ORIGINAL PAPER

doi: 10.5455/medarh.2021.75.35-40
MED ARCH. 2021 FEB; 75(1): 35-40
RECEIVED: JAN 27, 2021
ACCEPTED: FEB 25, 2021

The Outcome of Sepsis Patients Admitted to the Intensive Care Unit: Experience of 100 Cases

Alaa Abood Najim Al-Wadees[1], Ali Najeh Al-Khayyat[1], Qusay Abdulazahraa Yaqoob[2]

[1]Department of Surgery, Faculty of Medicine, Jabir Ibn Hayyan Medical University, Iraq

[2]Department of Surgery, College of Medicine, Kufa University, Iraq

Corresponding author: Ali Najeh Al-Khayyat, MD. Department of Surgery, Faculty of Medicine, Jabir Ibn Hayyan Medical University, Iraq, E-mail:awwady79@yahoo.com, ORCID ID: https://orcid.org/0000-0002-3185-5541

ABSTRACT

Introduction: The term sepsis has a deep root all over medical history. It defined by a many physician and myth such as Homer's Iliad. Sepsis defined as a clinical syndrome as an outcome from both systemic inflammatory response syndrome and infection. It can complicate by disturb the function of the organ (severe sepsis) and shock (septic shock). **Aim:** Our study aims to recognize sepsis cases in Al-Sader Medical city during 2019 and evaluate the management's management and the weak point in this management. **Methods:** It is a cross-sectional study done in Al-Sader Medical city; data collected from the archived files in the hospital during 2019, 100 cases reported in this period diagnosed and admitted as sepsis or admitted with other diagnosis evolved sepsis. **Results:** We found that one-third of the patients diagnosed as sepsis admitted to the intensive care unit, the mean duration of management 15.8 days. Many investigations did for these patients, the treatment which given to the patients was iv. fluids and antibiotics for entire patients, we also noted that death occurs in more than half of the patients in our study and death were prevalent among patient with a negative result in blood culture also the male patient was more predominant than the female patient and Najaf residency is more than three-quarters of them. Finally, we found that admission to the intensive care unit from units other than emergency or intensive care unit itself found is nearly one-third of the patient diagnosed as sepsis and the respiratory system was commonly involved and presented as pneumonia. **Conclusion:** More than half of the diagnosed cases died. The maximum common source of admission was from other hospital units, the severe sepsis and no growth of blood culture closely associated with death.

Keywords: sepsis; management of sepsis; sepsis in ICU; prognosis of sepsis.

1. INTRODUCTION

Sepsis is a consequence of clinical illness of infection and systemic inflammatory response. It occurs as a result of organ dysfunction (severe sepsis) with shock (septic shock) (1-2). Although introducing septic shock assent requires, frank hypotension, however, some have argued that evidence of hypoperfusion such as elevated levels of lactate in the blood >=4mmolll. In the United States, more than 750,000 people develop severe sepsis each year when close to 30 per cent die in the infirmary (3). Ideally, about 2/100 of hospitalized patients having severe sepsis and only 10% of patients in the group intensive care unit (ICU) have severe sepsis on admission or through staying in ICU (4-5). The Sepsis Occurrence in Acutely Ill Patients (SOAP) study across Europe recorded that greater than 35% of ICU patients got sepsis at several points through ICU stay, with a death rate of 27% (6). Almost all microbes lead to sepsis in compromised immune patients. In increment to the frequent pathogens, sepsis can as well evolve secondary to opportunistic microorganisms in the low immune patients. The utmost kind of infection is pneumonia that leads to severe sepsis (44%), followed by primary bacteremia (17%), infection of the genital tract (9%), infection of abdominal (9%), and, minimum ordinary, infections of soft tissue and wound infections (7%). About 1/3 of the sepsis patients have a negative culture study (7). Bacteria are the dominant cause of severe sepsis. The clever doctor discovered that sepsis's early manifestation could be superficial and nonspecific, such as unexplained tachypnea, changes of intellectual condition hyperglycemia, and diaphoresis. As well as significant to identify old age and suppressed immune patients with sepsis often do not own increase WBC count or fever.

