A COMPARATIVE STUDY OF SURVIVORS AND NON-SURVIVORS OF SEPSIS IN ICU- A STUDY FROM NORTH-EAST INDIA

Deepak Chaudhury[1], Lakshimi Borgohain[2], Chandraprakash[3], Subhankar Paul[4], Ilias Ali[5]

[1]Assistant Professor, Department of Emergency Medicine, Gauhati Medical College and Hospital.
[2]Associate Professor, Department of Psychiatry, Assam Medical College and Hospital.
[3]Former Postgraduate Trainee, Department of Emergency Medicine, Gauhati Medical College and Hospital.
[4]Postgraduate Trainee, Department of Emergency Medicine, Gauhati Medical College and Hospital.
[5]Professor and HOD, Department of Emergency Medicine, Gauhati Medical College and Hospital.

ABSTRACT

BACKGROUND

Sepsis is life-threatening organ dysfunction caused by a dysregulated host response to infection, which is one of the most important cause of mortality and morbidity in critically ill patients. In this study, comparative analysis of various parameters of survivors and non-survivors of sepsis has been done.

MATERIALS AND METHODS

This prospective, observational study was undertaken in the Department of Emergency Medicine ICU of Gauhati Medical College and Hospital, over a period of one year from August 2014 to July 2015 after obtaining Institutional Ethical Committee Clearance.

RESULTS

Among 50 sepsis patients analysed, there was 36% mortality and male predominance (56%). Though there was no statistical difference in presence of co-morbidities and symptomatology or biochemical parameters between two groups, but tachycardia, low GCS, higher SOFA and APACHE II scoring and requirement of mechanical ventilators were significantly higher among non-survivors.

CONCLUSION

Assessment of clinical signs and initial serological and radiological investigations are of utmost importance to detect more critically ill patients as early as possible to intervene earlier for saving the life of the sepsis patients.

KEYWORDS

Anti-TPO Antibody, Thyroid Gland Swelling, FNAC.

HOW TO CITE THIS ARTICLE: Chaudhury D, Borgohain L, Chandraprakash, et al. A comparative study of survivors and non-survivors of sepsis in ICU- a study from North-East India. J. Evolution Med. Dent. Sci. 2017;6(49):3792-3796, DOI: 10.14260/Jemds/2017/820

BACKGROUND

Sepsis is a major healthcare problem as well as a predominant cause of mortality throughout the world even after tremendous advances in modern healthcare facilities. According to the global data, an estimated 20 - 30 million cases of sepsis occurs each year and about 50 persons die from sepsis every hour.[1] Patients who have survived from sepsis have twice the risk of mortality in the next 5 years when compared to hospitalised controls.[2] Sepsis survivors also suffer from tremendous physical, cognitive and affective health problems in future life.[2]

Sepsis is life-threatening organ dysfunction caused by a dysregulated host response to infection causing high Intensive Care Unit (ICU) mortality and morbidity.[3] Sepsis is often diagnosed too late, because the clinical signs-symptoms and laboratory parameters that are currently in use for the diagnosis of sepsis, eg. raised temperature, increased heart-rate or breathing rate or white blood cell count, are non-specific. In children, the signs and symptoms may be subtle and deterioration is rapid. Sepsis is poorly understood and under-recognised due to confusion about its definition among patients and healthcare providers, lack of documentation of sepsis as a cause of death in death certificates, inadequate diagnostic tools and inconsistent application of standardised clinical guidelines to diagnose and treat sepsis.[4] Cultures and serology reports are available mostly after 24 to 48 hours. In the crucial hours which determine the prognosis of the patient, the physician has to depend on clinical symptoms and demographic data to aid in diagnosis and management. Hence, our study was performed with an objective to have a comparison between the clinical, serological parameters as well as the supportive measures taken among the survivors vs non-survivors of septic patients in the ICU.

