Original Article

TO EVALUATE URINE ALBUMIN-CREATININE RATIO (UACR) FOR ALBUMINURIA IN PATIENTS WITH SEPSIS ADMITTED TO MEDICINE INTENSIVE CARE UNIT (MICU) AND ITS CORRELATION WITH SOFA SCORE

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DOI: 10.47750/pnr.2022.13.S06.531

Abstract

Aim: The aim of the present study was to evaluate Urine Albumin-Creatinine Ratio (UACR) for albuminuria in patients with sepsis admitted to Medicine Intensive Care Unit (MICU) and its Correlation with SOFA score.

Methods: The present study was conducted in the Department of General Medicine, Dr. D. Y. Patil Medical College, Hospital and Research Centre, Pimpri, Pune from August 2018 to September 2020. 40 patients were included in the present study.

Results: The result shows the distribution of cases according to age. It was observed that the maximum number of subjects with sepsis (45%) was in 18 – 40 years age group. 22.5% of patients belonged to the above 60 age group. Mean age of the study subjects was 44.45 ± 18.43 years. Majority of the patients admitted due to sepsis were male 24 (60%) and 16 patients (40%) were female. In our study, abnormal hemoglobin levels (<12.3) were found in 35 (87.5%) out of 40 patients with a mean of 10.22 ±2.16. Out of 40 patients 26 (65%) were found to have elevated CRP levels and mean CRP was 79.2975. Liver function tests revealed that out of 40 patients 20 had elevated total bilirubin levels with mean of 4.40 ±8.49.

Conclusion: In this study several possibilities for the future application of UACR in critically ill patients were highlighted. For early detection of patients with sepsis needing early targeted therapy, routine UACR surveillance could potentially help. Microalbuminuria, a non-invasive and easily available bed side investigation, can be used as a marker for prediction of mortality and morbidity.

Keywords: Sepsis, Urinary albumin/creatinine ratio, intensive care unit, SOF score.

Introduction

Patients requiring intensive care frequently have some degree of systemic inflammatory response syndrome (SIRS), which, when severe, places them at risk of multiple organ failure.[1,2] An early feature of the acute inflammatory process is capillary endothelial cell activation accompanied by a rapid increase in capillary permeability to plasma proteins such as albumin. The transcapillary escape rate of radio-labeled albumin from the circulation increases dramatically within 3 hours of cardiac surgery in patients with infection and malignancies.[3,4] Studies in normal subjects and in patients with diabetes mellitus or hypertension have also demonstrated an association between urine albumin and albumin transcapillary escape rate and evidence of systemic endothelial dysfunction.[5,6]

Sepsis occurs in 1%–2% of all hospitalized patients and sepsis is a major cause of morbidity and mortality and the Indiasecond leading cause of death worldwide.[7] Epidemiological studies are based on community or hospital studies, and the nature of data collection such as retrospective chart review, discharge diagnoses, diagnosis in death certificates, or prospective observational studies gives different figures. A robust epidemiological study methodology should be prospective in nature conducted over a prolonged period and should include heterogeneous case mix representative of the disease, thus allowing scope for generalizing the observed data. Epidemiological data on sepsis come mostly from western literature.[7-10]

Urine Albumin Creatinine Ratio (UACR) may be useful in predicting mortality and morbidity in septic patients. UACR is mainly done to detect the albumin in urine early in the disease course and to prevent the further process of the disease. The glycocalyx layer which usually acts a barrier to protein permeability gets affected leading to the increase excretion of albumin in the urine from the Glomerulus.[11] Urine albumin measurements have good specificity and sensitivity for the changes in the glomerular permeability. Many studies have shown that even small amount of albumin in urine (30-300 mg/day) have a prognostic significance. The organ dysfunction in critically ill septic patients can be scored by scores such as SOFA, APACHE II and APACHE IV. In the first 48hrs if the SOFA increases in the septic patients it predicts mortality of at least 50%.[12,13]

Sepsis is a response shown by the host to the infecting pathogen causes pathological, physiological, biochemical abnormalities. Sepsis can be classified as severe sepsis, when infection and the host response result in organ dysfunction (e.g., acute kidney injury, acute liver failure), or as septic shock, when there is persistent arterial hypotension due to acute circulatory failure in spite of volume resuscitation.[14,15]

The aim of the present study was to evaluate Urine Albumin-Creatinine Ratio (UACR) for albuminuria in patients with sepsis admitted to Medicine Intensive Care Unit (MICU) and its Correlation with SOFA score.