In that individual, hypothermia should specifically seek for, and if found, managed critically, other laboratory and physical feedback rapid an expert physician to deduce that an infected patient 'looks septic', setting the kind of implied infection and the existence of organ dysfunction. The predisposing situations like elderly, organ transplantation history, immunocompromised, trauma, diabetes mellitus and surgery quickly ascertained. Vital signs need careful observation. Though numerous patients with sepsis will be feverish, up to 1/2 of the septic patients can be hypothermic or norm thermic (8). Increasing heart rate is a common sign as increase respiratory rate, and pulmonary condition needs careful observation for respiratory failure evidence. A meticulous checking could lead your quick guide on the likely infection source and the patient's common clinical conditions.

Patients with sepsis evidence should have blood aspirated for basic laboratory investigations, including CBC, the whole metabolic panel, and hemostasis study. White blood cell count, metabolic acidosis, hepatic or renal dysfunction should seek. Also, lactate blood level gain in the septic patient with an increased level considering a guide for sepsis-related organ hypoperfusion. It is also beneficial to view the kidney tissue and the collecting system in the septic patient with suspected perinephric abscess and exclude an obstructive uproar they significantly; bedside ultrasonography may help other diagnostic aims such as evaluating a patient's intravascular volume status (9). Computed tomography (CT) is more useful. Multiple biomarkers are estimated for use in sepsis. Most are estimated as prognostic markers in sepsis; others for diagnosis so far, neither found enough specificity or sensitivity to be systematically used. Procalcitonin has been the utmost vastly studied, but has recognized false positives (e.g. Burns, severe injuries and shocks) and false negatives (early infection, localized abscesses). As a prognostic marker, procalcitonin levels have shown to correlate with death.

The real clinical function of biomarkers resides to set. In the PROWESS (Protein C Worldwide Evaluation in Severe Sepsis) trial, patients with UTI as their source of severe sepsis had a 28-day death of 21% contrast with patients with a respiratory origin who had a death rate of 34% ($p < 0.01$) (10). Circulatory arrangements emerge from the integration of vasodilatation, leak of the capillary, decreased cardiac function, and initial repair. Some patients now utilized human albumin post a debatable meta-analysis finished that albumin accompanied with a 6% more death (11). The function of non-catecholamine drugs, such as vasopressin, levosimendan, Methylene blue and the phosphodiesterase inhibitors, to prop the circulation in sepsis stays to be cleared. Timeliness of the interference and awareness to s signs of continue tissue hypoperfusion is significant. Survival improved when volume loading to standard endpoints added, where needful, blood, catecholamine, and even mechanical ventilation (12). Many individuals with severe sepsis, even without lung sepsis, want lung upholding because of the double action of more ventilator need, hypoxemia, and pulmonary muscle dysfunction (13). Several patients enhance acute respiratory distress syndrome. The mechanical ventilation time decreases due to daily sedation interruptions (14), an increase of 9% in survival in patients with acute respiratory distress syndrome using small tidal volumes (6 ml/kg ideal body weight) (15). Renal failure occurs within 20-50% of patients, relaying on severity. Some proof shows that high volume hemofiltration temporarily decreases the requirement for vasopressors (16). Whether this interprets any long-term advantages, in terms of either renal work or survival, it has no evidence. Nutrition is another part in which high-quality data are rare, especially among non-surgical patients. In general, soon, enteral nutrition is bespoke (17) but this was accompanied by rising death in the only study in non-surgical patients (18). The merger of glycogenosis and insulin resistance means that hyperglycemia is common in patients with sepsis and correlated with a poorer result (19). Strick glycemic monitor reduces disease and death in a prospective randomized controlled trial in surgical patients (20). First and initially, among specific managements are rapid suitable empirical antimicrobials. Managements within 4 hours of admission decrease death and hospitalization stay in ICU (21). Late in hypotensive patients raise death by 7.6% an hour (22).

2. AIM

Our study aims to recognize sepsis cases in Al-Sader Medical city during 2019 and evaluate the management's management and the weak point in this management.

3. PATIENTS AND METHODS

A prospective study took place at Al-Sader Medical City, Najaf, Iraq. The study occurred between October 2019 to February 2020, this study involved 100 patients admitted to Al-Sader Medical City during 2019 either diagnosed as sepsis or admitted due to other causes and enhanced sepsis after admission. The data collected from the archived files in the hospital. Any archived file reported a diagnosis of sepsis during 2019 included in this study. Cases of neonatal sepsis excluded from the study. The data collected by a paper including information about sepsis, taken from patients file and filled by the author. It included the following information, gender, residence, source of admission (Is classified as emergency room, other units, and ICU with another diagnosis), site of infection, duration of management, ICU admission, Investigation details, treatment received, blood culture result and fate.

