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Original Research Article

Study Of Clinical Profile Of Sepsis In Geriatric Patients And Predictors Of Mortality

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Abstract

Background: Sepsis is a global healthcare issue and continues to cause high mortality especially in elderly patients. The present study was undertaken to study the clinical profile of sepsis in geriatric patients and to determine the predictors of mortality. **Method:** A total 201 patients of either sex, age >60 years with clinical and laboratory evidence of sepsis as per the International Sepsis definitions Conference criteriawere included in the study. **Results:** Out of 201 patients, 73.1% had comorbidity. 27.3% patients were found to be in septic shock on admission with mean arterial pressure ≤65mmHg according to sepsis 3 defining criteria.About 21% patients had culture negative sepsis. 39% patients had gram negative sepsis; 12% patients had gram positive sepsis.Pneumonia was the most common observed infection (33.8%), followed by urinary tract infection (24.4%), cellulitis (13.4%).56.7% patients required mechanical ventilation (MV) with survival of only 40.5%. Need for MV was found to be highly related to mortality ($p<0.001$). About 34.3% patients were provided with renal replacement therapy (RRT) and out of 69 only 34(16.92%) survived despite therapy, ($p=0.004$).Out of all the factors studied upon univariate analysis Age, SBP, Oxygen saturation, PaO2/FiO2 ratio, GCS score, haemoglobin, serum lactate levels, SOFAS score on day 1,3,5 were found to be significant predictors of mortality. On Multivariate regression analysis, significant predictors of mortality as an outcome were age, GCS score on admission, lower haemoglobin, increased Serum lactate and SOFAS score on Day 1 & 5.**Conclusion:** Present study described the clinical profile and mortality predictive factors in geriatricpatients with sepsis. These informative predictors would inform clinical practice to adopt effective therapeutic strategies to improve patient outcomes.

Keywords: Sepsis; Elderly; Mortalitypredictor; Comorbidity; Pneumonia; PaO2/FiO2 ratio; GCS score

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Introduction

Sepsis is the life-threatening condition that arises when the body's response to an infection injures its own tissues and organs. Today's emergency rooms and intensive care units are struggling with sepsis that has reached epidemic proportions but is rarely recognized. The incidence and prevalence of sepsis increase with age.However, the incidence of severe sepsis in older patients was 26.2 cases per 1000 population [1, 2].Sepsis is more commonly seen in the geriatric population as compared with their younger counterpart and elderly exhibited significantly elevated mortality as evidenced by earlier studies. Infectious diseases account for widespread morbidity and mortality among the elderly. In 2012 alone, infectious diseases accounted for 13.5% (3.1 million) of all visits made by elders to U.S. EDs. Hospitalization rates for infectious diseases in this segment of our population have steadily risen over the past two decades[3, 4].

The clinical presentation of older patients with sepsis is often atypical, leading to a difficult and delayed diagnosis. Prompt diagnosis is crucial to the management of sepsis, as initiation of early-goal-directed therapy is the key to reducing mortality from severe sepsis especially in older patients. Unless antibiotics and life support are delivered quickly, the condition can lead to organ failure and death. Modern medicine and healthier lifestyles have increased the likelihood that younger adults will now achieve old age. However, this has led to rapidly increasing numbers of older people, presenting with sepsis and septic shock because of the developments in the medical sciences, extensive use and availability of antibiotics, effective use of ICU, life support and increased awareness of the clinicians about sepsis. It has been estimated that by 2050, globally 21.4% of people will be aged 60yrs or older (Office of registrar general and census commissioner, Ministry of home affairs, Govt of India). Vulnerability to various physiological stresses such as infection, inflammation, and oxidative damage increases with ageing and is causally related to problems in geriatric population [5, 6].

The definition of "old age" is often debated, but many experts agree that individuals who are 60 or older are considered geriatric. (Ministry of Statistics & Programme Implementation Government of India). Hence, we used age > 60 years in present study to define the geriatric population. In this study we examined the symptomatology of patients, role of chronic comorbid medical conditions, the primary site of infection, and the type of

infection as it relates to gender differences in the incidence of sepsis and the outcome of patients during hospital stay of minimum 5 days.

