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STUDY OF MICROALBUMINURIA IN SEPSIS WITH SPECIAL REFERENCE TO SAPS-II SCORE IN A TERTIARY CRITICAL CARE CENTER BY

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ABSTRACT

This study was done to evaluate the degree of microalbuminuria in sepsis in correlation with SAPS II Score and to test whether the degree of microalbuminuria could predict mortality in critically ill sepsis patients. The present study conducted on patients admitted to Medical ICU/Medical emergency ward, 64 patients who meet the inclusion and exclusion criteria were included in the study. The degree of Microalbuminuria was more among patients with organ dysfunction than those without. Significant microalbuminuria was indicative of Multi organ Dysfunction. Serial measurements may help in the clinical assessment of critically ill patients at risk of worse prognosis, even in resource poor areas.

Keywords
Microalbuminuria; sepsis; mortality; SAPS II score; Urine ACR

Introduction

SEPSIS is defined as SIRS (systemic inflammatory response syndrome) that has a proven or suspected microbial etiology.[1] Invasive bacterial infections are the prominent causes of death around the world, particularly among young children. Non-typhoidal salmonella species, Streptococcus pneumonia ,Haemophilus influenza , and Escherichia coli were the most commonly isolated bacteria. [2] Sepsis is marked by a severe host defense response that involves triggering of potent inflammatory cascades which release a plethora of pro-inflammatory molecules into the circulation. The endothelium becomes dysfunctional due to the sustained onslaught of the inflammatory molecules and the simultaneous oxidative stress. An early event is the loss of barrier integrity leading to systemic capillary leak. Increased capillary permeability is an early feature of Systemic Inflammatory Response Syndrome (SIRS).[3-6] The glomerular manifestation of this enhanced capillary permeability is increased excretion of albumin in the urine. In various studies microalbuminuria has been correlated with rapid changes in vascular integrity. Early prediction of mortality among critically ill sepsis patients and early institution of intensive therapy is of paramount importance which has significant implications on survival of the patient. [7] Various ICU scoring systems to predict mortality are in current use like the APACHE II and SAPS II score. These scoring systems are cumbersome and are done at 24 hours of admission during which precious time is lost in administering therapy.

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.[8-11] This study is an attempt to understand the usefulness of Urine Micro albumin and creatinine ratio in predicting the mortality of the patient and to compare it with validated ICU scoring systems such as SAPS II.

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Materials and Methods

Source of data

The present study will be conducted on patients admitted to Medical ICU/ Medical emergency ward, SreeBalaji Medical College and Hospital, Chennai.

Method of collection of data

Study design: Prospective, non-interventional study in a tertiary care hospital

Sample size: 64 (As reviewed with statistician)

Sampling Method : Simple Random Sampling

Duration of study : June 2014 to August 2015

Method of collection of specimens and processing:

Spot urine sample collected at 6 and 48 hours of admission to medical ICU/Medical Emergency ward. Sample will be tested for urine microalbumin by immunoturbidometric method and for urine creatinine by Jaffe method and urine microalbumin :creatinine ratio calculated.

Inclusion criteria: Patients admitted to the Medical ICU/Medical Emergency ward at SreeBalaji Medical College and Hospital, with features of SIRS(systemic inflammatory response syndrome) and suspected infection.

Two or more of the following if present: SIRS

Fever(>38 C)/Hypothermia(<36)

Tachypnea(Respiratory rate >24/min)

Tachycardia (Heart rate >90/min)

Leucocytosis (>12000/microL) or Leucopenia (<4000/microL) or >10% bands

Exclusion criteria:

Patients receiving nephrotoxic drugs

Patients with preexisting urinary tract infection

Patients with urologic trauma resulting in frank hematuria or urinary infectio n

Patients with preexisting chronic kidney disease (serum creatinine level ≥ 2.0 mg/dL)

Investigations

Haemoglobin

Urine microalbumin:urinecreatinine ratio(Urine ACR) done at

Data will be collected using a pretested proforma meeting the objectives of the study. Detailed history, physical examination and necessary investigation will be undertaken. The purpose of the study will be explained to the patient and informed consent obtained. Patient will be followed

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up during the course of the hospital stay and the outcome of the patient (i.e. Death /Survival) is recorded.

Data Analysis and Interpretation:

Data was entered into Microsoft excel and analyses were done using the Statistical Package for Social Sciences (SPSS) for Windows software (version 18.0; SPSS Inc, Chicago). Descriptive statistics such as mean and standard deviation (SD) for continuous variables, and frequency and percentage for categorical variables were determined. The chi-square test and fisher's exact test (when appropriate) was used to show the associations between predictor and outcome variables. The level of significance was set at 0.05.