Statistical analysis

Statistical analysis did use SPSS windows version 25 Software. The data collected as ranges, mean and standard deviation and, categorical data calculated by percentages and frequencies. Chi-square and Fisher's exact probability test used to test qualitative and frequency data. The relevant P-value was significant if it was less than 0.05.

Variable	No. (n=100)	Percentage (%)
Gender		
Male	56	56.0
Female	44	44.0
Residence		
Najaf city	76	76.0
Outside Najaf city	24	24.0

Table 1. Distribution of patients by gender and residence

Site of infection	No. (n=100)	Percentage (%)
Pneumonia	26	26.0
UTI	8	8.0
Infection	4	4.0
Abdominal	18	18.0
Meningitis	10	10.0
Skin	20	20.0
Bone	4	4.0
Wound	24	12.0
Catheter	4	4.0
Other infection	6	6.0

Table 2. Distribution of study patients by site of infection

4. RESULTS

Altogether 100 patients participated in the study. All of them admitted to the hospital during 2019 and the beginning of 2020, the distribution of study patients by gender and residence, as shown in Table 1. Our study, the highest percentage of study patients was male (56%) with a male to female ratio of 1.27:1. Regarding residence, more than three-quarters of study patients were living in Najaf city (76%). Figure 1 shows the distribution of study patients by the source of admission. The highest percentage of patients admitted from units other than emergency or ICU itself (62%). Regarding diagnosis, 38% of study patients diagnosed as sepsis (38%) (Figure 2). The distribution of study patients by the site of infection shown in Table 2. In this study, pneumonia represented the highest infection proportion in the study patients (26%).

The distribution of study patients by ICU admission is shown in Figure 3. More than 2/3 of patients were admitted to ICU (68%). The duration of management initiation ranged from 21 hours to three months, with a mean of 15.8 days and standard deviation (SD) of ± 19.2 days. The highest percentage of patients managed for less than one month (76%). The distribution of study patients by the investigation shown in Table 3. In this study, CBC did in all study patients (100%).

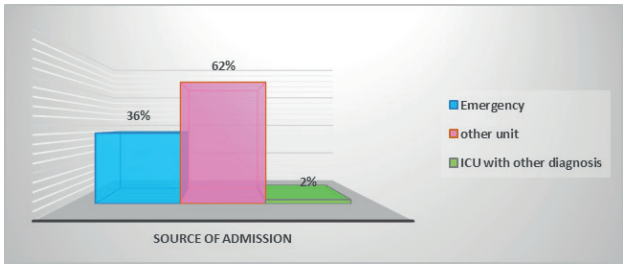

Figure 1. Distribution of the patients by source of admission

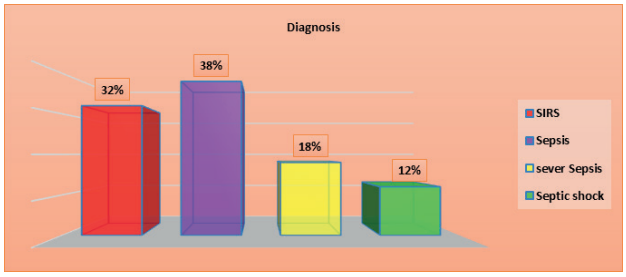

Figure 2. Distribution of the patients by diagnosis

Investigation	No. (n=100)	Percentage (%)
CBC	100	100.0
RFT	86	86.0
LFT	76	76.0
CXR	52	52.0
PT	16	16.0
PTT	16	16.0
INR	16	16.0
BT	54	54.0
ECG	24	24.0
Viral Screen	28	28.0
Blood Culture	88	88.0
Blood culture result n=88		
Isolated micro-organism	44	50.0
No Growth	44	50.0