Financial or Other, Competing Interest: None.
Submission 12-05-2017, Peer Review 07-06-2017,
Acceptance 13-06-2017, Published 19-06-2017.
Corresponding Author:
Dr. Deepak Chaudhury,
Panjabari, Lakhimipath,
House No. 3,
P.O. Khanapara- 781037,
Guwahati, Assam.
E-mail: deepak9891chaudhury@gmail.com
DOI: 10.14260/jemds/2017/820

MATERIALS AND METHODS

This prospective, hospital-based observational study was undertaken in the Emergency ICU of Gauhati Medical College and Hospital, over a period of one year from August 2014 to July 2015 after getting permission from Institutional Ethical Committee. The patients with sepsis, as defined by the American College of Chest Physicians/Society of Critical Care Medicine (ACCP/SCCM) Consensus Committee,[5,6] of above 18 years of age and primary admission to Emergency ICU were included in the study. However, patients with

pregnancy, primarily suffering from pancreatitis, adrenal insufficiency, burns, pulmonary embolism, cardiac tamponade, tumour-associated lactic acidosis, drug overdose and anaphylaxis, on treatment with immunosuppressive agents, patients leaving against medical advice were excluded from the study. Out of total 698 patients admitted during the study period, 87 patients were initially included according to our inclusion criteria. However, excluding the patients as per exclusion criteria of the study effective sample size became 50 for final analysis. The detailed history, clinical examination and all the relevant laboratory investigations were done. APACHE II[7] and SOFA[8] scoring were done for all the patients of sepsis admitted to emergency ICU for prognostication. APACHE II was calculated on day of admission to predict mortality and to assess the extent of multiorgan dysfunction, while extensive SOFA scoring was done daily. We have compared various profiles including clinical, serological scoring systems and organ supports between survivors' group (patients who were successfully discharged after recovery) and non-survivors group (patients who died in ICU during their course of treatment).

Statistical Methods

Continuous variables were presented on Mean ± SD (Min-Max) and results on categorical measurements were presented in Number (%). Significance was assessed at 5% level of significance. Student's 't' test (two-tailed, independent) has been used to find the significance of continuous variables between two groups and Chi-square/Fisher Exact test has been used to find the significance of categorical variables between two or more groups. All data were analysed with SPSS 16.0.

RESULTS

After applying the inclusion and exclusion criteria, clinical profiles of 50 patients with sepsis were studied, out of which 28 were males (56%) and 22 were females (44%) (Fig. 1).

18 patients (36%) died and 32 patients (64%) survived in this study (Fig. 2).

Age of patients varied from 18 years to 90 years (Fig. 3) with mean 48.36 years (SD ± 17.16). Highest numbers of cases were seen in the age group of 61 to 70 years, i.e. 12 patients (24%) followed by 41 to 50 years in 10 cases (20%), 21 to 30 years in 9 cases (18%) (Fig. 3). The youngest patient in the study is 18 years old, the oldest patient is 90 years.

24 patients (48%) had associated co-morbidities with diabetes being commonest of them (n= 14, 28%) (Fig. 4). Chest x-ray revealed 17 patients had lower zone consolidation and 5 had ARDS. ECG showed all 50 had sinus tachycardia with 2 also had P-pulmonale and 2 had LVH.

Pneumonia and urinary tract infections were the most common primary aetiologies of sepsis in our set of patients (Table 1). On admission 16 patients (32%) had anaemia, leucocytosis in 38 (76%) patients and leucopaenia in 4 patients (8%), 38 patients (76%) had hyponatraemia (Na < 135 mEq/L), 13 patients (26%) had hypokalaemia (K < 3.5 mEq/L) and 4 patients (8%) had hyperkalaemia (> 5.5), 41 patients (82%) had acidic pH (< 7.35) on the day of admission. Definite microbiological evidence of infection from culture of appropriate specimen and blood culture was found in 56% of patients with sepsis. Culture of appropriate specimen (as determined from history and clinical examination), e.g. sputum, urine, stool, pus, ascitic or pleural fluid, etc. could identify a definite microorganism in 38% of cases of sepsis (Fig. 5).

Furthermore, our study catered to the comparison of clinico-pathological parameters and organ supports in survivor and non-survivor group, which are presented in Table 2 to Table 5.

Primary Diagnosis of the Sepsis Patients	Number of Patients (N, %)
Pneumonia	19 (38%)
UTI	12 (24%)
Cellulitis with sepsis	5 (10%)
Bacterial peritonitis	4 (8%)
Pyelonephritis	3 (6%)
Empyema/Lung abscess	3 (6%)
Cholangitis	2 (4%)
Malaria	2 (4%)