Materials and Methods

A study design was a prospective cross sectional, observation study conducted in the Department of General Medicine at tertiary care centre during a period from November 2018 to November 2020.A total 201 cases of either sex, aged greater than 60years with clinical and laboratory evidence of sepsis as per the International Sepsis definitions Conference criteria and who admitted to medicine wards and ICU were included in the study.Postoperative and posttraumatic cases of sepsis, sepsis due to burn injury and patients with pericardial tamponade were excluded from the study.

All the selected patients were subjected to detailed clinical history and physical examination with special emphasis on sepsis-related examination. Data collected was noted in the predesigned preform. The study was approved by the ethical committee of the hospital and from all participants or from their closed relative's informed consent was taken. All patients were subjected to a standard protocol of clinical and laboratory assessment. **Clinical data:**Age, Sex, Comorbidities, Complete history, clinical examination including rectal temperature, mean blood pressure, heart rate, respiratory rate, GCS, and systemic examination.**Laboratory investigations:**Complete blood count (haemoglobin, whole blood count, platelet count, haematocrit level); Two specimen blood culture or site-specific culture if indicated; Kidney function test (urea, creatinine); Serum electrolytes (sodium, potassium level); Liver function test (total bilirubin, total protein level); Arterial blood gas analysis (PH, PaO2/FiO2);Chest X-ray / ultrasonography/ CT scan/ MRI if required**;** Serum lactate levels**;** CSF analysis if required**.**

All patients were evaluated for the criteria of sepsis by SOFA score and serial SOFA score on day 1, 3, 5 of admission was done and final outcome in the form of death, discharge was noted.The SOFA scoring system composed of scores from 6 organ systems that are graded from 0 to 4 according to the degree of dysfunction. The score accounts for clinical intervention and can be measured repeatedly. The rising scores correlate well with increasing mortality.All enrolled patients received empirical antibiotics upon diagnosis.The antibiotics were subsequently de-escalated according to the culture report. Other treatments were conducted as per the advice of attending physicians. All patients were followed up till they were treated of sickness or till they expired in hospital after a diagnosis of sepsis.

Statistical Analysis

Data was entered in Microsoft excel sheet and analysis was done with SPSS 20 version software. Categorical data was represented in the form of Frequencies and proportions. Paired t-test was used as test of significance. Continuous data was represented as mean and standard deviation. p value of <0.05 was considered significant.

Observation and Results

During the study period, a total of 201 patients were included in the study. The majority of patients belonged to the age group of 60–65 years (37.3%) with the mean age of patients was 68.4±5.61years with male predominance (122;60.7%) asshown in table 1.

Table 1: Age and gender distribution of patients

Demographic data		Frequency	Percentage
Age in years	60-65	75	37.3
	66-70	61	30.3
	71-75	38	18.9
	76-80	23	11.4
	>80	04	2.0
Gender	Male	122	60.7
	Female	79	39.3

Out of 201 patients, 73.1% had comorbidity. The diabetes mellitus was the most common comorbidity noted during study.Most common symptom noted was breathlessness (53.2), followed by fever (47.7%) and altered sensorium (31.8%), (Table 2).

Table 2: Comorbidities and clinical profile of sepsis in geriatrics

Parameters		Frequency	Percentage
Various common comorbidities	Diabetes mellitus	91	45.3
	Hypertension	84	41.8
	Ischaemic heart disease	32	15.9
	COPD	13	6.5
	CKD	16	8
	ICH	05	2.5
	Obesity	06	3.0
Rare comorbid conditions	SLE	02	1.0
	Chronic Liver Disease	06	3.0
	Old CVA	08	4.0
	Hypothyroidism	08	4.0
	Old Pulmonary TB	10	5.0

	Myasthenia Gravis	02	1.0
	Filariasis	02	1.0
Clinical profile	Fever	96	48.0
	Cough	55	27.36
	Breathlessness	107	53.23
	Altered sensorium	64	31.84
	Burning micturition	10	5.0
	Decreased urine output	53	26.36
	Vomiting	38	18.90
	Diarrhoea	13	6.46
	Pain in abdomen	23	11.44
	Swelling with discharge	11	5.47
	Swelling without discharged	25	12.43
	Other	38	18.90

CVA: Cerebrovascular Accident

ICH :Immunocompromised Host.