Table 3. Distribution of study patients by investigation

Variable	Outcome	Total (%) n= 100	P- value	
	Dead (%) n= 55	Cure (%) n= 45		
Source of Admission				
Emergency	23 (63.9)	13 (36.1)	36 (36.0)	0.14
ICU	2 (100)	0 (0)	2 (2.0)	
Other units	30 (48.4)	32 (51.6)	62 (62.0)	
Diagnosis				
SIRS	8 (25)	24 (75)	32 (32.0)	0.001
Sepsis	23 (60.5)	15 (39.5)	38 (38.0)	
Severe Sepsis	15 (83.3)	3 (16.7)	18 (18.0)	
Septic Shock	9 (75)	3 (25)	12 (12.0)	
Blood culture result n=88				
Micro-organism isolated	15 (34.1)	29 (65.9)	44 (50.0)	0.001
No Growth	31 (70.5)	13 (29.5)	44 (50.0)	

Table 4. Association between outcome and certain details

Concerning blood culture result, micro-organisms isolated in 50% of study patients. The distribution of study patients by treatment is shown in Figure 5. All study patients were received iv. fluid and antibiotics (100%). Figure 6 shows the distribution of patients by outcome. The highest percent of study patients were died (55%). The association between outcome and certain details shown in Table 4.

We noticed that the highest prevalence of death among patients with negative blood culture results (70.5%) with a significant association (P=0.001) between death prevalence and blood culture result. Regarding diagnosis, the highest prevalence of death seen among patients diagnosed with severe sepsis (83.3%) with a significant association (P=0.001) between the prevalence of death and

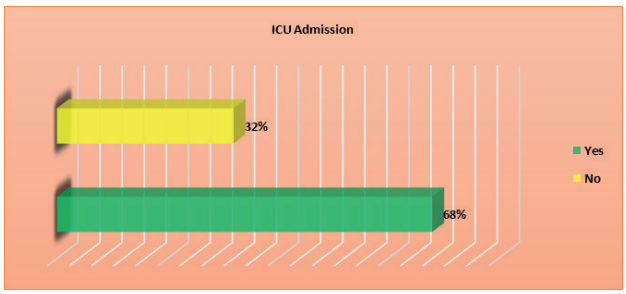

Figure 3. Distribution of study patients by site of infection

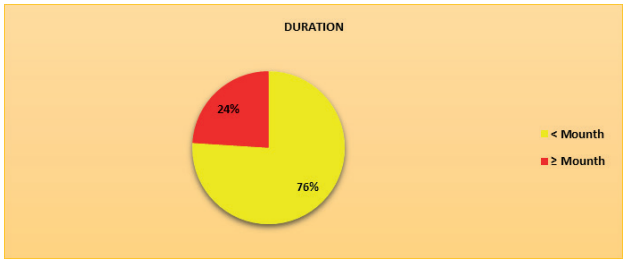

Figure 4. Distribution of study patients by duration of initiation of management

diagnosis. Correlation (P=0.14) between the prevalence of death and source of admission is no significant.

