CASE REPORT

The Journal of Palembang Nursing Studies
https://jpns-journal.com/index.php/jpns
OPEN ACCESS

One-hour sepsis bundle in patients with sepsis shock: A case report of nursing care implementation

Dian Rahmawati [1*]
Denissa Faradita Aryani [2]

[1] Faculty of Nursing, University of Indonesia, Depok, Indonesia
[2] Department of Surgical Nursing, Faculty of Nursing, University of Indonesia, Depok, Indonesia

***Correspondence**:
Dian Rahmawati
Faculty of Nursing, University of Indonesia, Jl. Prof. Dr. Bahder Djohan, Depok, West Java-16424, Indonesia.
Email: dian.rahmawati01@ui.ac.id

Volume 3(2), 109-116

http://dx.doi.org/10.55048/jpns122

e-ISSN 2827-8100
p-ISSN 2827-8496

Received : December 12, 2023
Revised : December 24, 2023
Accepted : April 21, 2024
Published: May 10, 2024

ABSTRACT

Background: Sepsis shock is a critical stage of sepsis characterized by impaired organ function and life-threatening consequences. Optimal management of sepsis shock necessitates a collaborative approach involving an interprofessional team inclusive of Intensive Care Unit (ICU) nurses. Prompt and accurate recognition of its clinical presentation is paramount for critical care nurses to ensure timely and effective intervention.
Objective: This case report aims to elucidate the nursing care analysis of sepsis shock patients through the application of the one-hour sepsis bundle.
Case: This case study revolves around a 69-year-old female admitted to the ICU due to sepsis shock secondary to pleural effusion and lung tumor. The patient exhibited hallmark indicators of sepsis shock, including hypotension necessitating vasoconstrictive support, fever peaking at 38.8°C, leukocytosis at 36.91 x 10^3/µL, elevated lactate levels at 2.7 mmol/L, and inadequate peripheral perfusion. Nursing diagnosis predominantly focused on assessing the risk of shock in the presence of sepsis and hypotension. The patient underwent immediate implementation of the one-hour sepsis bundle, commencing from the emergency room through ICU admission. Nursing interventions encompassed sepsis screening, continuous hemodynamic monitoring, fluid balance assessment, vigilance in maintaining airway patency, and meticulous infection control measures.
Conclusion: Subsequent to fluid resuscitation and initiation of inotropic and vasopressor support, notable improvements in hemodynamics were observed. However, persistent elevation in lactate levels underscored metabolic dysfunction, necessitating sustained vasopressor support beyond the seventh day of treatment due to refractory shock and multi-organ failure. The adoption of the one-hour sepsis bundle emerges as a recommended guideline for nursing management in sepsis shock patients.

Keywords: sepsis shock; critical care nurse; management; one-hour sepsis bundle

Rahmawati, D., & Aryani, D. F. (2024). One-hour sepsis bundle in patients with sepsis shock: A case report of nursing care implementation. *The Journal of Palembang Nursing Studies. 3*(2), 109-116. http://dx.doi.org/10.55048/jpns122

Nursing and Healthcare Practices

- *Nurse is responsible for monitoring the patient's response to organ support measures, early identification of sepsis and initiation of sepsis protocols. Supportive care interventions should be started within 1 hour of suspected sepsis.*
- *The impact of nurse-led multi professional team-based care in decreasing mortality, ICU length of stay and ICU readmission rates*
- *The fast communication of critical patient assessment findings should be prioritized by nurses to appropriate multidsciplinary teams for proper management.*

INTRODUCTION

Sepsis shock is characterized as an advanced stage of sepsis featuring impaired organ function, triggered by the body's response to infection, and accompanied by circulatory, cellular, and metabolic disturbances that pose life-threatening risks (Singer et al., 2016). Approximately 15% of sepsis patients progress to sepsis shock, with 10% requiring ICU admission and facing a mortality rate exceeding 50% (Dugar et al., 2020). Patients exhibiting signs and symptoms indicative of inadequate peripheral tissue perfusion, such as persistent hypotension and tachycardia, are at risk of shock and often necessitate intensive care unit (ICU) management. Untreated shock risks compromised blood flow to body tissues and subsequent multi-organ failure (Nduka & Parrillo, 2011).