Materials and Methods

The present study was conducted in the Department of General Medicine, Dr. D. Y. Patil Medical College, Hospital and Research Centre, Pimpri, Pune from August 2018 to September 2020. 40 patients were included in the present study.

The protocol of the study was approved by the institution's Scientific & Ethics Committee. All the study subjects were informed about the study procedure and data needed from them. Voluntary informed written consent was taken from all the participants who consented and were then included in the study.

Inclusion criteria

1. All patients of age more than 18 years admitted to the hospital
2. Patients of either sex
3. Patients fulfilled the criteria of Modified/Expanded definition of Sepsis and qSOFA score and SEPSIS-3 guidelines.

Exclusion criteria

1. All patients of Age less than 18 years
2. Pre-existing Kidney Disease
3. Type-I and Type-II Diabetes Mellitus
4. Connective Tissue Diseases
5. Immunocompromised patients
6. Pregnancy

Methodology

A detailed history taking and physical examination were done for all the study participants. Assessment of consciousness level, Glasgow coma scale score at the time of admission were also recorded in all patients. In GCS, the grading of severity is done as follows, mild (GCS score of ≤ 8) moderate (GCS score of 9-12) & severe (GCS score of 13-15).

Spot urine samples were taken within 6hrs of admission & 48 hours for quantification of urine microalbumin by using the immunoturbidometric method & creatinine by using Jaffe method and urine microalbumin: creatinine ratio was calculated which were referred to as UACR at admission and at 48hrs respectively. qSOFA was calculated for all the patients on admission. SOFA was calculated twice for all the patients once at the time of admission and again at 48hrs.

During the hospital stay, the patients were monitored and the outcome that is Death or survival was registered.

The collected data was entered in the MS-Excel and was analysed by applying relevant statistical tests mentioned above.

Statistical Analysis

Data collection and analysis was done and entered into Microsoft excel and Epi-info software. The frequency distribution and graphs were prepared for all the variables. Following statistical tests were applied - Pearson Chi-square test for the categorical variables and the student T test for the quantitative variables. The level of confidence interval & p-value were set at 95% and 5%.

Results

Table 1: Demographic details

Age group (years)	**Number (n=40)**	**Percentage (%)**
18-40	18	45.0
40-60	13	32.5
>60	9	22.5
Mean ± SD	44.45 ± 18.43	

Age group (years)	**Number (n=40)**	**Percentage (%)**
18-40	18	45.0
40-60	13	32.5
>60	9	22.5
Gender		
Female	16	40.0
Male	24	60.0

The above table shows the distribution of cases according to age. It was observed that the maximum number of subjects with sepsis (45%) was in 18 – 40 years age group. 22.5% of patients belonged to the above 60 age group. Mean age of the study subjects was 44.45 ± 18.43 years. Majority of the patients admitted due to sepsis were male 24 (60%) and 16 patients (40%) were female.

Table 2: Hematological parameters, liver function tests, coagulation parameters and renal function tests in study population

Variables (Normal range)	Number of subjects with abnormal values (n=40)	Maximum	Mean	Std. Deviation
Hb (12.3-15.3)	35	13.6	10.225	2.16
TLC (4000-10000)	40	57000	17915	10803.59
PLT (150000-450000)	28	450000	148275	1.052
CRP (<10mg/dl)	26	190.00	79.29	52.40
Liver function tests				
Total Bilirubin (0.10-1.2 mg/dL)	20	38.71	4.40	8.49
Direct Bilirubin (up to 0.3 mg/dL)	27	30.35	3.33	6.99
ALT (up to 33 U/Lt)	27	1575.00	198.47	347.84
AST (Up to 32U/Lt)	27	981.00	124.42	214.38
ALP (46-116 U/Lt)	19	489.00	151.20	95.12
Coagulation parameters				
PT INR (0.85-1.15)	27	3.70	1.52	0.60
APTT (20.72-27.89)	25	50.40	31.55	8.20
Renal function tests				
Urea (17-49 mg/dL)	29	320.00	83.20	56.52
Creatinine (0.6-1.2 mg/dL)	21	7.00	1.72	1.28