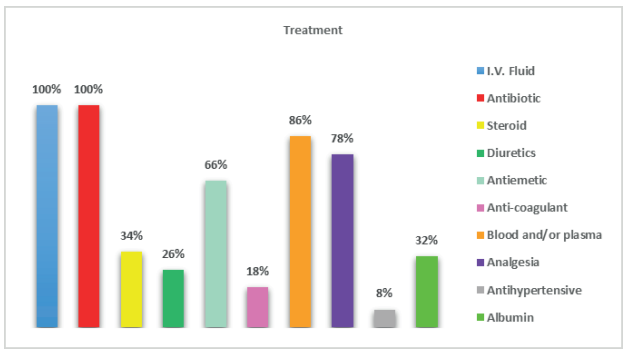

Figure 5. Distribution of study patients by treatment

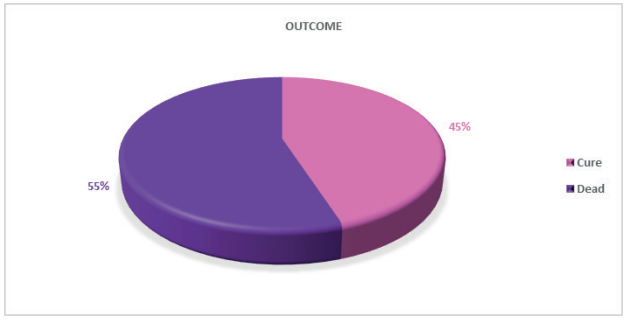

Figure 6. Distribution of study patients by the outcome

5. DISCUSSION

Despite the medical therapeutics advances sepsis, septic shock severe sepsis, stay the major cause of mortality and morbidity ICUs (22). Several studies have reported the characteristics, incidence, and results of severe sepsis and septic shock from various locations and nations (23). Not surprisingly, the death scope ratio excessively changes through the universe, and considerable changes in the manner of causative microorganisms and sites of infection observed (24). These actualities mirror the significance of local epidemiological research on sepsis to raise our learning about features of sepsis in varied locations and health care systems to get better patient care and prognosis (25). In our study, the total number of study patients in this research was 100. All of them admitted to the hospital in 2019. Patients entering the ICU during the current study constitute more than two-thirds of the patient (68%). By comparing this results with others, different results gain from a study conducted in Turkey (2006), as they observed that only 40.7% of the patients admitted to an ICU from the emergency department (26), also lower results observed in a study conducted in Mainland China in 2014, in which screened 3063 admissions of patients had or suspected to have sepsis and 1297 patients of those admitted to the ICU (42.3%) (23). The mean duration and SD were 15.8 days ± 19.2 days, with three-quarters of them, admitted for less than one month for management (76%).Many types of investigation done for the patients, CBC did for all patients and culture isolated microorganisms in half of them (50%), these results were higher than a Turkish study conducted on 69 patients with sepsis in 2006, They noted that the median duration of residence in hospital from the time of entry was 13 days (134 days). That was five days (44-day interval) from the duration of the diagnosis. (26) In Taiwan, a study conducted in 2015 showed that 269 patients with authenticating microbiological outcomes, Gram-negative bacteria, Gram-positive bacteria, and fungi separated in 65%, 25%, and 10% of the severe sepsis patients (27), another Chinese study conducted in 2014 and involved 484 patients enhanced severe sepsis, their results showed that median ICU length of stay was seven days, whilst hospital length of stay was 18 days. In addition, they found that 148 patients (30.6%) had microbiological documents related to severe septicemia and septic shock diagnosed in their study (26). In the current study, IV fluid and antibiotics (AB) administrated to all patients, which differs from Turkish study in 2006, in which 17 of 69 patients with sepsis (24.6%) began with initial AB monotherapy, while twenty-one of those patients received combination treatment which means that only 45% of the patients started AB administration (26), while another study done in 2015 agreed to the current results as they gave AB to all patients when they were diagnosed with or suspected to get an infection or sepsis (28).More than half of the current study's patients died (55%), furthermore, death was prevalent among patients with negative results in blood culture (70.5%) and noticed a significant association (P=0.001) between the prevalence of death and blood culture result, also death was prevalent in almost of patients with severe sepsis (83.3%) in which a significant association between them(P=0.001). In contrast, no significant association between death and source of admission had observed (P=0.14). The outcome of sepsis in a 2006 Turkish study found that 55/63 patients (87.3%) died as a result of hospitalization. The death rate was 92.2% for at least one organ dysfunction (liver, lung, kidney and hematologic), compared to 44.4% for no organ (26). In which the death ratio was higher in their study as compared to the current results. Still, lower results observed in a study conducted in a study in 2015 in which they