Table 3 show the descriptive data of the study population. Out of 201 patients, 67 (33.33%) patients had MAP more than 90mmHg suggestive of normotension & 134 (66.67%) patients were in hypotension on admission. Out of 134 patients 55 (27.3%) patients were found to be in septic shock on admission with mean arterial pressure less or equal to 65mmHg according to sepsis 3 defining criteria.

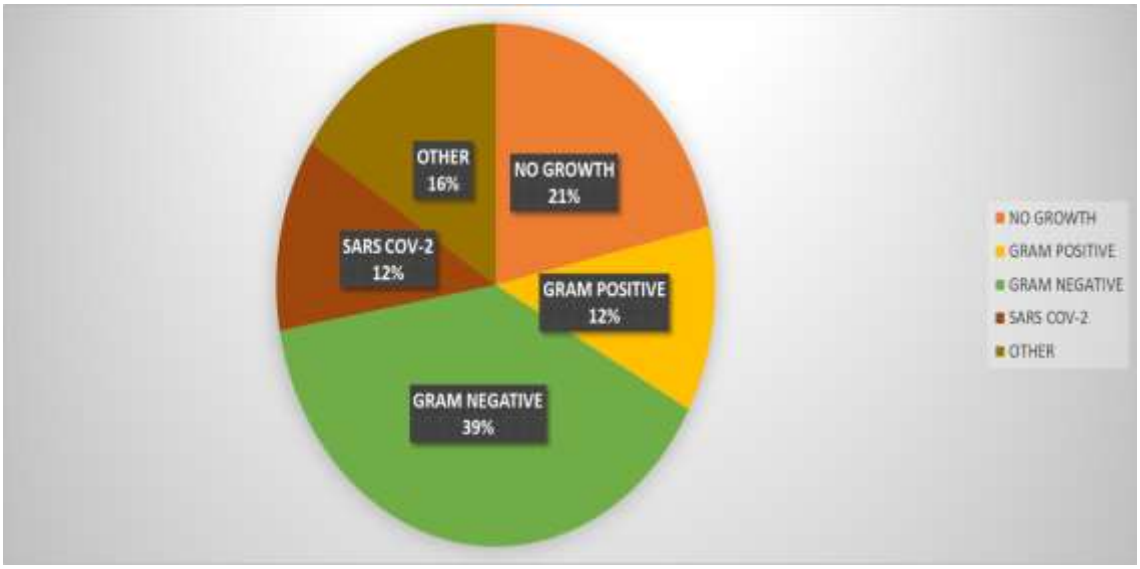
Table 3: Descriptive data of the study population

Parameter	Range	Mean ± SD
AGE	60-80	68.44 ± 5.6
SBP	50-160	105.01 ± 24.9
DBP	20-110	65.68 ± 18.29
MAP	30-123	77.8 ± 21.25
GCSScore	2-15	11.40 ± 3.26
O2 Saturation	39-100	83.9 ± 14.35
PAO2/FIO2 Ratio	26-500	216.29 ± 126.17
Temperature	96-103	98.9 ± 1.67
TLC	1900-38500	17200 ± 8002.9
HB	2.7-15.8	9.29 ± 2.37
PLT	10×10^3- 372×10^3	$160.1 \times 10^3 \pm 94.5 \times 10^3$
pH	6.7-7.6	7.30 ± 0.17
Sr Lactate	0.7-12.80	2.98 ± 1.72

Around 39% patients had gram negative sepsis, 12% patients had gram positive sepsis, 12% patients had SARS COV-2 virus infection, 16% had isolates other than gram

positive or gram-negative organism. 21% patients had no growth on blood or local culture despite prolong incubation of 72hrs, (Figure 1).

Figure 1: Culture Isolates of Study Population



The most common gram-positive organisms isolated on culture were Streptococcus pneumoniae in 9 (4.5%) followed by Enterococcus faecalis in 8 (4%) while the gram-negative organisms isolated on culture during study were klebsiella pneumoniae (26) followed by E. coli (26), pseudomonas aeruginosa (11), Enterobacter (8) and Acinetobacter (6). 24 (11.9%) cases were SARS COV-2 positive as shown in table 4.