The 2018 Surviving Sepsis Campaign (SSC) guidelines introduced a One-Hour sepsis bundle due to the association of a three-hour delay with a significant rise in hospital mortality (Evans et al., 2021). While this protocol is standard practice, the nurse's comprehension of the patient's condition is equally critical. Nurses must delve deeper into comorbidity information and pertinent actions to assist healthcare providers in adjusting treatment plans appropriately and conducting subsequent assessments to gauge patient response (Gripp et al., 2021). Critical care nurses must promptly recognize early signs of sepsis and identify patients at high risk of mortality. Upon suspecting severe sepsis, nurses should administer the qSOFA test (Quick Sequential Organ Failure Assessment). A positive score of two or more prompts the critical nurse to notify the attending physician for patient assessment and initiation of sepsis bundle protocols. Implementation of the one-hour sepsis bundle includes measuring lactate levels, repeating measurements if initial levels exceed 2 mmol/L, obtaining blood cultures before antibiotic administration, administering broad-spectrum antibiotics, initiating rapid fluid resuscitation for hypotension, and administering vasopressors if the patient remains hypotensive (Gripp et al., 2021).

Effective management of sepsis and sepsis shock relies on true team-based care. Adequate staffing, appropriate personnel, and a collaborative environment where nurses are regarded as equal partners are essential for reducing mortality rates associated with this critical condition. Therefore, nurses play a pivotal role in implementing the one-hour sepsis bundle. This case report aims to elucidate the nursing care analysis of sepsis shock patients through the application of the one-hour sepsis bundle.

CASE

A 69-year-old female presented with a medical diagnosis of sepsis shock secondary to massive pleural effusion with a right lung tumor classified as T4 N2 M1B (hepar, pleural effusion) St-IV, accompanied by delirium, suspected metabolic encephalopathy, differential diagnosis of intracranial syndrome, suspected paraneoplastic syndrome, and clinical pulmonary tuberculosis. Since July 2023, the patient reported experiencing shortness of breath, prompting hospital admission. A chest radiograph revealed right pleural effusion, followed by pleural puncture and suspicion of tuberculosis (TB). The patient commenced TB treatment, but symptoms persisted, leading to a CT scan on July 1, 2023, which suggested the presence of a mass, prompting further investigation via bronchoscopy.

Additional complaints included dry cough, absence of fever and rhinorrhea, and abdominal pain. Past medical history included hypertension (positive), asthma (negative), clinical tuberculosis (positive) treated with drugs, and cardiac ablation in 2019. Family

Rahmawati, D., & Aryani, D. F. (2024). One-hour sepsis bundle in patients with sepsis shock: A case report of nursing care implementation. *The Journal of Palembang Nursing Studies. 3*(2), 109-116. http://dx.doi.org/10.55048/jpns122

Table 1. Monitoring hemodynamic

Parameter	Time						
	17:00	17:05	17:15	17:30	17:35	17:40	17:45
Systolic	71	71	70	72	77	82	86
Diastolic	53	49	49	54	57	57	65
MAP	59	56	56	60	64	65	72
HR	99	109	108	105	100	99	96
RR	35	34	30	32	30	28	29
SpO2 (%)	92	96	97	95	95	96	97
Temperature (°C)	35.6					35.9	
Oxygen Support	Room Air	NC 5 Lpm	NC 5 Lpm	NC 5 Lpm	NC 5 Lpm	NC 5 Lpm	NC 5 Lpm
Note	Patient arrived at ER			Fluid resuscitation			

MAP (Mean Arterial Pressure), HR (Heart Rate), RR (Respiratory Rate), SpO2 (Oxygen Saturation), Temp (Temperature), NC (Nasal Cannula), Lpm (Liter per minute).

Table 2. Monitoring hemodynamic after supporting inotropic

Parameter	Time				
	18:00	19:00	20:00	20:30	21:00
Systolic	92	97	99	99	101
Diastolic	50	56	58	48	50
MAP	64	68	67	65	67
HR	98	82	76	79	83
RR	28	29	32	30	29
SpO2 (%)	96	97	96	97	97
Temperature (°C)	35.9			36	36
Oxygen Support	NC 5 Lpm	NC 5 Lpm	NC 5 Lpm	NC 5 Lpm	NC 5 Lpm
Note	Start norephinephrine 0.5 mcg/Kg/minutes				

MAP (Mean Arterial Pressure), HR (Heart Rate), RR (Respiratory Rate), SpO2 (Oxygen Saturation), Temp (Temperature), NC (Nasal Cannula), Lpm (Liter per minute).

