micro litre)
5) Or total WBC count (<4000 /micro litre) or bands >10%

Patients fulfilling the Inclusion criteria were enrolled in the study after taking written informed consent of the patient. Patients with hematuria, significant proteinuria, pre-existing chronic kidney disease, anuria, pregnant females, menstruating females, urinary tract infection were excluded.

Each patient's bio data, detailed clinical history including history of comorbidities and past illnesses was collected after which a detailed clinical examination was performed. All routine investigations including complete blood count, routine urine microscopic examination, renal function tests, liver function tests, serum electrolytes, random blood sugar, electrocardiogram, blood cultures, arterial blood gas analysis and spot urinary albumin creatinine ratio (UACR) were ordered and treatment was initiated as per the protocol. Based on the results of above investigations, a SOFA score was calculated for each patient and the patients were then divided into two groups based on the same. One group having Sepsis: SOFA score>=2, Second group without sepsis: SOFA Score <=2. Presence of microalbuminuria and culture positivity was compared amongst both the groups.

RESULTS

Out of the 60 patients enrolled in our study, 23(38.3%) were males and 37(61.7%) were females.

Most patients were in the 21-30 years age group, but there was no obvious predisposition for a particular age group. 53 patients (88.3%) had sepsis as diagnosed using the SOFA score, but only 7 patients (13.2%) had a positive blood culture test. The median SOFA score was 5.

Urine analysis showed 38 patients (63.3%) had microalbuminuria and 7 (11.7 %) patients had macroalbuminuria. The median value of UACR in sepsis patients was 101.56 and 10.08 in non-sepsis patients.

Table 1: Categorization of patients according to clinical diagnosis based on urine albumin-to-creatinine ratio (UACR) (n = 60)

Clinical category according to UACR	n	%
Normal	15	25.0
Microalbuminuria	38	63.3
Macroalbuminuria	7	11.7
Total	60	100.0

Table 2: Categorization of patients according to diagnosis of sepsis (n = 60)

Sepsis diagnosis	n	%
No sepsis	7	11.7
Sepsis	53	88.3
Total	60	100.0

We considered any participant with a SOFA score of ≥ 2 as having sepsis.

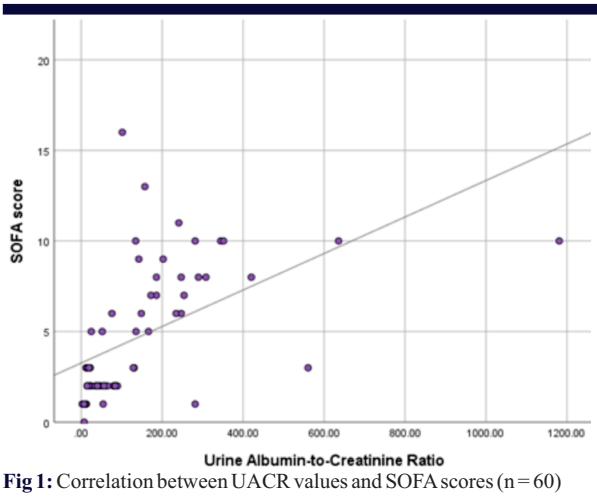

Fig 1: Correlation between UACR values and SOFA scores (n = 60)

Correlation between UACR values and SOFA scores was carried out to see the linear relationship between the two.

Table 3: T-test Between Microalbuminuria And Blood Culture Categories (n = 38; Only In Participants With Microalbuminuria)

	Blood culture report	N	Mean	SD	SE Mean	p-value
Urine Albumin-to-Creatinine Ratio	Negative	32	134.92	82.78	14.63	0.934
	Positive	6	131.90	73.46	29.99	

Independent samples t-test was applied between participants with microalbuminuria who had a positive blood culture report and patients of microalbuminuria with a negative blood culture report. No significant difference between mean UACR values in participants who had positive blood culture reports and those who had negative blood culture reports could be discerned (p-value = 0.934).

Table 4: Chi square test between UACR categories and sepsis (as defined by SOFA score ≥ 2) (n = 60)

		Categorization of SOFA scores to indicate sepsis		Total (%)
		No sepsis (%)	Sepsis (%)	
Categorization of UACR	Normal	5 (71.4)	10 (1.9)	15(20.0)
	Microalbuminuria	2 (28.6)	36 (67.9)	38(63.3)
	Macroalbuminuria	0 (0.0)	7 (13.2)	7(11.7)
Total		7	53	60

$\chi^2 = 9.269$; p-value = 0.010

For the purpose of understanding differences in patients with normal UACR scores, microalbuminuria and macroalbuminuria with respect to sepsis status we first categorised patients as having and not having sepsis. Subsequently, we carried out a chi-square test.

