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The Prevalence of Sepsis and Septic Shock in a Middle-Income Country: Experience of Two Tertiary Hospitals in Jordan

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ABSTRACT

Aim: This study was conducted to describe the prevalence rates for sepsis and septic shock and the length of stay (LOS) among adult patients in intensive care units (ICUs) at two tertiary hospitals in Jordan.

Study design: A cross-sectional descriptive design was used.

Materials and methods: A total of 914 patients admitted to adult medical and surgical ICUs at two tertiary hospitals for three months were screened for sepsis and septic shock, and followed up during their hospitalization. The data were collected using a flowchart for screening patients with sepsis/ septic shock. In addition, another tool was used to assess patients' socio-demographics and clinical variables.

Results: The overall three-month period prevalence rate for both sepsis and septic shock was 16.6%. Of these, 48.7% of patients developed sepsis and 51.3% had septic shock. The mean LOS in hospital of patients with sepsis/ septic shock was 21.4 days, compared to 10.5 days for patients without sepsis/ septic shock ($p < .001$). The mean LOS in ICU of patients with sepsis/ septic shock was 11.1 days, while for patients without sepsis/ septic shock it was 4.4 days ($P < .001$). The mean Sequential Organ Failure Assessment (SOFA) score was 7.6 ± 3.8 (range = 2.0 – 18.0) for patients with sepsis/septic shock.

Conclusion: The prevalence rate of sepsis and septic shock was comparable to, or lower than, the prevalence rate at adult ICUs of hospitals in different countries. Sepsis and septic shock were significant health problems among patients in the adult ICUs in Jordan, doubling their LOS.

Keywords: Sepsis, Septic shock, Prevalence, Length of stay.

Introduction

Sepsis is a life-threatening organ dysfunction induced by a dysregulated host response to infection (1). It is a heterogeneous disease in which multiple severe symptoms may develop rapidly and can progress into septic shock, which is characterized by hypotension, poor perfusion and the need for vasopressors (2-4). Sepsis affected 48.9 million patients worldwide in 2017 (5). Globally, it affected 29.5% of patients who were admitted to intensive care units (ICUs) (6).

In 2016, there were 1,498 cases of sepsis per 100,000 persons among a sample of hospitalized patients in the United States of America (USA) (7). A meta-analysis showed that the pooled incidence of sepsis was 189 hospital-treated sepsis cases per 100,000 person-years, with a mortality rate of 26.7%. More precisely, the incidence of sepsis was 58 per 100,000 person-years, and their in-hospital mortality rate was 41.9% (8). In 2017, it was estimated that sepsis was responsible for 11.0 million deaths globally (5), most commonly in middle and low-income countries (9). It was found that the percentages of in-hospital mortality of adult patients in US hospitals with severe sepsis and septic shock were 14.9% and 34.2%, respectively (10). Moreover, the in-hospital mortality rate was 17% among patients with severe sepsis and septic shock in an ICU in Spain (n= 1136) (11).

In Jordan, few retrospective studies have reviewed the epidemiology and clinical features of neonatal sepsis (12-14). Data on sepsis/ septic shock prevalence and clinical outcomes among adults in Jordan is lacking. In 2020, the World Health Organization (WHO) called for improved research evidence on epidemiological information and sepsis burdens, especially in

middle- and low-income countries (15). One study from Jordan addressed sepsis in the adult population and showed that the total cost of pharmacological drugs prescribed to Jordanian cancer patients with severe sepsis and septic shock in one year was over 291,030 Euros (16). This study aimed to describe the prevalence rates of sepsis and septic shock and the length of stay (LOS) among critically ill adult patients at two tertiary hospitals in Jordan.

Materials and Methods

A cross-sectional design was used to collect data from two tertiary hospitals in Jordan. The first hospital has a capacity of 582 beds and four adult ICUs. The four adult ICUs admit sepsis/ septic shock patients and thus were included in the study. These ICUs were: the main medical ICU (24 beds), two surgical ICUs (18 beds) and one post-intervention ICU (7 beds mixed-type unit with medical and surgical cases). The second hospital has 651 beds, and seven adult ICUs with a total of 120 beds. The two ICUs that admit sepsis/ septic shock patients were selected: the general surgical ICU (12 beds) and the medical ICU (16 beds). Data were collected in the period between 13 February 2019 and 2 June 2019.