noticed that patients who enhanced sepsis had higher ICU death and higher hospital death compared to those admitted but without sepsis development (41.4% vs 5.1% and 44.8% vs 8.2% respectively) with a significant statistical association between them (P < 0.001) (29) and another lower results observed in a study conducted in Germany 2013 in which the In-hospital mortality of the patients had severe sepsis were 43.6%, in those has sepsis the mortality was 24.3%. The highest proportion of death noticed in those who had septic shock 58.8% (29) and a study in Taiwan other lower results observed when the total twenty-eight-day death rate was 61% (27). A study conducted in China in 2014 showed that amongst the 484 patients enrolled in the research, 139 deaths in ICU, and 23 died through hospital staying post-transfer to hospital wards. 20 patients (4.1%) were yet in the hospital at the end of observation and consider survivors. The crude ICU and hospital death rates in this Chinese study were 28.7% and 33.5%; respectively, no significant association spotted between ICU stay and the sepsis prevalence (P=0.067) (26). In SOAP study (Sepsis Occurrence in Acutely Ill Patients) study, ICU death rate was 32.2% for severe sepsis and 54.1% for septic shock (30). In France, patients with severe sepsis had a hospital death rate of 59%. In contrast, patients with septic shock had a hospital death of 61.2% (31). Furthermore, overall ICU and hospital death rates were 26.5% and 37.5% for patients with severe sepsis in New Zealand, and Australia (32), this discrepancy in results may explain by many factors age of patients, change in the definition of severe sepsis, correlated morbidity, types and sites of infection, affected organisms, standard of antibiotic treatment, organ dysfunction severity, the seriousness of acute illness might be different and patients with ICU-acquired sepsis had more death rate. In the current research, the male gender was predominant in more than half of the patients (56%) with a male to female ratio of 1.27:1. Najaf residency noticed in more than three-quarters of them (76%), these findings were consistent with a 2006 Turkish study in which men represented 54% of the patients in the study (27), while different results observed in a study conducted in 2015, where a total of 2,025 patients were included in the research as they notice that patients who enhanced sepsis had a trend towards older age (67 ± 13 years) and a direct towards more male gender (69.0% vs 51.5%) with a male: female ratio was 1.3:1 [29]. The average age of patients with severe sepsis was 64.3 years, and about two-thirds of them were men with a male: female ratio was 1.8:1 (26). Lastly, higher results were observed in a Chinese study in 2014 when they noticed that male constituted more than two-thirds of the patients containing 336 males (69.4%), and their median age was 66 years. Greater than half of the patients entrance into ICU because of pulmonary problems (53.5%), and 2/3 patients (67.4%) had at minimum one underlying disease or chronic organ malfunction system, no significant association observed between gender and prevalence of sepsis (P=0.115). In contrast, a significant one observed between age and sepsis prevalence (P<0.001) (25). Admission from units other than emergency or ICU itself found in nearly two-thirds of the patients (62%) and more than third of the patients diagnosed as sepsis (38%). The respiratory system was commonly involved and presented as pneumonia in 26% of the study's patients. When compared to Turkish study in 2006, a higher proportion of patients 85·2% of those who diagnosed with sepsis in the surgical or medical wards, in the same study, the respiratory system was the commonly involved system as pneumonia diagnosed in 44.9 % of them (30), all these results were higher than those observed in our study. A result is lower than those gain in the current study observed in a study conducted in 2015, where a total of 2,025 patients included in the study, of those 29 patients (1.4%) enhanced sepsis, furthermore traumatic brain injury and intracranial haemorrhage complicated by sepsis were the commonest sources of sepsis presented in 5 patients for each (17.2) (30). Different results observed in Taiwan, in a study conducted in 2015 when they noticed that amongst 7795 patients assumptive to the ICUs through the research time, the respiratory tract (38%) and abdomen (33%) were the utmost recurrent area of infection, also noticed that 536 (6.9%) had severe sepsis and compromised the study people, the comparatively lower happening rate in this study as compared to our study (18% in severe sepsis), may be demonstrate by the tough inclusion stander and characteristics of the total patient people. As they included patients diagnosed with severe sepsis or septic shock on ICU admission and did not eliminate those who remained in the ICU for <24 h for routine postoperative follow up as the whole study people (31), also another lower incidence observed in a study conducted Japan in 2014 when severe sepsis constituted about 4.3% of the sepsis cases admitted to ICU (32), while the incidence was higher in a study conducted in United kingdom in 2003 in which severe sepsis found in 27% of the patients (33).Lastly, a Chinese study conducted in 2014 screened 3063 patients admitted through the study duration and 1297 patients (42.3%) included. Four hundred eighty-four patients enhanced severe sepsis or septic shock. In the same study, the lung (85.7%) and the abdomen (18.0%) were the utmost popular infections, with pneumonia was the commonest infection observed. One hundred sixty-seven patients (34.5%) had two or more site of infection.

6. CONCLUSION

More than half of patients who diagnosed as sepsis in the hospital died. A most common source of admission was from other units in the hospital. Severe sepsis and negative blood culture findings were significant risk factors of death in patients with sepsis. Upon finishing the research, we concluded that early goal-directed therapy plays no function in decreasing death rates amongst patients in our practice, especially when these patients get admitted to the ER. There should be an increased level of awareness promoted among the general population. People need to understand and recognize early signs and symptoms consistent with sepsis diagnosis and report

them to an authorized healthcare facility immediately; This will significantly decrease mortality.

- **Author's contribution**: All authors were involved in all steps of preparation this article. Final proofreading was made by the first author.
- **Conflict of interest**: None declared.
- **Financial support and sponsorship**: Nil.