The outcome of the chi-square test indicates a significant difference in the number of participants having normal UACR, microalbuminuria and macroalbuminuria with respect to sepsis ($\chi^2 = 9.269$; p-value = 0.010). A significantly larger proportion of participants with sepsis had microalbuminuria, as compared to participants who did not have sepsis (67.9% v/s 28.6%).

DISCUSSION

Sepsis is a life threatening condition commonly encountered by clinicians which mandates early diagnosis and initiation of targeted therapy. Recently updated definitions of sepsis and septic shock have been proposed which better identify patients who are likely to have a poor outcome, and therefore give an opportunity to escalate care. Despite these advances, there is still no molecular signature able to diagnose sepsis (Evans 2018) [7]. The tests which are being used at present for diagnosis of sepsis, namely Blood culture, Procalcitonin, C reactive protein, etc. all have their drawbacks and limitations.

Blood culture, although a gold standard for diagnosis of sepsis is time consuming and not a sensitive test. Procalcitonin although sensitive for sepsis, also gets elevated in other inflammatory conditions, hepatic dysfunction, inhalation injury, trauma, burns, heat stroke, fungal infections and anti T cell therapy. CRP is an inexpensive test, but not specific for sepsis as it is an acute phase reactant and rises in several conditions (Carrigan et al., 2004) [8] (Becker et al., 2008) [9]. As compared to PCT and CRP, levels of microalbuminuria increase within hours of inflammatory injury (Molnár et al., 2000) [10] (Nawal et al., 2022) [11]

In our study the mean age of patients was found to be 36.4 years. A study conducted by S Todi et al. (2010) [12] showed a mean age of 58.17 years (SD 18.66) and a study done by Angus et al. (2001) [13] showed mean age of 57.0 , as patients with age > 60 years constituted 34.8% of the study population. Gender distribution in our study showed that 23(38.33%) were males and 37(61.67%) were females. In a study conducted by S Todi et al. (2010) [12] in India which studied the epidemiology of sepsis in which male patients constituted 57.71%. Study done by Angus DC et al. (2001) [13] showed male patients constituted 51.9%. In the current study, we divided the patients into two groups, one group had patients with sepsis and the other had patients without sepsis. In the current study, the median levels for ACR were 101.56mg/g for the sepsis and 10.08 mg/g for the non-sepsis groups, respectively. The levels of microalbuminuria were significantly elevated among the patients with sepsis as compared to those without sepsis. In the present study, on carrying out the correlation between UACR and SOFA score, the Pearson's correlation coefficient was found to be 0.530 (p-value <0.005) indicating moderate positive correlation, i.e. rising values of UACR correlate with rising values of SOFA scores and vice versa. The findings were similar to as observed by Basu et al. (2010) [14, 15] in two of their studies and also in a study by Bhadade et al. (2014) [6]

The reason for increased incidence of microalbuminuria in critically ill patients 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 (Todi et al., 2010) [12]. The effects of disruption of the integrity of the endothelial barrier is manifests as altered glomerular endothelial permeability in the kidneys, allowing increased amounts of albumin to escape into the glomerular ultrafiltrate. The tubular reabsorption 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 (Basu et al., 2010) [14]. This probably explains the positive association observed between microalbuminuria and SOFA scores.

In our study, only 13.2% patients with sepsis were found to have a positive blood culture. The findings are similar to a study conducted by Marco Previsdomini et al. (2012) [16] where they had blood culture positive in 20% of ICU patients. No significant difference between mean UACR values in patients who had positive blood culture reports and those who had negative blood culture reports could be discerned (p-value = 0.934). The limitations of our study was the small sample size, also here we had included patients with Diabetes Mellitus and Hypertension which could confound microalbuminuria levels. Also patients with urosepsis were excluded from this study.

CONCLUSION

Microalbuminuria is an inexpensive, rapid diagnostic tool which gets elevated in patients of sepsis. The presence of microalbuminuria not only correlates well with the presence of sepsis but its levels correlate well with the severity of sepsis. There is no significant positive correlation between presence of microalbuminuria and positivity of blood culture.

REFERENCES

1. Evans, L., Rhodes, A., Alhazzani, W., Antonelli, M., Coopersmith, C. M., French, C., Machado, F. R., Mcintyre, L., Ostermann, M., Prescott, H. C., Schorr, C., Simpson, S., Wiersinga, W. J., Alshamsi, F., Angus, D. C., Arabi, Y., Azevedo, L., Beale, R., Beilman, G., Belley-Cote, E., Levy, M. (2021). Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock 2021. Critical care medicine, 49(11), e1063–e1143. https://doi.org/10.1097/CCM.0000000000005337
2. Global report on the epidemiology and burden of sepsis: current evidence, identifying gaps and future directions. Geneva : World Health Organization (http://www.wipo.int/amc/en/mediation/rules/).
3. Rudd, K. E., Johnson, S. C., Agesa, K. M., Shackelford, K. A., Tsoi, D., Kievlan, D. R., Colombara, D. V., Ikuta, K. S., Kissoon, N., Finfer, S., Fleischmann-Struzek, C., Machado, F. R., Reinhart, K. K., Rowan, K., Seymour, C. W., Watson, R. S., West, T. E., Marinho, F., Hay, S. I., Lozano, R., … Naghavi, M. (2020). Global, regional, and national sepsis incidence and mortality, 1990-2017: analysis for the Global Burden of Disease Study. Lancet (London, England), 395(10219), 200–211. https://doi.org/10.1016/S0140-6736(19)32989-7