The data collection instrument consisted of two parts. The first part of the instrument was a flowchart for screening patients with sepsis/ septic shock, which was adapted from the study of the International Taskforce (Sepsis-3) (1). This flowchart was composed of two parts: the first was used to differentiate between patients with sepsis and patients with septic shock. Patients who had a SOFA score ≥ 2 with documented or suspected infection were considered to have sepsis. Those who required vasopressors to keep mean arterial pressure (MAP) ≥ 65 mmHg and serum lactate level ≥ 2 mmol/L were considered to have septic shock. However, if the serum lactate level was not available, the following criteria were used to diagnose septic shock: having hypotension, characterized by systolic arterial pressure < 90 mmHg, MAP < 60 mmHg, or a "*reduction in systolic blood pressure of more than 40 mmHg from baseline, despite adequate volume resuscitation, in the absence of other cause of hypotension*" (17). Apart from septic shock, all causes of hypotension were excluded. The assessment of patients was carried out on admission and during each shift. The second part of the flowchart was the SOFA criteria. The second part of the instrument assessed the patients' socio-demographic and clinical variables. This study was approved by the Institutional Review Board (IRB) at both hospitals. Participation was based on informed consent, and patients' anonymity and confidentiality were maintained.

Statistical Analysis

Descriptive statistics were used to describe sample characteristics and clinical variables. A Chi-square test was performed, and other descriptive statistics were obtained to determine the prevalence of sepsis/ septic shock. Moreover, an independent sample t-test was performed to test the different LOS rates in hospitals and ICUs among the two groups of patients.

Table 1. Socio-demographic and Clinical Characteristics of the Patients

Characteristic	All patients (n=914)	Patients without Sepsis/ SS (n=762)	Patients with Sepsis/ SS (n=152)	p
Hospital Settings, n (%)				
Hospital 1	489 (53.5)	414 (54.3)	75 (49.3)	.26
Hospital 2	425 (46.5)	348 (45.7)	77 (50.7)	
ICU Type, n (%)				
Medical	412 (45.1)	337 (44.2)	75 (49.3)	<.001
Surgical	414 (45.3)	370 (48.6)	44 (28.9)	
Mix	88 (9.6)	55 (7.2)	33 (21.7)	
Gender, n (%)				
Male	491 (53.7)	422 (55.4)	69 (45.4)	.02
Female	423 (46.3)	340 (44.6)	83 (54.6)	
Age in years, mean (SD)	58.0 (19.9)	56.5 (20.0)	65.9 (17.8)	<.001

SD, standard deviation; SS, septic shock; ICU, intensive care unit

Table 2. Clinical Characteristics of Patients with Sepsis/Septic Shock at the Time of Enrollment, (n=152)

Characteristic	n (%)
Where was the patient when sepsis/SS was first suspected?	
Emergency department	87 (57.2)
Hospital ward	65 (42.8)
Have a urinary catheter (Foley's catheter)	54 (35.5)
Have a central venous catheter	20 (13.2)
Mechanical ventilation	17 (11.2)
Suspected Sepsis Source (infection focus):	
Respiratory	64 (42.1)
Urinary	26 (17.1)
Skin/Soft Tissue/Wound	23 (15.1)
Abdominal	14 (9.2)
CNS	10 (6.6)
Unknown/Not identified	10 (6.6)
Blood Stream	2 (1.3)
Multiple Sites	2 (1.3)
Bone/Joints	1 (0.7)

SS, septic shock; CNS, central nervous system; ICU, intensive care unit

Results

The study sample consisted of all the 914 patients admitted to the six adult ICUs at both hospital settings during data collection. Patients who were 18 years or older were included; 489 (53.5%) in hospital one, and 425 (46.5%) in hospital two. Initially, a total of 914 patients were screened and 183 patients were suspected of having sepsis. Sepsis/ septic shock was confirmed in 152 (16.6%) patients; 78 (51.3%) patients had only sepsis and 74 (48.7%) patients had septic shock only. Compared to patients without sepsis/ septic shock, patients with sepsis/ septic shock were older and there were more females than males (see Table 1). The respiratory system was the primary infection site in 64 (42.1%) patients with sepsis/ septic shock. Table 2 presents the socio-demographic and clinical characteristics of patients with sepsis/ septic shock.