Table 4: Showing Different Organisms Isolated on Blood/Local Culture

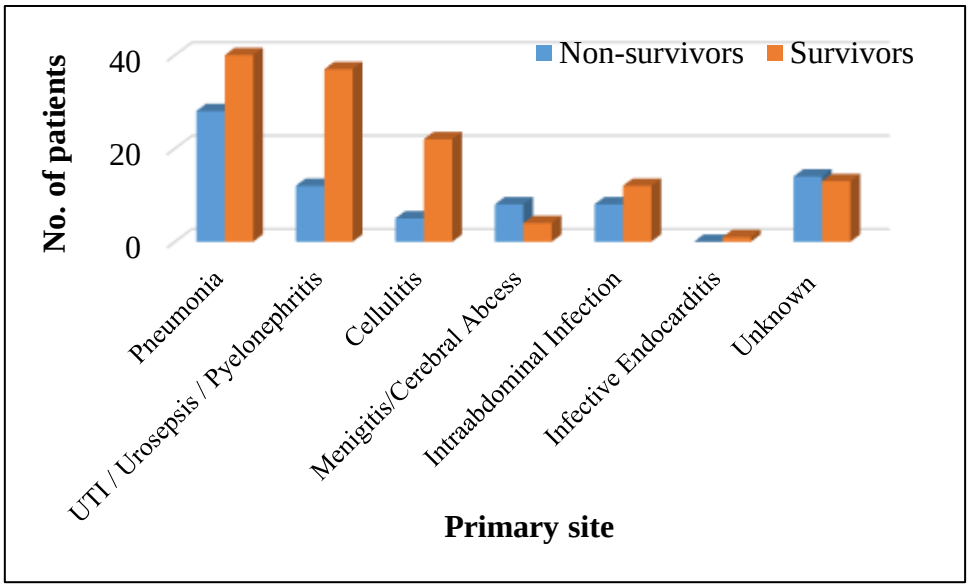
Organism		**Frequency**	**Percentage**
	No growth	43	21.4
Gram Positive Organisms Grown on Culture	GPC Staphylococcus Aureus	02	1.0
	GPC Streptococcus Pneumoniae	09	4.5
	GPC Enterococcus Faecalis	08	4.0
	GPC Streptococcus Pyogenes	03	1.5
	GPC Streptococcus Viridans	01	.5
Gram Negative Organisms Grown on Culture	GNB Klebsiella Pneumoniae	26	12.9
	GNB E. COLI	26	12.9
	GNB Pseudomonas Aeruginosa	11	5.5
	GNB Enterobacter SPP	08	4.0
	GNB Acinetobacter Baumanni	06	3.0
	GNB Salmonella Typhi	02	1.0
Others	SARS COV-2	24	11.9
	Rickettsial Infection	08	4.0
	Mycobacterium Tuberculosis	07	3.5
	Dengue Virus	06	3.0

	Candida Albicans	05	2.5
	M. Avium Complex	02	1.0
	Pneumocystis Carinii	02	1.0
	Plasmodium Falciparum	02	1.0

Out of 201 patients,114(56.7%) patients required mechanical ventilation and out of 114 patients only 45 survived, 69 (60.53%) patients who were on mechanical ventilation expired. Need for mechanical ventilation was highly significant in terms of mortality (p value < 0.001; OR = 21.04). Out of 201 patients, 69(34.3%) patients were provided with renal replacement therapy and out of 69 only 34(16.92%) survived despite therapy. Need for renal replacement therapy was highly significant predictor of mortality with p value 0.004; OR = 2.36.

Pneumonia was the most common observed infection (33.8%), followed by urinary tract infection (24.4%), cellulitis (13.4%) as depicted in figure 1.Higher incidence of pneumonia amongst non survivors was found highly significant factor with p value of 0.019 (OR=2). Also, Unknown site of infection was associated with higher mortality with p value of 0.005 (OR=5.59).

Figure 2: Comparison of primary focus of infection in between Survivors & Non-Survivors



Out of all the factors studied upon univariate analysis Age, SBP, Oxygen saturation, PaO2/FiO2 ratio, GCS score, haemoglobin, serum lactate levels, SOFAS score on day 1,3,5 were found to be significant predictors of mortality.On Multivariate regression analysis,

significant predictors of mortality as an outcome were age, GCS score on admission, lower haemoglobin, increased Serum lactate and SOFAS score on Day 1 & 5, (Table 5).