RESULTS

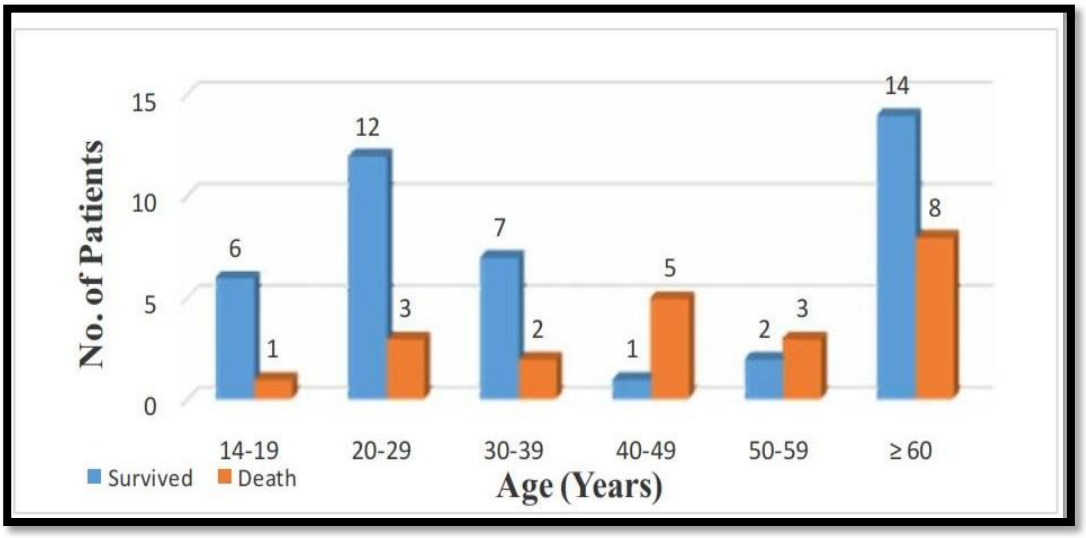

Figure 1: Distribution of patients according to their age groups

Age (Years)

In this study conducted at SreeBalaji Medical College and Hospital., a total of 64 patients were included in the study. Majority of the patients was more in the age group of 60-80 years (34.8%).

Table 1: Distribution of patients according to their sex

Sex	Death		Survived		Total	
	No.	%	No.	%	No.	%
Male					37	57.81
Female					27	42.18

In this study out of 64 patients, 27 patients were females (42.18%) as compared to 37 males (57.81%).

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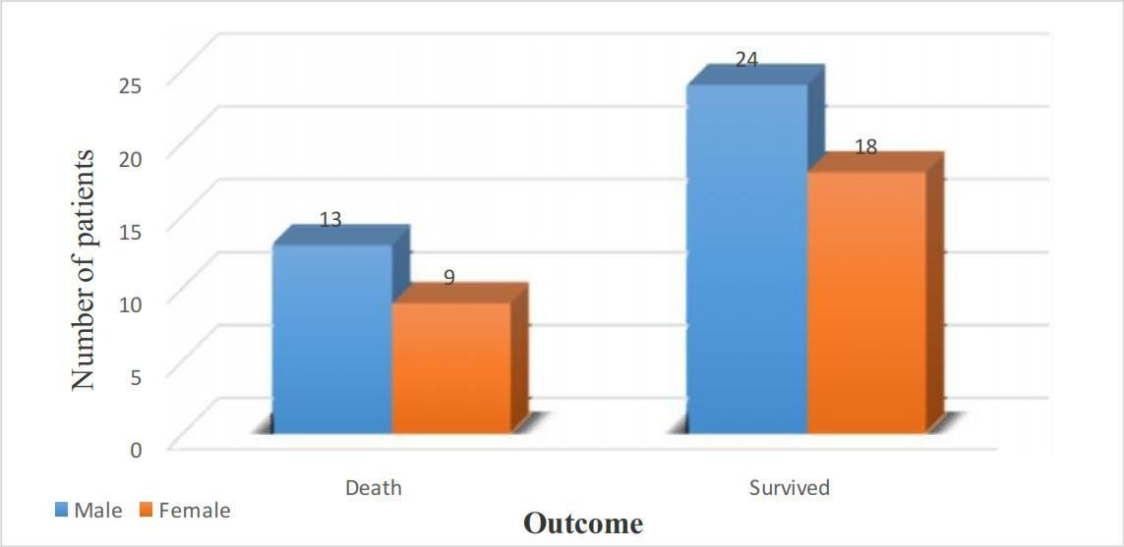

Figure 2: Distribution of patients according to the Outcome

In this study out of 64 patients, 22 patients (34.4%) did not survive and 42 patients (65.6%) survived.