Table 3. SOFA Score for Different Organ of Patients with Sepsis/ Septic Shock (n=152)

SOFA Score for Different Organ Systems	n (%)
SOFA Score for Respiration	
PaO2/FiO2 ≥ 400 mmHg	15 (10.0)
PaO2/FiO2 < 400 mmHg	19 (12.7)
PaO2/FiO2 < 300 mmHg	49 (32.7)
PaO2/FiO2 < 200 mmHg with respiratory support	49 (32.7)
PaO2/FiO2 < 100 mmHg with respiratory support	18 (12.0)
SOFA Score for Coagulation (Platelet count)	
≥150000/µL	107 (70.4)
< 150000/µL	23 (15.1)
< 100000/µL	14 (9.2)
< 50000/µL	6 (3.9)
< 20000/µL	2 (1.3)
SOFA Score for Liver (Bilirubin Level)	
< (1.2 mg/dL or 20µmol/L)	102 (67.1)
= (1.2-1.9 mg/dL or 20-32 µmol/L)	23 (15.1)
= (2-5.9 mg/dL or 33-101µmol/L)	14 (9.2)
= (6-11.9 mg/dL or 102-204µmol/L)	1 (0.7)
> (12 mg/dL or 204µmol/L)	5 (3.3)
Not performed	7 (4.6)
SOFA Score for the Cardiovascular System	
MAP ≥ 70 mmHg	72 (47.4)
MAP < 70 mmHg	12 (7.9)
Dopamine < 5 µg/kg/min or Dobutamine (any dose)	3 (2.0)
Dopamine 5.1-15 µg/kg/min or Epinephrine ≤0.1 µg/kg/min or Norepinephrine ≤ 0.1 µg/kg/min.	38 (25.0)
Dopamine > 15 µg/kg/min or Epinephrine >0.1 µg/kg/min or Norepinephrine > 0.1 µg/kg/min	27 (17.8)
GCS	
15	57 (37.5)
13-14	33 (21.7)
10-12	20 (13.2)
6-9	30 (19.7)
<6	12 (7.9)
Serum creatinine result	
< (1.2 mg/dL or 110 µmol/L)	59 (38.8)
= (1.2-1.9 mg/dL or 110-170 µmol/L)	36 (23.7)
= (2-3.4 mg/dL or 171-299 µmol/L)	36 (23.7)
= (3.5-4.9 mg/dL or 300-440 µmol/L)	15(9.9)
> (5 mg/dL or 440µmol/L)	6 (3.9)
Urine output	
> 500 mL/day	128 (84.2)
< 500 and ≥ 200 mL/day	10 (6.6)
< 200 mL/day	14 (9.2)

SOFA, sequential organ failure assessment; PaO2, partial pressure of oxygen; FiO2, fraction of inspired oxygen; MAP, mean arterial pressure; GCS, Glasgow coma score.

The results also showed that only 43 (36.4%) blood cultures were positive (93.5% bacteria and 6.5% fungi), and 46 (38.0%) patients had positive urine cultures (63.9% bacteria, 27.7% fungi, and 8.5% mixed-bacterial growth). In addition, 31 (55.4%) patients had positive sputum culture (63.6% bacteria, 24.2% fungi, and 12.2% mixed-bacterial growth including candida species).

The mean SOFA score was 7.6 ± 3.8 (range = 2.0 – 18.0). Specifically, the mean SOFA scores among patients with sepsis and patients with septic shock were 5.3 ± 2.5 (range= 2.0 – 13.0) and 10.1 ± 3.4 (range = 3.0-18.0), respectively (p <.001). The SOFA scores showed that 90% of patients with sepsis/ septic shock had an abnormal ratio of partial pressure of oxygen (PaO2)/ fraction of inspired oxygen (FiO2) that was less than 400, and 70.4% of the patients with sepsis/septic shock had normal platelet count ≥150000 per microliter (see Table 3).

Independent sample t-test analysis showed that the mean hospital LOS of patients with sepsis/ septic shock was 21.4 days, compared to 10.5 days for patients without sepsis/ septic shock [t(178.99)= - 5.9, p <.001]. The mean ICU LOS of the patients with sepsis/ septic shock was 11.1 days and for the patients without sepsis/ septic shock was 4.4 days [t(195.35) =-6.9, p <.001].

Discussion

The results of this study showed that the total three-month period prevalence of sepsis and septic shock was 16.6% (48.7% developed sepsis and 51.3% had SS). The SOFA score of patients with septic shock was higher than patients with sepsis. Both the mean hospital and ICU length of stay of patients with sepsis/ septic shock were approximately twice of patients without sepsis/septic shock.