Table 5: Comparison of Different variable between Survivors & Non-Survivors

Variable	Non-Survivors	Survivors	P value
Age	67.04±5.09	69.27±5.75	**0.006**
Temperature	99.11±1.86	98.81±1.54	0.23
MAP	74.33±22.92	79.86±20.01	0.074
SBP	99.97±24.98	108.01±24.46	**0.026**
DBP	63.36±19.81	67.06±17.25	0.166
Oxygen Saturation	79.73±17.26	86.41±11.67	**0.01**
GCS	9.77±3.52	12.38±2.66	**0.00**
Total Leukocyte Count	16755±8941	17465±7412	0.545
Haemoglobin	9.71±1.93	9.11±2.28	**0.056**
Serum Sodium	136.09±11.77	136.45±8.14	0.799
Creatinine	3.09±3.53	3.38±4.07	0.612
PaO2/Fio2	163.57±118.84	247.81±120.16	**0.00**
Platelet count	169.36±99.22	154.67±91.57	0.288
pH	7.24±0.210	7.34±0.134	**0.00**
Serum Lactate	3.36±1.22	2.76±1.93	**0.017**
SOFAS Day 1	8.32±3.38	6.61±3.00	**0.00**
SOFAS Day 3	9.06±3.92	5.58±2.40	**0.00**
SOFAS Day 5	9.14±5.16	4.23±2.19	**0.00**

Discussion

In the present study, age (p value 0.009) was significantly associated with outcome which is similar to the study done by Nasa et al[7]. Hence, early aggressive care to acknowledge and manage severe sepsis is required to boost the outcome in elderly. The male predominance seen in current study,and this reflects that the male population was more prone to sepsis. Most common symptom noted was breathlessness (53.2%), followed by fever (47.7%), altered sensorium (31.8%), cough (27.3%), decreased urine output (26.3%), vomiting (18.9%), abdominal pain (11.44%). These findingsare comparable to Arun VG et al

[8] and Bhattacharya et al study [9].A large number of the patients(73.1%) had associated co-morbidities at the time of diagnosis of sepsis. Diabetes was the most prevalent comorbid condition (45.3%) followed by hypertension (41.8%). A similar observation has been made previously by Martin GS et al [10]. However, presence of comorbidity was not significantly associated with the outcome in present study which is similar to the study of Bhattacharya et al [9]. Only HIV positive serostatus (p value =0.013) as a comorbidity had significant statistical difference in our study. To the best of our knowledge, the presence of HIV as a comorbidity has not been reported in literature.

The mean SBP on admission observed in patients during study was 105.01±24.9mmHg.27.3% patients were found to be in septic shock on admission with mean arterial pressure less or equal to 65mmHg according to sepsis 3 defining criteria. Significant relationship was observed between septic shock on admission (p value 0.041; OR 1.90) to mortality in current study. Furthermore, the multivariate analysis revealed that septic shock was significantly associated with higher risk of death in patients aged ≥65 years, suggesting that septic shock is an important risk factor for mortality in elderly patients receiving MV in the ICU.

Mean observed GCS score for study population was 11.40±3.26. Out of all, 31.8 % of patients complained altered level of consciousness as one of the symptoms. Supporting the above finding, 49.8% patients had score between 9-13 suggesting moderate neurological dysfunction. Presence of altered level of consciousness was found to be significantly associated with the outcome of sepsis with a p value of 0.006 (OR = 2.308). Lower GCS score recordings were also significantly associated with outcome with p value of 0.002. This finding is compared with the study of Boonmee P et al [11].

Mean recorded haemoglobin was 9.29±2.37 gm/dL. Reduced haemoglobin was significantly associated with outcome of mortality with p value of 0.007 which is similar to the study by Muady et al [12].Mean recorded platelet count was 160.1 X 103±94.5 X 103 /mm3. Platelet count was not found to be a significant predictor of outcome in our study. This is similar to the study by Liu et al [13]. This could possibly be explained by the fact that automated cell counters are not sensitive enough to report the appropriate platelet count.Mean oxygen saturation recorded amongst study population was 83.9±14.35%. Mean recorded oxygen saturation amongst the population who died was recorded to be 79.73±17.33%. Reduced oxygen saturation on admission was found to be significantly associated with outcome (p value 0.000) this is similar to study by Boonmee et al [11].