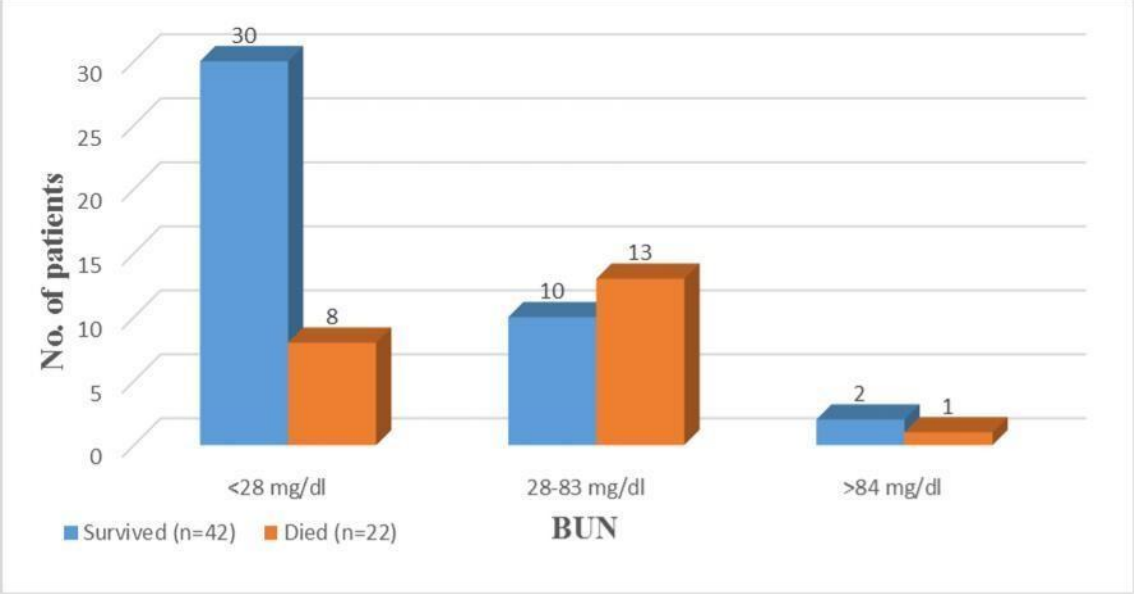

Figure 3: Distribution of patients according to their Blood urea nitrogen

In this study out of 64 patients, BUN was < 28mg/dl in 38 patients (59.4%) and 28 -83 mg/dl in23 patients (35.9%) and
>84 mg/dl in 3 patients (4.7%).

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Table 2: Distribution of patients according to their chronic disease status

Chronic Disease	Death		Survived		Total	
	No.	%	No.	%	No.	%
No chronic	19	29.6	40	62.5	59	92.2
Metastatic	0	0	2	3.12	2	3.1
AIDS	3	4.68	0	0	3	4.7
P value	0.032					

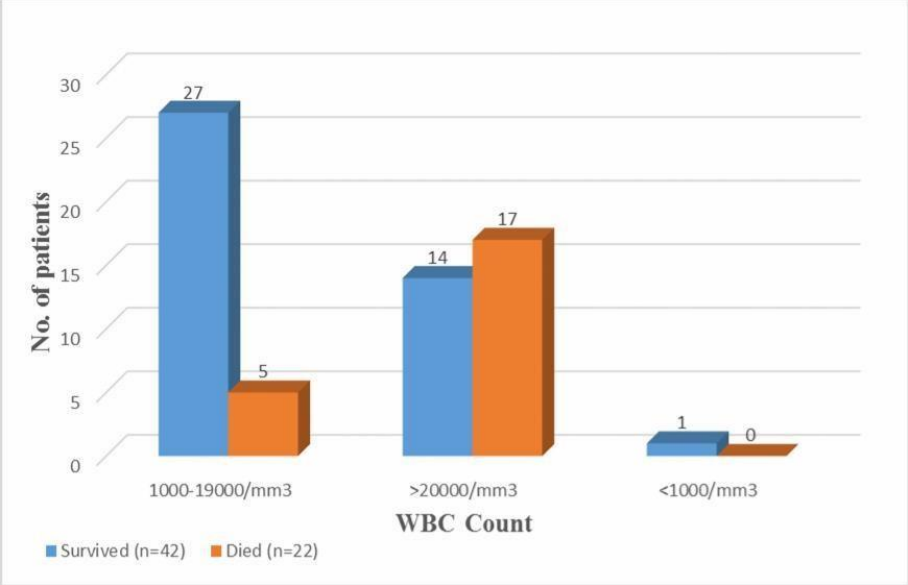

Figure 4: Distribution of patients according to their WBC Count

In this study out of 64 patients, 32 patients (50%) had WBC count of 1000-19000/mm3 and 31 patients (48.4%) had WBC count of > 20000/mm3 and 1 patient (1.6%) had WBC count of <1000/mm3.