Table 1. Diagnosis of Sepsis Patients

Variables	Non-Survived (n=18)	Survived (n= 32)	P value
Age in years (mean ± SD)	51.06 ± 19.59	46.84 ± 15.77	0.411
Fever (No. %)	18, 100.0%	32, 100.0%	1.000
Headache (No. %)	2, 11.1%	2, 6.2%	0.612
Cough (No. %)	5, 27.8%	8, 25.0%	1.000
Breathlessness (No. %)	7, 38.9%	9, 28.1%	0.532
Altered sensorium (No. %)	1, 5.6%	1, 3.1%	1.000
Vomiting (No. %)	4, 22.2%	8, 25.0%	1.000
Jaundice (No. %)	2, 11.1%	2, 6.2%	0.612
Oliguria (No. %)	4, 22.2%	12, 37.5%	1.000
Abdominal pain (No. %)	5, 27.8%	12, 37.5%	1.000
Chest pain (No. %)	2, 11.1%	3, 9.3%	1.000
Loose stools (No. %)	2, 11.1%	3, 9.3%	1.000
Temperature (mean ± SD)	102.48 ± 1.06	102.61 ± 1.01	0.658
Pulse rate (mean ± SD)	123.44 ± 13.51	117.63 ± 5.04	0.033*
Day 1 GCS	10.06 ± 5.57	14.19 ± 1.99	<0.001*
Respiratory rate (mean ±SD)	27.22 ± 5.54	26.5 ± 5.47	0.658
Co-morbidities	10 (55.5%)	14 (43.7%)	0.423

Table 2. Comparison between Clinical Parameters of Survivors and Non-Survivors

Variables	Non-Survived	Survived	P value
Haemoglobin	11.14 ± 4.02	10.89 ± 2.04	0.770
Haematocrit	37.54 ± 9.67	38.58 ± 4.39	0.605
Total Count	15827.78 ± 8423.69	22893.75 ± 24048.53	0.236
PH	7.24 ± 0.13	7.24 ± 0.1	0.989
Serum Bilirubin	2.19 ± 1.41	2.78 ± 2.55	0.375
Serum amylase	20.56 ± 11.55	17.69 ± 5.97	0.251
Serum creatinine (mg/dL)	1.76 ± 1.06	2.77 ± 2.43	0.101

Table 3. Comparison between Haematological and Biochemical Parameters between Survived and Non-Survived Patients

Scores	Non-Survived	Survived	P value
Sofa Day 1	10.17 ± 3.45	7.94 ± 2.64	0.014*
Sofa Day 3	13.42 ± 4.06	6.84 ± 2.96	< 0.001**
Sofa Day 10/ Last Day	13.5 ± 5.69	1.33 ± 1.23	< 0.001**
Apache II Score Day 1	23.28 ± 9.65	18.75 ± 7.34	0.068

Table 4. Comparison between Severity Scoring Systems, between Survivors and Non-Survivors

Variables	Non-Survived	Survived	P value
Inotropic support (No. %)	13 (72.2%)	15 (46.9%)	0.083
Mechanical Ventilator (No. %)	16 (88.9%)	14 (43.8%)	0.002*
Dialysis (No. %)	2 (11.1%)	8 (25.0%)	0.295
Duration of ICU Stay (No. %)	3.72 ± 3.08	3.75 ± 2.02	0.969

Table 5. Comparison of Supportive Measures between Survivors and Non-Survivors

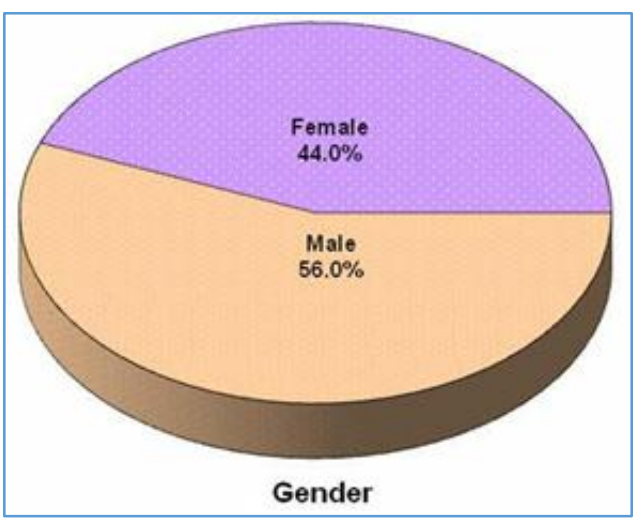

Figure 1. Pie Diagram showing Gender Distribution of Sepsis Patients in Our Study