Table 3. Laboratory result parameter of sepsis

Parameter	Date							Note
	24/09	27/09	29/09	30/09	01/10	02/10	03/10	
Leucocyte (4-10) 10^3/µL	23.7	36.91	33.71	23.45	24.24	23.41	13.9	High
Lactate (1-2 mmol/L)	2.0	2.7						High

history indicated the patient's sister passed away three years prior due to breast cancer. The patient, a former textile factory worker, was currently a housewife, while her husband smoked.

The initial assessment of the patient revealed a Quick Sequential Organ Failure Assessment (qSOFA) score of 3, meeting criteria with a respiratory rate of 35 breaths per minute, Glasgow Coma Scale (GCS) of 13, and blood pressure of 71 mmHg. Subsequent laboratory evaluations encompassed various organ systems to determine the Sequential Organ Failure Assessment (SOFA) score. The respiratory component scored 0 due to a PaO2/FiO2 ratio exceeding 400 (692), while the coagulation component also scored 0 with a platelet count of 237 x 10^3/µL. Liver function was assessed through SGOT and SGPT levels, with SGOT values at 85 U/L (normal range: 5-34) and SGPT at 30 U/L (normal range: 0-55). The cardiovascular section scored 4 due to hypotension requiring norepinephrine support at 0.5 mcg/KgBB/minute, while the level of consciousness scored 1 with a GCS of 13. Renal function, however, scored 0 as creatinine levels did not improve. The total SOFA score was 5, excluding bilirubin function assessment.

The patient received treatment in the emergency room for approximately 3 days, during which hemodynamic monitoring was conducted, with norepinephrine support administered at 0.5 mcg/KgBB/minute. On September 27, 2023, the patient underwent bronchoscopy at 1:30 p.m. Prior to the procedure, laboratory examinations for PT and APTT were performed, along with a transfusion of 300 mL of fresh frozen plasma (FFP). Preoperative preparation was overseen by an Anesthesiologist with ASA II status. Post-procedure, the patient was transferred to the ICU and, if necessary, received water seal drainage (WSD) and intubation with mechanical ventilation support.

The patient was admitted to the ICU on September 27, 2023, intubated from the operating room and equipped with water seal drainage (WSD). The admission to the ICU was categorized as priority 1, meeting criteria for critical patients with unstable hemodynamics requiring intensive therapy such as ventilatory support/assistance, infusion of vasoactive and continuous drugs, and post-surgical care. Upon arrival at the ICU, the patient exhibited cold extremities, cold sweat, a capillary refill time (CRT) of 2 seconds, and a feverish body temperature ranging from 37-38.8°C. The patient was breathing with mechanical ventilation support and receiving norepinephrine support at 0.7 mcg/KgBB/minute. Subsequently, laboratory examinations including full blood count, electrolytes, urea, creatinine, albumin, lactate, and thoracic X-rays were conducted, along with repeat blood culture sampling.

On the second day of ICU treatment, September 28, 2023, the patient's hemodynamic status remained unstable, prompting the addition of vasopressin therapy at 0.03 units/minute. Cold extremities and cold sweat persisted, with a CRT of 2 seconds. Additionally, edema was noted in both extremities, prompting the initiation of furosemide at 1 mg/hour. Furthermore, antibiotic therapy was escalated, with Cefepime administered at 2 grams three times daily.

From the third to the seventh day of treatment, sepsis shock management and hemodynamic monitoring were conducted while the patient remained in the ICU. However, the final evaluation of patient care on October 3, 2023, revealed a deteriorating condition. Despite receiving final support with Norepinephrine at 2 mcg/KgBB/min, Vasopressor at 0.03 units/minute, and Dobutamine at 10 mcg/KgBB/min, the patient's blood pressure did not improve and tended to decrease. On October 3, 2023, the morning assessment indicated a systolic blood pressure range of 67-97 mmHg, diastolic range of 28-52 mmHg, mean arterial pressure (MAP) of 36-54 mmHg, pulse pressure of 18-26 mmHg, and heart rate (HR) of 129-134 beats per minute. The patient exhibited cold extremities, weakening peripheral pulses, irregular heart rhythm, and hyperthermia with a fever temperature reaching 39.9°C. Regrettably, the patient was declared deceased on October 3, 2023, and nursing interventions were ceased.