REFERENCES

1. Botero JS, Pérez MC. The history of sepsis from ancient Egypt to the XIX century. Sepsis-an ongoing and significant challenge 2012. In Tech, doi: 10.5772/51484.
2. Bone RC, Balk RA, Cerra FB, Dellinger RP, Fein AM, et al. Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. Chest. 1992 Jun 1; 101(6): 1644-1655, doi: 10.1378/chest.101.6.1644.
3. Angus DC, Linde-Zwirble WT, Lidicker J, Clermont G, Carcillo J, Pinsky MR. Epidemiology of severe sepsis in the United States: analysis of incidence, outcome, and associated costs of care. Critical care medicine. 2001 Jul 1; 29(7): 1303-1310, doi: 10.1097/00003246-200107000-00002
4. Sands KE, Bates DW, Lanken PN, Graman PS, Hibberd PL, Kahn KL, et al. Epidemiology of sepsis syndrome in 8 academic medical centers. JAMA. 1997 Jul 16; 278(3): 234-240.
5. Linde-Zwirble WT, Angus DC. Severe sepsis epidemiology: sampling, selection, and society. Critical Care. 2004 Aug; 8(4): 222, doi: 10.1186/cc2917
6. Vincent JL, Sakr Y, Sprung CL, Ranieri VM, Reinhart K, Gerlach H, et al, Sepsis Occurrence in Acutely Ill Patients Investigators. Sepsis in European intensive care units: results of the SOAP study. Critical care medicine. 2006 Feb 1; 34(2): 344-353, doi: 10.1097/01.ccm.0000194725.48928.3a
7. Wheeler AP, Bernard GR. Treating patients with severe sepsis. New England Journal of Medicine. 1999 Jan 21; 340(3): 207-214, doi: 10.1056/NEJM199901213400307.
8. Rizoli SB, Mashall JC. Saturday night fever: finding and controlling the source of sepsis in critical illness. The Lancet Infectious Diseases. 2002 Mar 1; 2(3): 137-144, doi: 10.1016/s1473-3099(02)00220-7.
9. Samer Makki Mohamed Al-Hakkak et al. The role of ultrasound in the diagnosis of non-traumatic acute abdomen. International Journal of Pharmaceutical Research, Oct–Dec 2020, 12(4): 3706-3713.
10. Bernard GR, Vincent JL, Laterre PF, LaRosa SP, Dhainaut JF, Lopez-Rodriguez A, et al. Efficacy and safety of recombinant human activated protein C for severe sepsis. New England Journal of Medicine. 2001 Mar 8; 344(10): 699-709, doi: 10.1056/NEJM200103083441001.
11. Cochrane Injuries Group Albumin Reviewers. Human albumin administration in critically ill patients: systematic review of randomised controlled trials. BMJ. 1998; 317: 235-240, doi: 10.1136/bmj.317.7153.235
12. Rivers E, Nguyen B, Havstad S, Ressler J, Muzzin A, Knoblich B, et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med. 2001; 345: 1368-1377, doi: 10.1056/NEJMoa010307
13. Lanone S, Taille C, Boczkowski J, Aubier M. Diaphragmatic fatigue during sepsis and septic shock. Intensive Care Med. 2005; 31: 1611-1617, doi: 10.1007/s00134-005-2748-4.
14. Kress JP, Pohlman AS, O'Connor MF, Hall JB. Daily interruption of sedative infusions in critically ill patients undergoing mechanical ventilation. N Engl J Med. 2000; 342: 1471-7, doi: 10.1056/NEJM200005183422002
15. Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. N Engl J Med. 2000; 342: 1301-1308, doi: 10.1056/NEJM200005043421801.
16. Venkataraman R, Subramanian S, Kellum JA. Clinical review extracorporeal blood purification in severe sepsis, 2003; 7: 139-145, doi: 10.1186/cc1889.
17. Kreymann KG, Berger MM, Deutz NE, Hiesmayr M, Jolliet P, Kazandjiev G, et al. ESPEN guidelines on enteral nutrition: intensive care. Clin Nutr. 2006; 25: 210-223, doi: 10.1016/j.clnu.2006.01.021.
18. Krinsley JS. Association between hyperglycaemia and increased hospital mortality in a heterogeneous population of critically ill patients. Mayo Clin Proc. 2003; 78: 1471-1478, doi: 10.4065/78.12.1471.