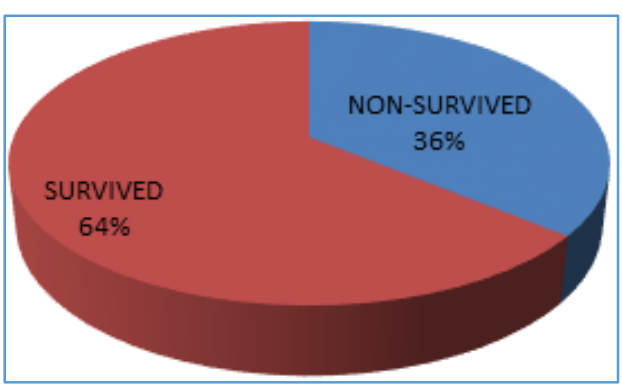

Figure 2. Pie Diagram showing Frequency of Morality in Sepsis Patients

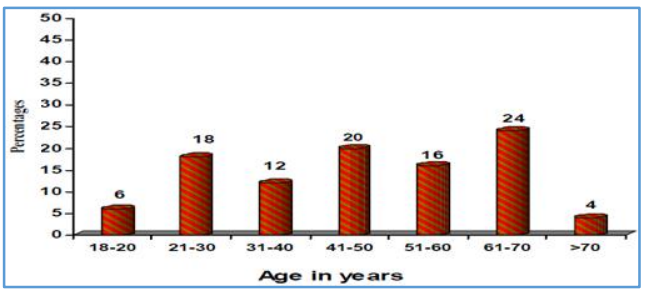

Figure 3. Bar Diagram showing Age Distribution of Study Population

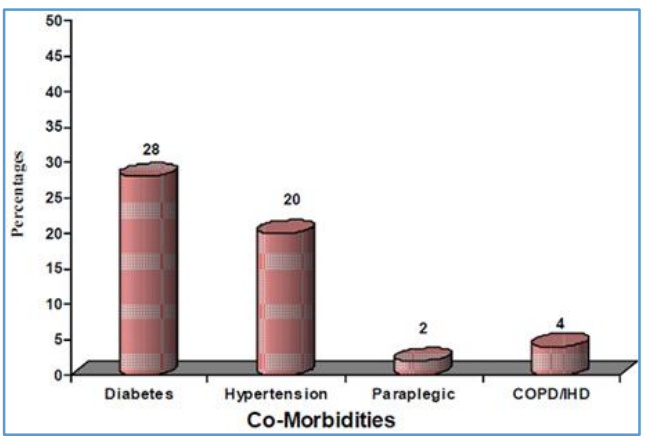

Figure 4. Various Comorbidities of Sepsis Patients in Our Study

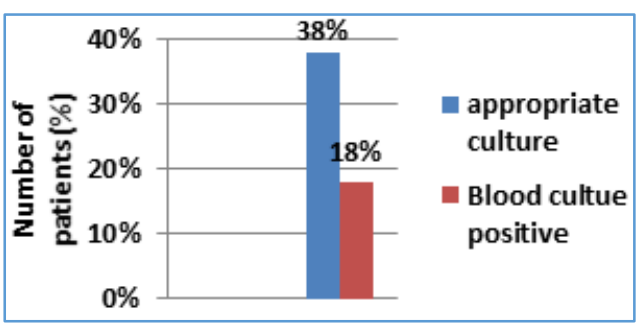

Figure 5. Microbiological Evidence in Sepsis Patients

DISCUSSION

The clinical profile of 50 patients with sepsis was studied with 28 males and 22 females in this cohort and mean age of 48.3 years. Similar study in India have also shown male preponderance with most patients in the fourth to fifth decade.[9]

Definite microbiological evidence of infection from culture of appropriate specimen and blood culture was found in 56% of patients with sepsis in our study, which is similar to the observation of Todi S et al[9] in a multicentric, prospective trial from 2006 to 2009 in Indian ITUs found culture positivity in 61.6% patients with sepsis. Vincent JL et al (2009) reported in a study involving 14,000 ICU patients in 75 countries that microbiological culture was positive in 70% of the infected patients.[10]

The mortality recorded in this study is 36%. In large

clinical trials, the mortality associated with severe sepsis and septic shock ranges between 13% and 50%.[11]

All patients had fever with breathlessness and oliguria being the next predominant symptom observed in 32% patients each. Among the several disorders encountered in sepsis, Acute Kidney Injury (AKI) mostly manifested clinically by decreased urine output is one of the most important, because it is a life-threatening condition, increases the complexity and cost of care, and is an independent risk factor for mortality.[12] There was no significant difference in symptomatology between survivors and non-survivors in our study.