Mean recorded ratio of PaO2/FiO2 was 216.29±126.17. Need for MV was decided on the basis of ratio, patients with ratio less than 100 were put on MV. Out of 201 patients,114(56.7%) required MV and out of 114 patients only 45 survived, 69 (60.53%) patients who were on MV expired. Need for MV was highly significant in terms of mortality ($p<0.001$; OR=21.04). This finding is in accordance with the study done by Greenberg et al [14].

Mean recorded pH was 7.30±0.17 and mean serum lactate that was recorded was 2.98±1.72. Mean lactate levels observed in present study were higher than normal, suggesting that lactic acidosis is an important component of sepsis. On bivariate analysis higher serum lactate was found to be significantly associated with mortality in patients. This is similar to the observations by Liu et al [13].Pneumonia and unknown site of infection were significantly associated with mortality in current study.

Blood culture or serology was negative for growth in 43 (21.3%) patients and positive in 78%. Around 39% patients had gram negative sepsis, 12% patients had gram positive sepsis, 12% patients had SARS COV-2 virus infection, 16% had isolates other than gram positive or gram-negative organism. Gram negative organisms were predominant isolates in following order- Klebsiella pneumoniae (26), E. coli (26) and Pseudomonas aeruginosa (11); this is similar to study by Tanriover et al [15].Amongst gram positive culture isolates Streptococcus pneumoniae in 9 (4.5%) and Enterococcus faecalis in 8 (4%) were the most common isolates followed by Streptococcus pyogenes in 3 (1.5%), Staphylococcus aureus in 2 (1%), Streptococcus viridans (0.5%).

Mean SOFAS score on day 1 of admission for the study population was 7.24±3.25 which progressively decreased as a result of intervention to 6.74±3.40 on day 3 and 5.35±3.75 on day 5. Mean SOFAS score on day 1 for those who died was 8.32±3.38 which further progressed to worsen on day 3 and day 5 to 9.06±3.93 and 9.14±5.26 respectively. This is higher in comparison to the scores for those who survived, who had mean SOFAS score on day1, day 3 and day 5 as 6.61±3.0, 5.58±2.40, 4.22±2.19 respectively. The score amongst survivors shows a decreasing trend post treatment, suggesting that the treatment was effective in this group in comparison to non survivors who had presented to hospital with higher scores and continued to worsen despite treatment and were resistant to intervention. This observation is similar to the study conducted by Ferreira et al[16]. Both the mean and highest SOFA scores were particularly useful predictors of outcome. However, the study by de Groot et al [17], has reported contrasting results where disease severity score like SOFA

was found to be poorly associated with mortality in older patients. Here, the AUCs of all disease severity scores were poor and ranged from 0.56 to 0.64 in older patients, significantly lower than the good AUC range from 0.72 to 0.86 in younger patients [8]. Hence, a modification of the currently available scores or an "age" factor may be required to obtain better diagnostic and prognostic performances, as reported in previous studies. Nonetheless, additional studies ought to be conducted to derive and validate acceptable early warning scores for this specific population.

Limitation

- A single, tertiary, university hospital situated at the city centre with moderate volume of visiting patients. This may limit the generalizability of the study findings.
- Only included patients suspected of sepsis in the ED and not patients whom we did not suspect but later went on to be diagnosed with sepsis during hospital admission.
- We used in-hospital mortality, which is all-cause mortality rather than sepsis-related mortality as the primary outcome. This might have overestimated the actual mortality due to sepsis since the elderly could have died from many other concurrent causes.
- We did not have records of some essential factors in critical septic patients such as serum procalcitonin, compliance with the sepsis bundle of care, or the severity of sepsis assessed by appropriate tools such as Acute Physiology and Chronic Health Evaluation II (APACHE II) score or NEWS score.
- Some of the factors might have failed to meet statistical significance due to small sample sizes in the analyses.

Conclusion

Elderly patients with sepsis in the ED may have higher in-hospital mortality. The factors associated with increased mortality in the elderly sepsis patient include age, immunocompromised status, altered mentation on admission, decreased urine output, lower GCS score, respiratory tract infection, unknown site of infection, ICU admission, mechanical ventilation, need for renal replacement therapy, high serum lactate and low haemoglobin.High SOFA score on admission and on day 5 of hospitalisation may be associated with increased mortality. These informative predictors would inform clinical practice to adopt effective therapeutic strategies to improve patient outcomes.

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