Table 3: Distribution of patients according to their HCO3 Status

HCO3(mEq/L)	Death		Survived		Total	
	No.	%	No.	%	No.	%
>20	3	4.68	11	17.1	14	21.9
15-19	5	7.81	4	6.25	9	14.1
<15	14	21.8	27	42.1	41	64.1
P value	0.243					

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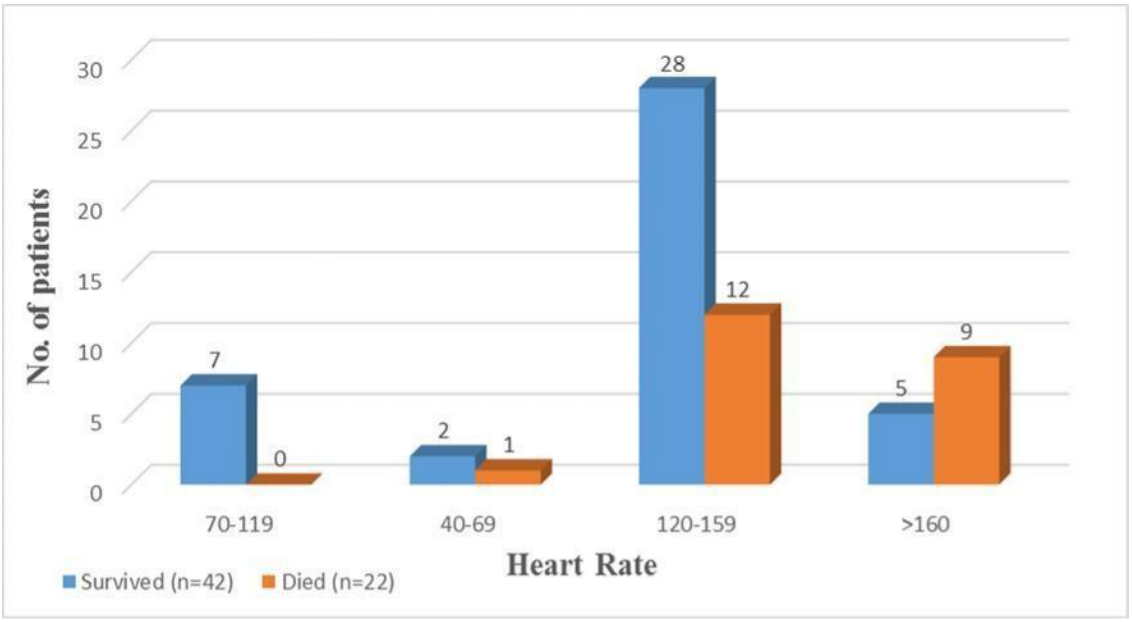

Figure 5: Distribution of patients according to their Heart rate

In this study out of 64 patients, 3 patients (4.7%) had heart rate of 40-69 bpm, 7 patients (10.9 %) had heart rate of 70 - 119, 40 patients (62.5%) had heart rate of 120 -159 bpm, 14 patients (21.9%) had heart rate of >160bpm.