The nursing diagnosis primarily focused on the risk of shock with associated risk factors for sepsis and hypotension. Ineffective peripheral perfusion was identified as a sign of decreased blood circulation at the capillary level, potentially disrupting the body's metabolism. Throughout the study, the patient exhibited somnolence, with notable findings including cold extremities, weak peripheral pulses, cyanosis in the toes, pale skin color, decreased skin turgor, and narrowed pulse pressure of 18 mmHg. Laboratory results upon admission on

September 24, 2023, indicated an increased leukocyte count of 22.04 x 10^3/µL, platelets at 237 x 10^3/µL, and a hemostatic imbalance reflected in elevated APTT values compared to control levels. Specifically, Prothrombin Time (PT) was 3.3 seconds (control: 9.8 - 12.6 seconds), while APTT was 38.6 seconds (control: 21.8 - 28 seconds).

The implementation of the one-hour sepsis bundle commences in the emergency room. Upon the patient's arrival at 5:05 p.m, the nurse positions the patient in semi-Fowler position, ensures airway patency, and sets up bedside monitors for measuring blood pressure, respiratory rate, heart rate, and oxygen saturation. Initial oxygen saturation is recorded at 91-92% with room air, prompting the nurse to administer oxygen at a rate of 6 liters per minute, resulting in a rise in saturation to 95-97%. Blood pressure readings indicate hypotension with a systolic/diastolic measurement of 71/49 mmHg, accompanied by peripheral acral coldness, pallor, weak peripheral pulses, and delirium awareness. The nurse collaborates with the doctor to establish peripheral vein access, with a 20G catheter inserted into the right cubital vein using aseptic technique. Arterial blood gas and lactic acid samples are obtained. The insertion of the catheter proceeds smoothly, facilitating the administration of fluid resuscitation with 0.9% NaCl solution, initially at a rate of 250 mL over 10 minutes, followed by the remaining 250 mL over the subsequent hour, starting at 5:30 p.m.

Hemodynamic monitoring is conducted every 5 minutes during the first 15 minutes of fluid administration, revealing a gradual improvement. However, the mean arterial pressure (MAP) fails to reach 65 mmHg during the subsequent 15-minute period. Consequently, the nurse, in collaboration with the doctor, inserts a 20G venous catheter into the left cubital vein and initiates norepinephrine therapy at a starting dose of 0.5 mcg/KgBB/minute due to the inadequate response to fluid resuscitation for 30 minutes (see Table 1). Subsequently, a urinary catheter is inserted to monitor urine output, which is observed to be yellow. At 8 p.m., lactate levels are measured at 2.0 mmol/L, prompting the nurse and doctor to conduct comprehensive blood tests, electrolyte assessments, urea, creatinine measurements, blood cultures, and thoracic X-rays. At 9 p.m., the doctor prescribes levofloxacin 750 mg, which the nurse administers at 10 p.m. Urine output is monitored by nursing staff, with a diuresis rate of 0.5 mL/KgBB/hour.

DISCUSSION

Risk factors contributing to the development of lung tumors include gender differences, particularly in non-smoking women, who are susceptible to low transversion EGFR mutations due to genetic and environmental factors such as exposure to cigarette smoke and carcinogenic environments, leading to oxidative DNA damage and an increase in DNA and EGFR mutations, thus promoting the growth and spread of malignant cells and tumors (Agalioti et al., 2015).

Tumor metastasis to the pleural cavity can result in pleural effusion, characterized by a massive accumulation of fluid in the pleural space. The clinical presentation of pleural effusion varies depending on the quantity of fluid and the underlying cause. The significant fluid accumulation predisposes to bacterial colonization, potentially triggering infections, with common complications including pneumonia, sepsis, and pleural sepsis, the latter of which can progress to sepsis shock (Gayen, 2022).