The present study's findings showed the overall period-prevalence rate of sepsis and septic shock together was 16.6%. This prevalence rate was comparable to the prevalence rate of sepsis and septic shock at adult ICUs in Saudi Arabia, which was 15% (18). It was also comparable to the point-prevalence rate of 17.9 % of severe sepsis and septic shock in adult ICUs in Germany (19). However, due to the limited settings of the present study and using a different screening approach for sepsis and septic shock, the prevalence rate of sepsis and septic shock was lower than the previously reported rate of 37.3% of severe sepsis and septic shock in adult ICUs in China (20), the prevalence rate of 30.8% of severe sepsis and septic shock in 132 medical and surgical ICUs in Turkey (21), and the prevalence rate of 29.5% of sepsis among adult patients admitted to 730 ICUs in 84 countries (6).

The respiratory system was the most common site of infection among patients with sepsis/ septic shock. This might be because the majority of patients had medical illnesses, rather than surgical illnesses. This finding was supported by Baykara et al. (21) and Silva et al. (22). Furthermore, the urinary system was the second-most common site of infection among patients with sepsis/ septic shock. Different research studies in the literature were conducted in various hospitals around the world and enrolled patients with different illnesses and comorbidities, which might explain the variance in clinical characteristics among patients from different studies. For example, most of the patients of the current study had medical illnesses rather than surgical illnesses, which made urinary tract infections more prevalent than abdominal infections, which are common among patients who undergo abdominal surgery. This finding of the current study contradicts the findings of previous research studies, which indicated that the abdomen was the second-most common site of infection among adult patients admitted to ICUs with sepsis/ septic shock (22-24).

The mean SOFA score of adult patients with sepsis/ septic shock was 7.6, confirming that patients with sepsis/ septic shock had

multiple organ failure. This finding was comparable to the mean SOFA score of 7.5 (range=5.0-10.0) among adult patients with severe sepsis/ septic shock who were admitted to 22 ICUs in China (20). Nevertheless, there is a difference between this score and the SOFA scores reported in the literature, which could be attributed to enrolling patients with different health characteristics. For example, the score was slightly less than the mean SOFA score of 9.16 ± 3.16 among adult patients with sepsis/ septic shock in an ICU in Turkey (25).

Sepsis progressed into septic shock among approximately half of the patients. This finding represents a midway between the results of the previous studies. It may have occurred because patients with a wide variety of medical and surgical conditions were enrolled in the current study and the practices of treating patients with sepsis can differ from one setting to another. The finding of the current study was broadly consistent with data from Japan (45.2%) (23), but lower than what had been reported in Pakistan (59.3%) (26) and double the number reported in Italian ICUs (22.5%) (27).

The findings showed significantly longer hospital LOS among patients with sepsis/ septic shock than patients without sepsis/ septic shock. It was reported that patients with sepsis who stayed for a long period inside hospitals might develop conditions other than sepsis alone, which increased the risk of mortality (28). In addition, it was shown that patients who survive sepsis might develop functional and cognitive disabilities, and be prone to recurrent readmission and long-term use of healthcare resources, which together could increase healthcare costs (29). The findings of the current study were comparable to the findings of the SepNet Critical Care Trials Group in 133 ICUs in Germany (19), who reported longer hospital LOS among sepsis/ septic shock patients. Consistent with this are the findings reported from Japan by Ogura et al. (23). Furthermore, the mean hospital LOS of the patients without sepsis/ septic shock was comparable to the mean hospital LOS of 13 days among patients without severe sepsis/ septic shock in 133 ICUs in Germany (19).

The findings of the current study showed a significant difference in the mean ICU LOS between patients with sepsis/ septic shock (11.1 days) and patients without sepsis/ septic shock (4.4 days). This finding was expected because septic shock is a complicated state of sepsis. The finding was comparable to the mean ICU LOS of patients with severe sepsis, which was ten days (range=6.0-19.0) (30) and 10.3 days among patients with sepsis (31). However, it was inconsistent with the median ICU LOS of 6.4 days (SD=8.8) among patients with sepsis in the USA (32). Patients enrolled in the current study tended to have other comorbidities and complications besides sepsis, which might lead to increasing their LOS.

This study's limitations include the relatively small number of patients and the diversity of ICUs studied. It included medical and surgical patients. Also, the serum lactate level was not performed on all patients and an alternative definition of septic shock was used. Additional studies are needed to further understand sepsis/ septic shock among adult patients in all ICUs in the Jordanian healthcare context. Moreover, nurses and physicians working in ICUs need to focus on improving the sepsis screening and outcomes of patients with sepsis/ septic shock.