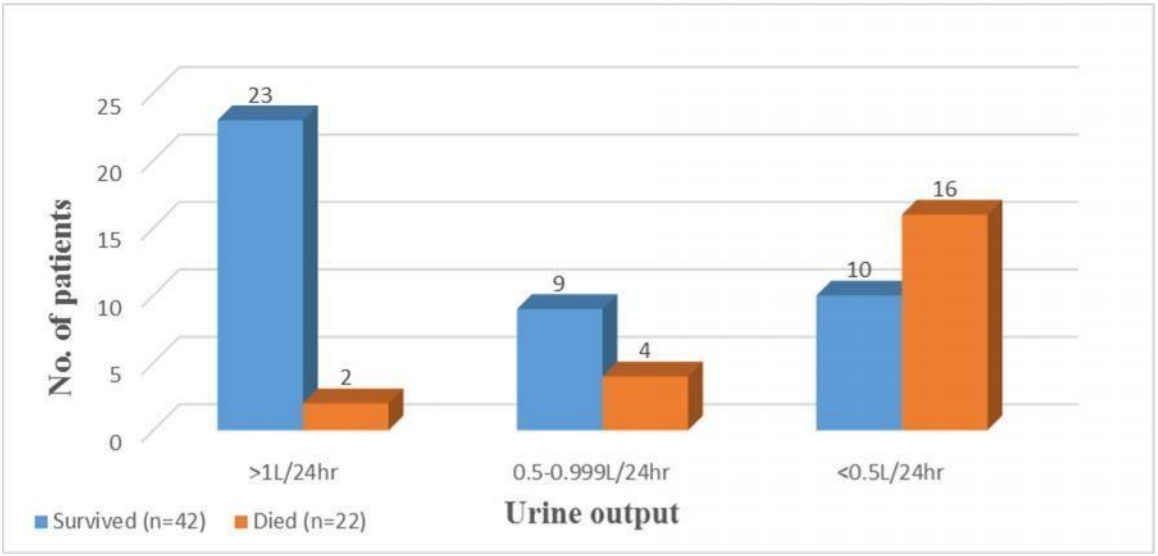

Figure 6: Distribution of patients according to their Urine output

In this study out of 64 patients, 25 patients (39.1%) had urine output of >1L/24 hr. 13 patients (20.3%) had urine output of 0.5-0.999L/24 hr and 26 patients (40.6 %) had urine output of < 0.5 L/24 hr.

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Table 4: Distribution of patients according to their Serum potassium level

Serum potassium (mEq/L)	Death		Survived		Total	
	No.	%	No.	%	No.	%
<3	3	4.68	2	3.12	5	7.81
3-4.9	16	25.00	38	59.37	54	84.34
>5	3	4.68	2	3.12	5	7.81
P Value	0.063					

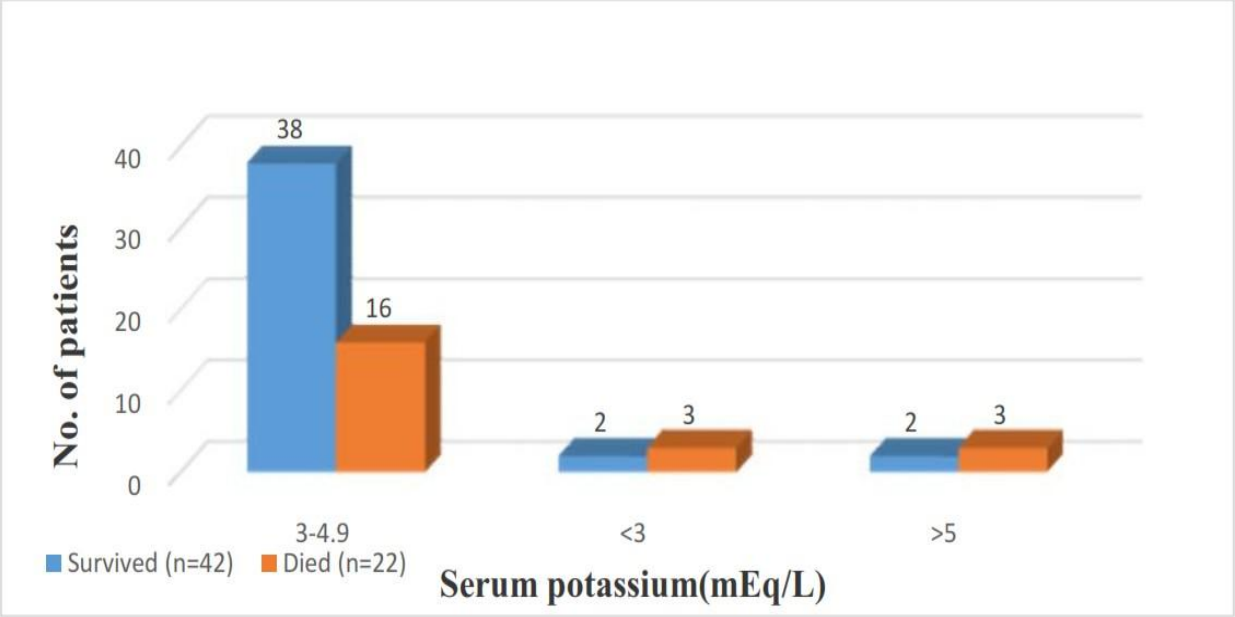

Figure 7: Distribution of patients according to their Serum potassium level

In this study out of 64 patients, 5 patients (7.81%) had potassium <3 mEq/L , 54 patients (84.4%) had potassium between 3-4.9 mEq/L and 5 patients (7.81%) had potassium >5 mEq/L

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Table 5: Distribution of patients according to their Serum Bilirubin