19. Van den Berghe G, Wouters P, Weekers F, Verwaest C, Bruyninckx F, Schetz M, et al. Intensive insulin therapy in critically ill patients. N Engl J Med 2001; 345: 1359-1367, doi: 10.1056/NEJMoa011300.
20. Houck PM, Bratzler DW, Nsa W, Ma A, Bartlett JG. Timing of antibiotic administration and outcomes for Medicare patients hospitalized with community-acquired pneumonia. Arch Intern Med. 2004; 164: 637-644, doi: 10.1001/archinte.164.6.637.
21. Kumar A, Roberts D, Wood KE, Light B, Parrillo JE, Sharma S, et al. Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. Crit Care Med. 2006; 34: 1589-1596, doi: 10.1097/01.CCM.0000217961.75225.E9.
22. Harrison DA, Welch CA, Eddleston JM. The epidemiology of severe sepsis in England, Wales and Northern Ireland, 1996 to 2004: secondary analysis of a high quality clinical database, the ICNARC Case Mix Programme Database. Crit Care. 2006; 10: R42, doi: 10.1186/cc4854.
23. Zhou J, Qian C, Zhao M, et al. Epidemiology and outcome of severe sepsis and septic shock in intensive care units in mainland China. PLoS One. 2014; 9: e107181, doi: 10.1371/journal.pone.0107181.
24. Mayr FB, Yende S, Angus DC. Epidemiology of severe sepsis. Virulence. 2014; 5: 4-11, doi: 10.4161/viru.27372.
25. Lagu T, Rothberg MB, Shieh MS, et al. Hospitalizations, costs, and outcomes of severe sepsis in the United States 2003 to 2007. Crit Care Med. 2012; 40: 754-776, doi: 10.1097/CCM.0b013e318232db65.
26. Tanriover MD, Guven GS, Sen D, Unal S, Uzun O. Epidemiology and outcome of sepsis in a tertiary-care hospital in a developing country. Epidemiology and Infection. 2006 Apr; 134(2): 315-322, doi: 10.1017/S0950268805004978.
27. Huang CT, Tsai YJ, Tsai PR, Yu CJ, Ko WJ. Epidemiology and outcome of severe sepsis and septic shock in surgical intensive care units in Northern Taiwan Medicine. 2015 Nov; 94(47), doi: 10.1097/MD.0000000000002136.
28. Sadaka F, Cytron MA, Fowler K, Javaux VM, O'Brien J. Sepsis in the neurologic intensive care unit: epidemiology and outcome. Journal of clinical medicine research. 2015 Jan; 7(1): 18, doi: 10.14740/jocmr1935w
29. Fleischmann C, Thomas–Rueddel DO, Hartmann M, Hartog CS, Welte T, Heublein S, Dennler U, Et al. Hospital incidence and mortality rates of sepsis: an analysis of hospital episode (DRG) statistics in Germany from 2007 to 2013. Deutsches Ärzteblatt International. 2016 Mar; 113(10): 159, doi: 10.3238/arztebl.2016.0159.
30. Vincent JL, Sakr Y, Sprung CL, Ranieri VM, Reinhart K, et al. Sepsis in European intensive care units: results of the SOAP study. Crit Care Med. 2006; 34: 344-353, doi: 10.1097/01.ccm.0000194725.48928.3a.
31. Finfer S, Bellomo R, Lipman J, French C, et al. Adult-population incidence of severe sepsis in Australian and New Zealand intensive care units. Intensive Care Med. 2004; 30: 589-596, doi: 10.1007/s00134-004-2157-0.
32. Ogura H, Gando S, Saitoh D, Takeyama N, Kushimoto S, Fujishima S, Et al. Epidemiology of severe sepsis in Japanese intensive care units: a prospective multicenter study. Journal of Infection and Chemotherapy. 2014 Mar 1; 20(3): 157-162, doi: 10.1016/j.jiac.2013.07.006.
33. Padkin A, Goldfrad C, Brady AR, Young D, Black N, Rowan K. Epidemiology of severe sepsis occurring in the first 24 hrs in intensive care units in England, Wales, and Northern Ireland. Critical care medicine. 2003 Sep 1; 31(9): 2332-2338, doi: 10.1097/01.CCM.0000085141.75513.2B.