The mean age among non-survivors was a little high compared to survivors (51.7 v/s 46.84), which was not statistically significant (p= 0.411); 7 patients among non-survivors and 9 patients among survivors had breathlessness which was statistically similar (p= 0.532). The non-survivors had a higher pulse rate (mean 123.44 v/s 117.63, p= 0.033) and a lower blood pressure and therefore a greater requirement for inotropes (72.2% vs 46.9%, p= 0.08). Compared to survivors in our study, mortality rate among septic shock patients was 72.2%. Septic shock was associated with a higher mortality as shown with studies in Europe by Jacobson et al[13] and 72.1% in Croatia by Degoricija et al.[14] However, an Indian study by Todi et al had recorded a mortality of 59.26% in patients with severe sepsis and septic shock.[9]

Although, the observed high respiratory rate in non-survivors than survivors (27.22 v/s 26.5) was not statistically significant (p= 0.658), but there was significantly more need of mechanical ventilation in non-survival patients (88.9% vs 43.8%, p= 0.002).

Among other clinical parameters, mean GCS among survivors was high compared to non-survivors on all days (Day 1, 14.19 v/s 10.19) and was statistically very significant (p < 0.001), which is in accordance with the finding by Vosylius et al[15] and Bastos et al[16] that admission GCS was an independent predictor of mortality. Presence of comorbidities were statistically not significant among survivors and non-survivors (p= 0.423).

Among the haematological parameters, leucocytosis and leucopaenia are often associated with mortality and normal white blood cell counts are associated with survival.[13,17] In our study, however, non-survivors had a mean total count of 15,827/μL and survivors had a mean total count of 22,893/μL at admission, which was not statistically significant though.

Biochemical parameters were not statistically different among survivors and non-survivors. In our study, mean serum creatinine did not significantly differ among non-survivors and survivors on Day 1 and also on initial few days (Day 1, 1.76 v/s 2.77, p= 0.101). Even mean serum bilirubin was significantly different among survivors and non-survivors (Day 1, 2.19 v/s 2.78, p= 0.375).

In this study, though mean APACHE II score was high among non-survivors than survivors (23.28 v/s 18.75), but it was of no statistical significance. However, many studies have shown that high APACHE II score at the time of admission was associated with high mortality.[12]

SOFA score has been validated extensively for prognostification. In our study, extensive study of SOFA score was done from Day 1 to the last day. The SOFA score on Day 1 was high among non-survivors and low among survivors which was statistically significant (10.17 v/s 7.94, p= 0.014). However, the most significant difference was observed on Day 3. The SOFA score was very high among non-survivors as compared to survivors, which was statistically very significant (13.42 v/s 6.84, p < 0.001). This was similar to many studies that have been done. Vosylius et al[15] in their study on 117 ICU patients with sepsis showed that the changes in the severity of organ dysfunction were closely related to the outcome of the patients admitted to ICU and Day 3 SOFA score was better than Day 1 SOFA score for outcome prediction.

Vincent et al[18] in their study in 40 ICU's in 16 countries showed that the total SOFA score increased in 44% of the non-survivors, but in only 20% of the survivors. Saulius Vosylius[15] in Vilnius, Lithuania observed that SOFA score on Day 1 and Day 3 was significantly higher in non-survivors than those in survivors.

In our study 13 out of 18 (72.2%) among non-survivors required inotropic support, whereas 15 out of 32 (46.9%) among survivors required inotropic support suggesting statistically significant hypotension among non-survivors (p= 0.083); 16 out of 18 (88.9%) among non-survivors required ventilator support, whereas 14 out of 32 (43.8%) among survivors required ventilator support suggesting significant respiratory system involvement among non-survivors (p= 0.002). The mean duration of ICU stay did not vary between non-survivors and survivors (3.72 v/s 3.75). It may be attributable to early death among non-survivors and early recovery among survivors. However, dialysis was required more among survivors than non-survivors (25% v/s 11.1%, p= 0.295), but was not statistically significant.

The mean duration of ICU stay did not vary between non-survivors and survivors (3.72 v/s 3.75). It may be attributable to early death among non-survivors and early recovery among survivors.