Serum Bilirubin (mg/dL)	Death		Survived		Total	
	No.	%	No.	%	No.	%
<4	11	17.18	39	60.93	50	78.1
4-5.9	10	15.62	2	3.12	12	18.8
>6	1	1.56	1	1.56	2	3.1
P Value	<0.001					

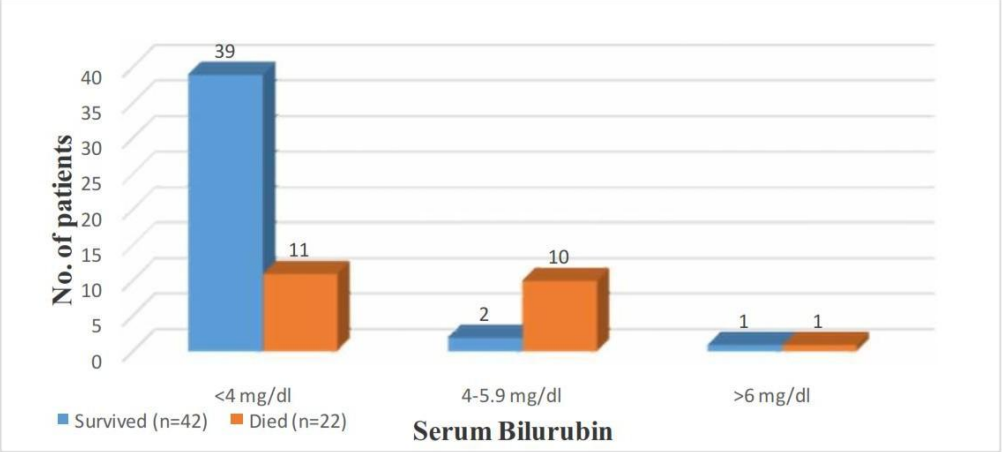

Figure 8: Distribution of patients according to their Serum Bilirubin

In this study of 64 patients, 50 patients (78.1%) had serum bilirubin below 4 mg/dL, 12 patients (18.8%) had serum bilirubin between 4 -5.9 mg/dL and 2 patients (3.1%) had bilirubin above 6 mg/dL.

Table 6: Distribution of patients according to their respiratory rate

Tachypnea	Death		Survived		Total	
	No.	%	No.	%	No.	%
Present	19	29.68	35	54.68	54	84.4
Absent	3	4.68	7	10.93	10	15.6
P Value	0.751					

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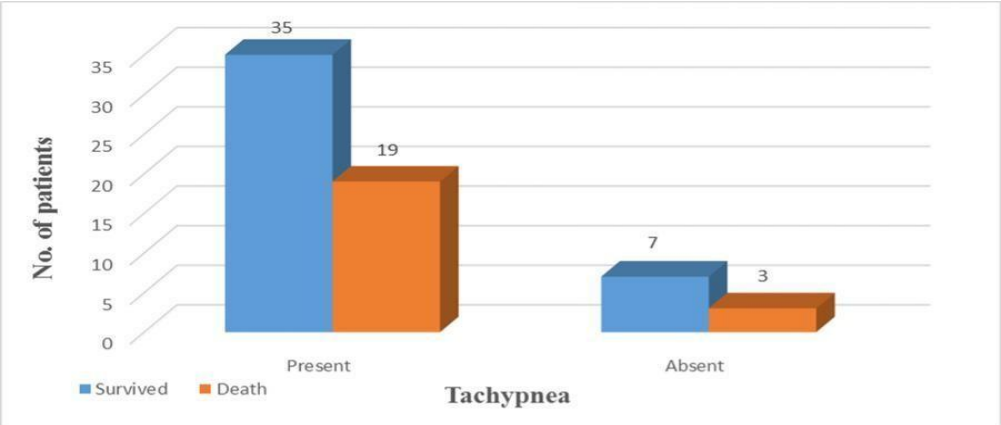

Figure 9: Distribution of patients according to their respiratory rate

In this study of 64 patients, 54 patients (84.4%) had tachypnea and 10 patients (15.6%)did not have tachypnea.