In cases of sepsis shock, nursing diagnosis primarily focuses on the risk of shock, considering factors associated with sepsis and hypotension. Ineffective peripheral perfusion indicates compromised blood circulation at the capillary level, leading to metabolic disruptions. Vascular leakage and excessive arterial dilation contribute to reduced vascular resistance, leading to decreased blood pressure and compromised perfusion and distribution of blood to organs and tissues, culminating in distributive shock (Wilhelms et al., 2020).

One common form of distributive shock is sepsis shock, resulting from blood vessel leakage and bacterial invasion. Pathogens within the bloodstream possess lipoprotein molecules that damage vascular endothelial cells, triggering the release of vasodilators like nitric oxide and activating complement proteins, which stimulate histamine release from mast cells. This cascade activates immune cells, including macrophages and neutrophils, leading to the production of pro-inflammatory cytokines like tumor necrosis factor and IL-1. While these cytokines aid in immune defense, they also exacerbate endothelial cell damage, leading to increased vascular permeability and vasodilation, resulting in vascular fragility and leakage (Wiewel et al., 2016).

Early evaluation of patients suspected of infection involves assessing several criteria, including a respiratory rate ≥ 22 times per minute, systolic blood pressure ≤ 100 mmHg, and alterations in consciousness status. A qSOFA score exceeding 2 warrants further assessment of the SOFA score (Dugar et al., 2020). Elevated lactate levels in laboratory tests indicate hypoperfusion, which can lead to anaerobic metabolism and metabolic acidosis (Evans et al., 2021).

Fluid resuscitation plays a crucial role in stabilizing tissue hypoperfusion in sepsis shock. Administering crystalloid fluids aims to achieve early resuscitation and replenish intravascular volume in patients with sepsis shock, with nursing vigilance to ensure effective tissue perfusion (Rababa et al., 2022). Patients may require additional fluids following initial resuscitation, with maintenance fluids administered over 24 hours, and nurses monitor fluid intake and output to mitigate the risk of fluid overload (Bertoncini et al., 2016).

According to the 2021 Surviving Sepsis Campaign (SSC) guidelines, fluid administration is the primary therapy for resuscitating patients with sepsis or sepsis shock accompanied by hypotension and elevated serum lactate levels. The recommended resuscitation fluid is 30 mL per kilogram of body weight of crystalloid fluid (Evans et al., 2021). However, fluid resuscitation is administered using a challenge test technique, wherein approximately 200-250 mL of crystalloid fluid is infused over 10 minutes, with close monitoring of hemodynamic changes. This approach is warranted, considering the patient's presenting symptoms of dyspnea, diminished breath sounds on the right lung, ronchi sounds on the left lung, and CT scan findings indicative of pleural effusion.

The challenge test technique represents the safest approach to fluid administration when the potential benefits are uncertain. This technique involves administering intravenous fluid boluses under tightly controlled conditions and assessing the patient's hemodynamic response. It aims to strike a balance between the advantages of enhanced oxygen delivery to tissues and the risk of exacerbating edema formation. If no clinical benefit, such as an increase in cardiac output, is observed, fluid administration should cease immediately. Given the potential for deteriorating lung function with excessive fluid administration, adherence to the challenge test protocol is imperative (Jean-Louis et al., 2020).

Patients presenting with elevated blood pressure and lactate levels exceeding 2 mmol/L require prompt administration of vasopressors to maintain tissue perfusion (Evans et al., 2021). Norepinephrine is a first-line inotrope used in sepsis shock, acting as an adrenergic receptor agonist to induce peripheral vasoconstriction, thereby raising blood pressure and peripheral resistance while augmenting tissue blood flow to sustain tissue perfusion (Evans et al., 2021).

Low mean arterial pressure (MAP) is typically indicative of decreased organ perfusion. However, targeting high MAP levels with vasopressors may heighten the risk of atrial fibrillation without improving survival rates in patients with sepsis shock (Evans et al., 2021). Therefore, it is advisable to aim for a MAP target of 65 mmHg during early resuscitation in sepsis shock patients requiring vasopressors (Evans et al., 2021). Following vasopressor administration, hemodynamic parameters in the patient indicate a blood pressure range of 100-112 mmHg, with a MAP exceeding 65 mmHg, and a urine production rate of 1.7 mL/kgBW/hour for 5 hours. Consequently, norepinephrine administration effectively maintains systolic blood pressure and achieves the desired MAP target.