4. Hammond, N. E., Kumar, A., Kaur, P., Tirupakuzhi Vijayaraghavan, B. K., Ghosh, A., Grattan, S., Jha, V., Mathai, D., Venkatesh, B., & Sepsis in India Prevalence Study (SIPS) Investigator Network (2022). Estimates of Sepsis Prevalence and Outcomes in Adult Patients in the ICU in India: A Cross-sectional Study. Chest, 161(6), 1543–1554. https://doi.org/10.1016/j.chest.2021.12.673
5. Liu, C., Suo, S., Luo, L., Chen, X., Ling, C., & Cao, S. (2022). SOFA Score in relation to Sepsis: Clinical Implications in Diagnosis, Treatment, and Prognostic Assessment. Computational and mathematical methods in medicine, 2022, 7870434. https://doi.org/10.1155/2022/7870434
6. Bhadade, R. R., deSouza, R., Harde, M. J., & Sridhar, B. (2014). Microalbuminuria: a biomarker of sepsis and efficacy of treatment in patients admitted to a medical intensive care unit of a tertiary referral center. Journal of postgraduate medicine, 60(2), 145–150. https://doi.org/10.4103/0022-3859.132320
7. Evans T. (2018). Diagnosis and management of sepsis. Clinical medicine (London, England), 18(2), 146–149. https://doi.org/10.7861/clinmedicine.18-2-146
8. Carrigan, S. D., Scott, G., & Tabrizian, M. (2004). Toward resolving the challenges of sepsis diagnosis. Clinical chemistry, 50(8), 1301–1314. https://doi.org/10.1373/clinchem.2004.032144
9. Becker, K. L., Snider, R., & Nylen, E. S. (2008). Procalcitonin assay in systemic inflammation, infection, and sepsis: clinical utility and limitations. Critical care medicine, 36(3), 941–952. https://doi.org/10.1097/CCM.0B013E318165BABB
10. Molnár, Z., Szakmány, T., Köszegi, T., & Tekeres, M. (2000). Microalbuminuria and serum procalcitonin levels following oesophagectomy. European journal of anaesthesiology, 17(7), 464–465.
11. Nawal, C. L., Barasara, S., Chejara, R. S., Meena, P. D., Singh, A., & Meena, V. K. (2022). Microalbuminuria: As an Indicator of Sepsis and to Predict Mortality in Patients Admitted to Intensive Care Unit. The Journal of the Association of Physicians of India, 70(3), 11–12.
12. Todi, S., Chatterjee, S., Sahu, S., & Bhattacharyya, M. (2010). Epidemiology of severe sepsis in India: an update. Critical Care, 14(Suppl 1), P382. https://doi.org/10.1186/cc8614
13. Angus, D. C., Linde-Zwirble, W. T., Lidicker, J., Clermont, G., Carcillo, J., & Pinsky, M. R. (2001). Epidemiology of severe sepsis in the United States: analysis of incidence, outcome, and associated costs of care. Critical care medicine, 29(7), 1303–1310. https://doi.org/10.1097/00003246-200107000-00002
14. Basu, S., Bhattacharya, M., Chatterjee, T. K., Chaudhuri, S., Todi, S. K., & Majumdar, A. (2010). Microalbuminuria: A novel biomarker of sepsis. Indian journal of critical care medicine : peer-reviewed, official publication of Indian Society of Critical Care Medicine, 14(1), 22–28. https://doi.org/10.4103/0972-5229.63034
15. Basu, S., Chaudhuri, S., Bhattacharyya, M., Chatterjee, T. K., Todi, S., & Majumdar, A. (2010). Microalbuminuria: An inexpensive, non invasive bedside tool to predict outcome in critically ill patients. Indian journal of clinical biochemistry : IJCB, 25(2), 146–152. https://doi.org/10.1007/s12291-010-0027-9
16. Previsdomini, M., Gini, M., Cerutti, B., Dolina, M., & Perren, A. (2012). Predictors of positive blood cultures in critically ill patients: a retrospective evaluation. Croatian medical journal, 53(1), 30–39. https://doi.org/10.3325/cmj.2012.53.30