Table 7: Distribution of patients according to their pulse rate

Tachycardia	Death		Survived		Total	
	No.	%	No.	%	No.	%
Present	19	29.68	35	54.68	54	84.4
Absent	3	4.68	7	10.93	10	15.6
P Value	0.497					

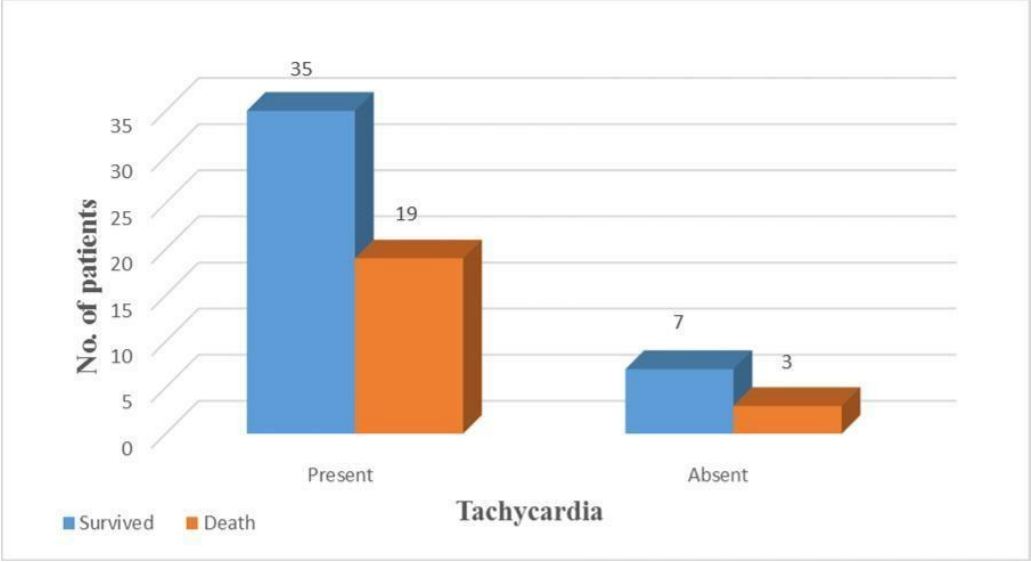

Figure 10: Distribution of patients according to their pulse rate

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In this study of 64 patients, 60 patients (93.8%) had tachycardia and 4 patients (6.2%) did not have tachycardia.

Table 8: Co-relation between micro-albuminuria and SAPS II Score

	Co-relation Co-efficient	P Value
Urine ACR 1 and SAPS II Score	0.858	<0.0001
Urine ACR 2 and SAPS II Score	0.841	<0.0001
Urine ACR 1 and Urine ACR2	0.976	<0.0001

Discussion

In the present study done at, SreeBalaji Medical College and Hospital, Patients who were admitted to MICU and Medical emergency ward with features of SIRS and suspected infection were included in the study after inclusion and exclusion criteria. [12] Spot urine sample collected at 6 and 48 hours of admission to medical ICU/Medical Emergency ward. Samples are tested for urine microalbumin by immunoturbidometric method and for urine creatinine by Jaffe method. SAPS II score calculated within 24 hours of admission. Discussion will be done under the following headings. Patients were distributed from age 14 to 80 years with age >60 years constituting 34.8%.Mean age of the study population was 43.53 years (SD 19.81).A study conducted by S Todi et al (2010) [9] showed mean age of 58.17 years (SD 18.66) and a study done by Angus DC et al showed mean age of 57.0[8] .Patients with age > 60 years constituted 34.8% of the study population. This is in consistence with the fact that sepsis is more common among the elderly age group.

Table 9: Comparison of mean age of patients with other studies

Study	Angus DCet al[8]	S todi et al[9]	Rodriques et al[32]	Present study
Mean age(Years)	57.0	58.17	45	43.52

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Table 10: Comparison of % of sepsis patients > 60 years with other studies.

Study	S sreedharan et al[63]	Present study
% Patients >60 years	28.9%	34.8%

SEX

In the present study 27 patients (42.18%) were female and 37 patients were male (57.81%).This is consistent with study conducted by S Todi et al[9] which studied epidemiology of sepsis in India with male patients constituting 57.71%, study done by Angus DC et al[8] showed male patients constituted 51.9% and the study done by S Sreedharan et al[13] showed male patients constituted 60.5%.This study shows that sepsis is more common among males compared to females.

Table 11: Comparision of sex distribution of patients with other studies.

Study	Angus DC et al[8]	S todi et al[9]	S sreedharan et al[63]	Present study
% Male	51.9%	57.71%	60.5%	57.81%
% Female	48.1%	42.29%	39.5%	42.19%

CO-MORBID ILLNESS

In this study done out of 64 patients, 7 patients (10.93%) had COPD and 11 patients (17.18%) had type 2 Diabetes mellitus, 12 patients had(18.75%) had local infection as a source of infection and 2 patients (3%) were Immunocompromised (HIV). A study done by Angus DC et al[9] showed that COPD was the most common underlying co-morbidity which was present in 12.3% of the patients. This shows that lung is the most common source of infection leading to sepsis.