In the management of sepsis and sepsis shock, obtaining screening results for infectious agents through microbiological culture is crucial. Cultures should be examined before initiating continued antimicrobial therapy in patients suspected of sepsis or sepsis shock within 1 hour (Gripp et al., 2021). The patient underwent culture examination within the specified timeframe on 24/09/2023. Antibiotic administration in sepsis shock must be immediate, as delays exceeding 1 hour can elevate the risk of mortality (Gripp et al., 2021). Administration of broad-spectrum antibiotics is strongly recommended prior to culture results, with subsequent adjustment based on microbial identification if available (Evans et al., 2021). The patient received Levofloxacin 750 mg once daily, a third-generation fluoroquinolone antibiotic effective against various bacterial infections, particularly those of respiratory origin, even in the absence of culture confirmation, as evidenced by thoracic x-ray abnormalities and suspected respiratory involvement due to symptoms and clinical history of TB.

Antibiotic therapy was administered for approximately three days, from the emergency room to ICU admission (September 24 to

September 27, 2023). However, the antibiotic regimen proved ineffective, as evidenced by elevated infection markers on September 27, 2023, indicating worsening leukocytosis and lactate levels (Table 3). Subsequently, antibiotic escalation to Cefepime 2 grams thrice daily was initiated following collaborative assessment by the nursing and medical teams. This approach aligns with SSC 2021 guidelines emphasizing antimicrobial stewardship to mitigate antimicrobial resistance by optimizing therapy and narrowing its spectrum based on pathogen identification and susceptibility (Evans et al., 2021).

Nursing evaluation criteria encompass mean arterial pressure (MAP) ≥65 mmHg, central venous pressure (CVP) 8–12 mmHg, central venous oxygen saturation (ScvO2) ≥70% or mixed venous oxygen saturation (SvO2) ≥65%, urine output ≥0.5 ml/kg/hour, peripheral warmth, and improved skin perfusion (Res et al., 2021). Despite maintaining MAP above the target, the patient required inotropic and vasopressor support to achieve hemodynamic stability. Although ScvO2 assessment was not performed, lactate levels served as an indicator of global hypoperfusion. Persistent lactate elevation suggests metabolic failure leading to lactic acidosis, consistent with clinical signs of hypoperfusion necessitating continued inotropic and vasopressor support throughout the treatment period due to refractory shock and multi-organ failure (Woyka et al., 2018).

Although there were delays in nursing implementations due to external factors, adherence to sepsis guidelines facilitated timely management initiation within 3-6 hours despite the 1-hour bundle not being fully achieved. Delays were primarily attributed to logistical challenges in medication procurement, collaborative decision-making with physicians, and administrative processes. Early sepsis identification and protocol initiation, coupled with rapid communication of critical patient assessments, are imperative for prompt multidisciplinary intervention, potentially reducing mortality, ICU length of stay, and readmission rates.

CONCLUSION

Implementation in patients with sepsis shock requires the collaboration of a multidisciplinary team comprising healthcare professionals and nurses. Early assessment, resuscitation, and administration of inotropic therapy are essential for maintaining adequate perfusion pressure. However, the management of the one-hour sepsis bundle in this case proved ineffective due to persistent hypotension, resulting in delays in antibiotic administration in both the emergency room (ER) and ICU. These delays, attributed to processes such as drug procurement, collaborative decision-making with physicians, and hospital management regulations, can have detrimental effects on patients, leading to disrupted organ perfusion and multi-organ damage. Therefore, the implementation of the One Hour Sepsis bundle is recommended as a nursing management guideline for patients with sepsis shock.

Declaration of Interest

The authors declare no conflict of interest.

Acknowledgment

None

Funding

None

Data Availability

The data that support the findings of this study are not publicly available due to privacy restrictions but are available from the corresponding author upon reasonable request.