Conclusion

The overall prevalence of sepsis and SS in Jordan is consistent with the previously reported numbers in the world, with half of the patients going into SS. The presence of sepsis and SS resulted in prolonged ICU and hospital LOS. Moreover, the SOFA score was higher among patients with SS than patients with sepsis.

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AUTHOR CONTRIBUTIONS:

Concept: SAO; **Design:** JAA; **Supervision:** JAA; **Resources:** BK; **Materials:** BK; **Data Collection and/or Processing:** SAO, SMA; **Analysis and/or Interpretation**: SAO; **Literature Search:** SAO; **Writing Manuscript**: SAO, BK, JAA, SMA; **Critical Review:** JAA, BK.

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Informed Consent: From the patients and from the closest relatives of patients who were unable to give consents.

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References

1. Singer M, Deutschman C, Seymour C, et al. The third international consensus definitions for sepsis and septic shock (Sepsis-3). Jama 2016;315(8):801-10. doi: 10.1001/jama.2016.0287.
2. Neviere R, Parsons P, Finlay G. Sepsis syndromes in adults: Epidemiology, definitions, clinical presentation, diagnosis, and prognosis. UpToDate. Wolters Kluwer; 2020 Accessed 11 February 2020.
3. Rebeaud F. Timely Identification of Sepsis. Retrieved from: https://www.mlo-online.com/diagnostics/biomarkers/article/13009232/timely-identification-of-sepsis; 2017:26-8. Accessed 14 January 2019.
4. Neviere R. Sepsis syndromes in adults: Epidemiology, definitions, clinical presentation, diagnosis, and prognosis. UpToDate. Wolters Kluwer; 2018. Accessed 11 September 2018.
5. Rudd K, Johnson S, Agesa K, et al. Global, regional, and national sepsis incidence and mortality, 1990–2017: analysis for the Global Burden of Disease Study. The Lancet 2020;395(10219): 200-211. doi: 10.1016/S0140-6736(19)32989-7.
6. Sakr Y, Jaschinski U, Wittebole X, et al. Sepsis in intensive care unit patients: worldwide data from the intensive care over nations audit. Open Forum Infect Dis Oxford University Press US. 2018:ofy313. doi: 10.1093/ofid/ofy313.