SIRS CRITERIA

In the present study 40 patients (62.5%) had all the 4 criteria for SIRS, 20 patients (31.3%) had 3 criteria and 4 patients (6.3%) had 2 criteria.

ORGAN DYSFUNCTION

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Cardiovascular system: 24 Patients (37.5 %) had cardiovascular system dysfunction in the form of SBP < 90 mmHg, median ACR1 and ACR2 were 143.80 μg/mg and 121.68 μg/mg among patients with cardiovascular dysfunction and 77.62 and 48.28 among patients with no cardiovascular dysfunction. P value was statistically significant.
Renal system: 26 patients had renal dysfunction in the form of urine output <0.5L/24 hr. Median ACR1 and ACR2 were 140.19 μg/mg and 118.05 μg/mg among patients with renal dysfunction and 76.61 μg/mg and 46.90 μg/mg among patients with no renal dysfunction.P value was statistically significant.
Haemotologic system: 20 patients (31.25 %) had haematologic dysfunction in the form of platelet count <80000/cumm.The degree of microalbuminuria was more among patients with organ dysfunction than among patients with no organ dysfunction. Urine microalbumin was significantly elevated among those with organ dysfunction than those without organ dysfunction and the degree of elevation was more in those with multiorgan dysfunction than those with single organ dysfunction.. Hence urine microalbumin is a marker of multiorgan organ dysfunction.[14,15]

MORTALITY
Mortality percentage in this study was 34.4%.This is consistent with various studies including study done by Rangel-Frausto MS et al[16,17] which showed mortality ranging from 20-35% and study conducted by Greg S et al 2006[18] which showed case fatality increased linearly with age and age was an independent predictor of mortality. Mortality was maximum among those aged >40 years. Out of 22 patients who died, 16 patients (72.7%) were aged>40 years. Mortality was higher among male patients 59.09% than among female patients (40.09%). A study done by Angus DC et al showed that women had less age specific incidence and mortality rates compared to men.[9] Among the patients who died 11 (50%) patients out of 22 had an infectious source in the lung. Other causes included localized infection in the form of cellulitis or abscess or an abdominal source of infection. Urinary tract infections were excluded from the study as it was an exclusion criteria of the study.[19] Study done by Angus DC et al[9] showed that 44% of the cause of mortality had a respiratory source of infection, 17.3 % had bacteremia from an unidentified source and 8.6 % had an abdominal source and 6.6 % had local wound as a source of infection.[20,21] showed that most common primary sources of infection resulting in sepsis are the lungs, the abdomen, and the urinary tract. Total 22 patients who died 5 patients were diabetic and 2 patients were immune compromised.

CONCLUSION

Total of 64 patients were included in the study. Patients were distributed from age 14 to 80 years with mean age of 43.52 years. Elderly patients constituted the majority. Out of 64 patients 37 were males and 27 were females. Mortality percentage in this study was 34.4 %. Mortality was more in males compared to females and it was more in elderly patients. 40 patients (62.5%) had all the 4 criteria for SIRS, 20 patients (31.3%) had 3 criteria and 4 patients (6.3%) had 2 criteria. Out of 64 patients, 7 patients (10.93%) had COPD and 11 patients (17.18%) had type 2 Diabetes mellitus, 12 patients had(18.75%) had local infection as a source of infection and 2 patients (3%) were Immunocompromised (HIV). Urine microalbumin was significantly elevated among those with organ dysfunction than those without organ dysfunction and the degree of elevation was more in those with multiorgan dysfunction than those with single organ

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dysfunction. Among the variables of SAPS II, the variables which had statistically significant p values for mortality were urine output and GCS score with P value of 0.0001, serum bilirubin (p value 0.001) and Systolic blood pressure (p value 0.003). SAPS II score ranged from 13 to 87. Median SAPS II score among survivors were 42.0 and among non survivors were 63.5. Non survivors has a higher SAPS II score compared to survivors. P value was statistically significant with p of 0.0001. Urine ACR 1 was 66.4 μg/mg among survivors and 166.5 μg/mg among non survivors and ACR 2 was 34.6 among survivors and 151.4 among non survivors. Both were statistically significant with p value of 0.0001. Absence of significant microalbuminuria among sepsis patients at admission is predictive of survival and significant microalbuminuriaat admission is predictive of mortality which is equivalent to the time tested SAPS II score. Significant microalbuminuria is also predictive of organ dysfunction in sepsis. Early institution of intensive therapy to these patients can improve survival rates. 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. Hence microalbuminuria can be used as a dynamic marker of critical illness.

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Ethical approval: The study was approved by the Institutional Ethics Committee

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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