In our study, abnormal hemoglobin levels (<12.3) were found in 35 (87.5%) out of 40 patients with a mean of 10.22 ±2.16. It was found that all the patients presented with abnormal leucocyte count with lowest being 800 and highest being 57,000 with an average of 17,915. Out of 40 patients 28 (70%) were found to have platelet count less than 150000 with lowest being 20000 with an average of 148275. Out of 40 patients 26 (65%) were found to have elevated CRP levels and mean CRP was 79.2975. Liver function tests revealed that out of 40 patients 20 had elevated total bilirubin levels with mean of 4.40 ±8.49. Out of 40 patients 27 had elevated AST and ALT levels with a mean 124.42 and 198.47 respectively. Out of 40 patients 19 had elevated ALP levels with a mean of 151.20. 27 out of 40 patients had deranged PT INR levels with a mean of 1.52 and 25 out of 40 patients had deranged APTT levels with a mean of 31.55 with maximum being 50.40. Out of 40 patients renal function tests showed that mean urea was 83.20 with raised urea levels in 29 patients and mean creatinine was 1.72 with raised creatinine levels in 21 patients.

Table 3: Blood culture findings and endotracheal tube culture findings in study population

Findings	**Frequency**	**Percent**
No growth	36	90
S.Typhi	2	5.0
Leptospira	1	2.5
klebsiella	1	2.5
Endotracheal tube culture findings		
No growth	10	66.66
Klebsiella	3	20
Pseudomonas	2	13.33
Total	15	100

Blood culture in the present study was performed to assess the bacteremia and it was found that 36 patients showed no growth and 10 percent of patients have shown growth. Out of which 2 patients showed positive growth for Salmonella Typhi and 1 patient found Leptospira positive and 1 patient found klebsiella positive. Blood culture showed a positivity of 10%. Endotracheal tube cultures have shown that 5 patients have showed positive cultures out of 15 intubated patients. Out of 6 patients, 3 were positive for Klebsiella and 2 were positive for Pseudomonas showing a positivity of 33.33 percent for cultures.

Table 4: UACR (urine albumin creatinine ratio) findings in study population

UACR	**<30**	**30-300**	**Mean**	**Std. Deviation**	**Minimum**	**Maximum**
At admission (n=40)	19	21	79.7250	70.67368	11.00	210.00
At 48hrs (n=40)	18	22	93.92	104.22	14.00	284.00

It was found that 52.5% had UACR 30-299 mg/dl and 47.5% had UACR <30mg/dl at the time of admission. At the time of 48hrs after admission, it was found that 45% had UACR of <30mg/dl and 55% had UACR of values 30-299. Mean UACR at admission was 79.7250 with standard deviation of 70.67 while the mean value of UACR at 48hrs was 93.92 with standard deviation of 104.22.

Table 5: SOFA SCORE FINDINGS

SOFA score	< 9	9 -11	> 11	Mean ± SD
At admission (n=40)	29 (72.5%)	6 (15%)	5 (12.5%)	5.37 ± 3.99
At 48 hours (n=40)	23 (57.5%)	4 (10%)	13 (32.5%)	9.30 ± 5.06

SOFA score was less than 9 in 72.5% patients at the time of admission but at 48 hours, it was in 57.5%. SOFA score was 9 to 11 in 15% patients on admission and it was 10% at 48hrs. It was more than 11 in 12.5% patients on admission and it was 32.5% at 48hrs.

Table 6: qSOFA findings of study population

Parameters	n	Mean	Std. Deviation	<2	>2
qSOFA	40	1.30	0.93	23	17

qSOFA was <2 among 57.5% and >2 among 42.5% patients. Mean value of qSOFA was 1.30 with a maximum score of 3 and a standard deviation of 0.93.

Table 7: CORRELATION OF UACR WITH qSOFA, SOFA AT ADMISSION

UACR at admission	Q SOFA	SOFA at admission
79.72 ± 70.67	1.3 ± 0.93	5.37 ± 3.99
Pearson Correlation	0.740	0.932
P value	0.0001	0.0001

Correlation analysis found that there was strong correlation between UACR and qSOFA (r =0.740) and UACR and SOFA (r =0.932) at the time of admission using Pearson correlation co-efficient and this correlation was statistically significant for both correlation ($p<0.05$).

Discussion

Sepsis is not only a great health problem but also an important socioeconomic challenge worldwide. It lowers patients' living quality and increases the mortality significantly.[7] Identification of sepsis, its prognosis, and outcome prediction are of paramount importance in medical practice. At present, available tools for prediction of prognosis in ICU are the APACHE scores,[16] which predict mortality, and the SOFA score,[17] which predicts morbidity. These scoring systems rely on several physiological indices and chemical analyses. In addition to difficulty in estimation, several drawbacks and limitations have been shown to these scoring systems.[18]

In our study patients were distributed among age of 18-72yrs. For younger age (18 – 40years) group prevalence of sepsis was 45 % and age >60 years it was 22.5%. Mean age of the study subjects was 44.45 years (SD 18.43).