7. Kempker AJ, Rudd KE, Wang HE, et al. Sepsis epidemiology across the International Classification of Diseases, to International Classification of Diseases, chasm—a direct application of the Institute for Health Metrics and Evaluation case definition to hospital discharge data. Crit Care Med 2020;48(12):1881-1884.
8. Fleischmann-Struzek C, Mellhammar L, Rose N, et al. Incidence and mortality of hospital-and ICU-treated sepsis: results from an updated and expanded systematic review and meta-analysis. Intensive Care Med 2020;46(8):1552–1562.
9. World Health Organization (WHO). Improving the prevention, diagnosis and clinical management of sepsis. Retrieved from: http://www.who.int/servicedeliverysafety/areas/sepsis/en/; 2017. Accessed 11 December 2018.
10. Paoli C, Reynolds M, Sinha M, et al. Epidemiology and costs of sepsis in the United States: An analysis based on timing of diagnosis and severity level. Crit Care Med 2018;46(12):1889-1897.
11. Azkárate I, Choperena G, Salas E, et al. Epidemiology and prognostic factors in severe sepsis/septic shock: Evolution over six years. Med Intensiva (Engl Ed) 2016;40(1): 18-25.
12. Khassawneh M, Khader Y, Abuqtaish N. Clinical features of neonatal sepsis caused by resistant gram-negative bacteria. Pediatr Int: Official J of the Japan Pediatr Soc 2009;51(3):332-6. doi: 10.1111/j.1442-200X.2008.02767.x.
13. Younis N. Neonatal sepsis in Jordan: bacterial isolates and antibiotic susceptibility patterns. Rawal Med J 2011;36(3):1-16.
14. Yusef D, Shalakhti T, Awad S, et al. Clinical characteristics and epidemiology of sepsis in the neonatal intensive care unit in the era of multi-drug resistant organisms: a retrospective review. Pediatr and Neonatolog 2018;59(1):35-41. doi: 10.1016/j.pedneo.2017.06.001.
15. World Health Organization. WHO calls for global action on sepsis - cause of 1 in 5 deaths worldwide. Retrieved from: https://www.who.int/news/item/08-09-2020-who-calls-for-global-action-on-sepsis---cause-of-1-in-5-deaths-worldwide#:~:text=5%20deaths%20worldwide-,WHO%20calls%20for%20global%20action%20on%20sepsis%20%2D%20cause,1%20in%205%20deaths%20worldwide&text=The%20World%20Health%20Organization's%20first,%2D%20and%20middle%2Dincome%20countries; 2020 Accessed 20 September 2020.
16. Nazer L, Al-Shaer M, Hawari F. Drug utilization pattern and cost for the treatment of severe sepsis and septic shock in critically ill cancer patients. Internatio J of Clin Pharm 2013;35(6):1245-50. doi: 10.1007/s11096-013-9860-2.
17 Levy M, Fink M, Marshall J, et al. 2001 sccm/esicm/accp/ats/sis international sepsis definitions conference. Intensive Care Med 2003;29(4):530-8. doi: 10.1097/01.CCM.0000050454.01978.3B.
18. Baharoon S, Telmesani A, Tamim H, et al. Community-versus nosocomial-acquired severe sepsis and septic shock in patients admitted to a tertiary intensive care in Saudi Arabia, etiology and outcome. J of Infect and Public Health 2015;8(5):418-24. doi: 10.1016/j.jiph.2014.12.003.
19. SepNet Critical Care Trials G. Incidence of severe sepsis and septic shock in German intensive care units: the prospective, multicentre INSEP study. Intensive Care Med 2016;42(12):1980-9. doi: 10.1007/s00134-016-4504-3.
20. 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(9):e107181.
21. Baykara N, Akalin H, Arslantas MK, et al. Epidemiology of sepsis in intensive care units in Turkey: a multicenter, point-prevalence study. Crit Care 2018;22(1):93. doi: 10.1186/s13054-018-2013-1.
22. Silva EP, Duarte Vd, Soares MM, et al. Survival analysis of patients with sepsis in Brazil. Revis da Soc Brasil de Med Tropic 2019;52. http://dx.doi.org/10.1590/0037-8682-0121-2018.
23. Ogura H, Gando S, Saitoh D, et al. Epidemiology of severe sepsis in Japanese intensive care units: a prospective multicenter study. J of Infect and Chemother 2014;20(3):157-62. doi: 10.1016/j.jiac.2013.07.006.
24. Zahorec R, Firment J, Strakova J, et al. Epidemiology of severe sepsis in intensive care units in the Slovak Republic. Infect 2005;33(3):122-8. doi: 10.1007/s15010-005-4019-2
25. Balcan B, Olgun Ş, Torlak F, Sağmen SB, Eryüksel E, Karakurt S. Determination of factors affecting mortality of patients with sepsis in a tertiary intensive care unit. Turk Thorac J. 2015;16(3):128. doi: 10.5152/ttd.2015.4510.
26. Ullah AR, Hussain A, Ali I, et al. A prospective observational study assessing the outcome of Sepsis in intensive care unit of a tertiary care hospital, Peshawar. Pak. J of Med Sci 2016;32(3):688. doi: 10.12669/pjms.323.9978.
27. Agodi A, Barchitta M, Auxilia F, et al. Epidemiology of intensive care unit-acquired sepsis in Italy: results of the SPIN-UTI network. Ann Ig 2018;30(2):15-21. doi: 10.7416/ai.2018.2247.
28. Doerken S, Mandel M, Zingg W, et al. Use of prevalence data to study sepsis incidence and mortality in intensive care units. The Lancet Infect Dis 2018;18(3):252. doi: 10.1016/S1473-3099(18)30081-1.
29. Hajj J, Blaine N, Salavaci J, et al. The "centrality of sepsis": a review on incidence, mortality, and cost of care. Healthcare 2018; 6(3): 90. doi: 10.3390/healthcare6030090.
30. Grozdanovski K, Milenkovikj Z, Demiri I, et al. Epidemiology of community-acquired sepsis in adult patients: a six year observational study. Prilozi 2018;39(1):59-66. https://doi.org/10.2478/prilozi-2018-0024.
31. Fernando S, Reardon P, Van Katwyk S, et al. Outcomes and Costs of Patients with Sepsis Transferred to a Tertiary Care Intensive Care Unit. Crit Care Med 2018;46(1):690. doi: 10.1097/01.ccm.0000529415.77199.43.
32. Rhee C, Dantes R, Epstein L, et al. Incidence and trends of sepsis in US hospitals using clinical vs claims data, 2009-2014. Jama 2017;318(13):1241-9. doi: 10.1001/jama.2017.13836.