REFERENCES

Agalioti, T., Giannou, A. D., & Stathopoulos, G. T. (2015). Pleural involvement in lung cancer. *Journal of thoracic disease, 7*(5), 1021–1030. https://doi.org/10.3978/j.issn.2072-1439.2015.04.23

Singer, M., Deutschman, C. S., Seymour, C. W., Shankar-Hari, M., Annane, D., Bauer, M., & Angus, D. C. (2016). The third international consensus definitions for sepsis and septic shock (Sepsis-3). *Jama, 315*(8), 801-810. https:// doi.org/10.1001/jama.2016.0287

Bertoncini, F., Di Massimo, D. S., & Gatta, C. (2016). Sepsis: Implication for nursing. *Italian Journal of Medicine, 10*(4), 360–363. https://doi.org/10.4081/itjm.2016.801

Dugar, S., Choudhary, C., & Duggal, A. (2020). Sepsis and septic shock: Guideline-based management. *Cleveland Clinic Journal of Medicine, 87*(1), 53–64. https://doi.org/10.3949/ccjm.87a.18143

Evans, L., Rhodes, A., Alhazzani, W., Antonelli,

M., Coopersmith, C. M., French, C., Machado, F. R., Mcintyre, L., Ostermann, M., Prescott, H. C., Schorr, C., Simpson, S., Wiersinga, W. J., Alshamsi, F., Angus, D. C., Arabi, Y., Azevedo, L., Beale, R., Beilman, G., Levy, M. (2021). Surviving sepsis campaign: International guidelines for management of sepsis and septic shock 2021. *Intensive Care Medicine, 47*(11), 1181–1247. https://doi.org/10.1007/s00134-021-06506-y

Gayen, S. (2022). Malignant pleural effusion: Presentation, diagnosis, and management. *The American Journal of Medicine, 135*(10). https://doi.org/https://doi.org/10.1016/j.amjmed.2022.04.017

Gripp, L., Raffoul, M., & Milner, K. A. (2021). Implementation of the surviving sepsis campaign one-hour bundle in a short stay unit: A quality improvement project. *Intensive and Critical Care Nursing, 63*, 103004. https://doi.org/10.1016/j.iccn.2020.103004

Ko, B. S., Choi, S. H., Shin, T. G., Kim, K., Jo, Y. H., Ryoo, S. M., & Kim, W. Y. (2021). Impact of 1-hour bundle achievement in septic shock. *Journal of clinical medicine, 10*(3), 527. https://doi.org/10.3390/jcm10030527

Nduka, O. O., & Parrillo, J. E. (2011). The pathophysiology of septic shock. *Critical Care Nursing Clinics of North America, 23*(1), 41–66. https://doi.org/10.1016/j.ccell.2010.12.003

Podder V, S. N. (2022). *Levofloxacine*. National Library of Medicine (StatPearls).

Rababa, M., Bani-Hamad, D., Hayajneh, A. A., & Al Mugheed, K. (2022). Nurses' knowledge, attitudes, practice, and decision-making skills related to sepsis assessment and management. Electronic *Journal of General Medicine, 19*(6). https://doi.org/10.29333/ejgm/12556

Jean-Louis, V., Ferguson, A., Pickkers, P., Jakob, S. M., Jaschinski, U., Almekhlafi, G. A., & Sakr, Y. (2020). The clinical relevance of oliguria in the critically ill patient: analysis of a large observational database. *Critical Care, 24*, 1. https://doi.org/10.1186/s13054-020-02858-x

Wiewel, M. A., Harmon, M. B., van Vught, L. A., Scicluna, B. P., Hoogendijk, A. J., Horn, J., & Wiersinga, W. J. (2016). Risk factors, host response and outcome of hypothermic sepsis. *Critical Care, 20*, 1-9. https://doi.org/10.1186/s13054-016-1510-3

Wilhelms, S. B., Walther, S. M., Sjöberg, F., & De Geer, L. (2020). Causes of late mortality among ICU-treated patients with sepsis. *Acta Anaesthesiologica Scandinavica, 64*(7), 961-966. https://doi.org/10.1111/aas.13592

Woyka, S. (2021). Korelasi kadar ScvO2 dengan skor sequential organ failure assesment (SOFA) pada pasien sepsis di intensive care unit (ICU) RSUD Dr. Moewardi Surakarta. *Majalah Anestesia & Critical Care, 39*(3), 152-158. https://doi.org/10.55497/majanestcricar.v39i3.230