A study done by S Todi et al.[19] showed mean age of 58.17±18.66yrs. In the present study 16 patients (40%) were female and 24 patients were male (60%). This is consistent with study conducted by S Todi et al.[19] epidemiology of sepsis in India with male patients constituting 57.71%, study done by Angus DC et al[20] showed male patients constituting 51.9%.

In the present study 9 patients had pus cells and 35 larger number of samples were negative. Urine cultures revealed 31 out of 40 showed no growth while 9(22.5%) patients showed positivity. Endotracheal tube cultures have shown that 5 patients have showed positive cultures out of 15 intubated patients showing a positivity of 33.33%. Another study by Rodriguez F et al[21] found that the most common diagnosis was UTI (28.6%) followed by pneumonia in 22.8% and soft tissue infections in 21.8% as a cause of sepsis in community acquired pneumonia and within hospital acquired, pneumonia was the most frequent diagnosis in 26.6% followed by UTI in 20.4% and soft tissue infections in 17.4% as a cause of sepsis.

Microalbuminuria (MA) is known to be a sensitive expression of the increased permeability of the systemic microcirculation. In our study UACR (Urine Albumin Creatinine Ratio) was collected on admission and at 48hrs of admission. 40 patients UACR done on admission ranged from 11 to 210 microgram/mg with mean value of 79.72 ± 70.67. UACR at 48 hours ranged from 14 – 284 microgram/mg with mean value of 93.92±103.22. In a study by Mulgund SR et al[22] mean UACR done on admission was 88.57 ± 48.9 microgram/mg mean UACR at 24 hours was 96.27±52.48 microgram/mg.

The qSOFA score in the present study ranged from 0-3 with the mean scoring of 1.3±0.93. Mean SOFA at admission was 5.37 ±3.99 and at 48 hrs was 9.3+5.06. SOFA score was less than 9 in 72.5% patients at the time of admission but at 48 hours, it was in 57.5%. SOFA score was 9 to 11 in 15% patients on admission and it was 10% at 48hrs. It was more than 11 in 12.5% patients on admission and in 32.5% at 48hrs. There was increase in SOFA as severity of sepsis increased. A study done by Jones AE et al., found SOFA score when applied to the patients admitted with sepsis and signs of hypoperfusion, showed fair to strong precision for predicting in-hospital mortality. It has a positive and significant association with in-hospital mortality over 72 hrs.[23]

In our study correlation analysis found that there was strong correlation between UACR and qSOFA ($r = 0.740$) and UACR and SOFA ($r = 0.932$) at the time of admission using Pearson correlation co-efficient and this correlation was statistically significant for both correlation ($p<0.05$). Also, there was strong correlation between UACR and SOFA ($r = 0.745$) at the 48 hours of admission using Pearson correlation co-efficient and this correlation was statistically significant ($p<0.05$). The SOFA scores were found to be higher in the ICU patients in whom the UACR is increasing compared to those patients in whom the UACR was found to be normal or decreasing. The Study by Saeed MA et al[24] found there was no significant correlation between microalbuminuria on admission and either SOFA or APACHE IV scores, whereas microalbuminuria after 24 h was significantly correlated with SOFA score but was not statistically significantly correlated with APACHE IV score. Moreover, SOFA but not APACHE IV score is higher in patients with an increasing trend of ACR. Findings of our study are in line with existing literature. The present study identified the UACR as a prognostic marker, SOFA score and qSOFA score in septic patients including their correlation with each other in the septic patients. Our study showed that in critically ill patients UACR has strong positive correlation with SOFA scores could be used as prognostic and mortality predictor. But at what cut-off level and when to be measured was not studied in detail.

Conclusion

In this study several possibilities for the future application of UACR in critically ill patients were highlighted. For early detection of patients with sepsis needing early targeted therapy, routine UACR surveillance could potentially help. Microalbuminuria, a non-invasive and easily available bed side investigation, can be used as a marker for prediction of mortality and morbidity. The 48hr UACR test forecasts the survival of patients admitted to ICU with sepsis and may also track the success of therapeutic procedures such as fluid resuscitation, sufficient antibiotics, vasopressors and inotropes affecting the endothelium. There was a correlation of UACR and SOFA both at admission and at 48hrs revealing that early treatment of patients with sepsis can help in reducing the mortality.

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