However, our study was limited by several factors. With a sample size of 50 patients, this model requires external validation by further large studies. Time of admission to ICU for each patient is different, thereby lead time bias was possible. History of prior antibiotic usage could not be ascertained by history. Nosocomial complications and socio-economic constraints are difficult to model in studies.

CONCLUSION

Sepsis with Multiorgan Dysfunction Syndrome (MODS) is a common cause of Intensive Care Unit (ICU) mortality and morbidity. Sepsis can be reversed, but as sepsis progresses to severe sepsis and septic shock the mortality rate substantially increases. Specimen culture reports are usually available quite later (with low yield) and so we have to intervene earlier and harder based on the clinico-pathological parameters. Scoring systems like SOFA and APACHE may be useful in these set of patients to prognosticate these patients early, but have variable sensitivity in clinical studies. Hence, assessment of clinical signs and initial serological and radiological investigations are of utmost importance to detect more critical patients as early as possible to save lives.

REFERENCES

[1] Kissoon N, Carcillo JA, Espinosa V, et al. World federation of pediatric intensive care and critical care societies: global sepsis initiative. Pediatr Crit Care Med 2011;12(5):494-503.

[2] Angus DC. The lingering consequences of sepsis: a hidden public health disaster? JAMA 2010;304(16):1833-4.

[3] Singer M, Deutschman CS, Seymour CW, et al. The third international consensus definitions for sepsis and septic shock (sepsis-3). JAMA 2016;315(8):801-10.

[4] International organizations declare sepsis a medical emergency. Issued by an expert panelrepresenting 20 adult and pediatric intensive care societies 2010. Available from: http://www.prnewswire.com/news-releases/international-organizations-declaresepsis-a-global-medical-emergency-104142073.html.

[5] Bone RC, Balk RA, Cerra FB, et al. Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. The ACCP/SCCM consensus conference committee. American college of chest physicians/society of critical care medicine. Chest 1992;101(6):1644-55.

[6] Levy MM, Fink MP, Marshall JC, et al. 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference. Crit Care Med 2003;29(4):530–8.

[7] Knaus WA, Draper EA, Wagner DP, et al. APACHE II: a severity of disease classification system. Crit Care Med 1985;13(10):818-29.

[8] Vincent JL, Moreno R, Takala J, et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the working group on sepsis-related problems of the European society of intensive care medicine. Intensive Care Med 1996;22(7):707-10.

[9] Todi S, Chatterjee S, Sahu S, et al. Epidemiology of severe sepsis in India: an update. Crit Care 2010;14(Suppl 1):P382.

[10] Vincent JL, Rello J, Marshall J, et al. International study of the prevalence and outcomes of infection in intensive care units. JAMA 2009;302(21):2323-9.

[11] Balk RA. Severe sepsis and septic shock. Definitions, epidemiology, and clinical manifestations. Crit Care Clin 2000;16(2):179-92.

[12] Merwe ED, Kidd M, Metzker S, et al. Validating the use of the APACHE II score in a tertiary South African ICU. SAJCC 2005;21(1):46-54.

[13] Jacobson S, Johansson G, Winsö O. Primary sepsis in a university hospital in northern Sweden: a retrospective study. Acta Anaesthesiol Scand 2004;48(8):960-7.

[14] Degoricija V, Sharma M, Legac A, et al. Survival analysis of 314 episodes of sepsis in medical intensive care unit in university hospital: impact of intensive care unit performance and antimicrobial therapy. Croat Med J 2006;47(3):385–97.

[15] Vosylius S, Sipylaite J, Ivaskevicius J. Sequential organ failure assessment score as the determinant of outcome for patient with severe sepsis. Croat Med J 2004;45(6):715-20.

[16] Bastos PG, Sun X, Wagner DP, et al. Glasgow coma scale score in the evaluation of outcome in the intensive care unit: findings from the acute physiology and chronic health evaluation III study. Crit Care Med 1993;21(10):1459-65.

[17] Oliveira AP, Barata CH, Murta EF, et al. Comparative study of survivor and non-survivor sepsis patients in a university hospital. Rev Soc Bras Med Trop 2008;41(1):50-4.

[18] Vincent JL, de Mendonça A, Cantraine F, et al. Use of the SOFA score to assess the incidence of organ dysfunction/failure in intensive care units: results of a multicenter, prospective study. Working group on sepsis related problems of the European society of intensive care medicine. Crit Care Med 1998;26(11):1793-800.