Health Notions
ISSN 2580-4936
Published by
Humanistic Network for Science and Technology

EDITORIAL TEAM

CHIEF EDITOR (VALID FROM JANUARY 1, 2020)

EDITORS (VALID FROM JANUARY 1, 2020)

ADMINISTRATOR (VALIF FROM JANUARY 1, 2020)

"HEALTH NOTIONS" ISSN: 2580-4936 (online version only), published by Humanistic Network for Science and Technology

Cemara street 25, 001/002, Dare, Ds./Kec. Sukorejo, Ponorogo, East Java, Indonesia, 63453

Health Notions
ISSN 2580-4936
Published by
Humanistic Network for Science and Technology

VOL 4, NO 2 (2020)

FEBRUARY

DOI: https://doi.org/10.33846/hn402

FULL ISSUE

View or download the full issue

COVER AND PROFILE

TABLE OF CONTENTS

ORIGINAL RESEARCH

"HEALTH NOTIONS" ISSN: 2580-4936 (online version only), published by Humanistic Network for Science and Technology

Cemara street 25, 001/002, Dare, Ds./Kec. Sukorejo, Ponorogo, East Java, Indonesia, 63453

KEYWORDS
Anger COVID-19 Diabetes Mellitus Hemoglobin Levels of Pregnant Women, Baby Weight, Literature Review Intensity of Labor Pain Keywords: diabetes mellitus, herbs, self-care Labor Pain In The First Stage Lower Extremity Amputation Maternity Nursing Maternity nursing Percutaneous Nephrolithotomy Pregnant Women RSUD Dr. Soetomo Risk Factors Vehicular accident, victim, delivery room, action room, Sayyidah Maryam drinking water refill stain, duration of operation, production capacity, raw water source mass immunization mixed gonadal dysgenesis readiness retrospective

DOI: http://dx.doi.org/10.33846/hn40205
http://heanoti.com/index.php/hn

RESEARCH ARTICLE
URL of this article: http://heanoti.com/index.php/hn/article/view/hn40205

Correlation Between Sepsis Bundle Compliance with Incidence of Acute Kidney Injury and Mortality in Sepsis Adult Patients

Eka Prasetiyawan[1(CA)], Arie Utariani[2], Edward Kusuma[3]
[1(CA)]Resident of Anesthesiology, Faculty of Medicine, Universitas Airlangga / Soetomo General Hospital, Indonesia; eprasetiyawan@gmail.com (Corresponding Author)
[2]Anesthesiologist, Faculty of Medicine. Universitas Airlangga / Soetomo General Hospital
[3]Anesthesiologist, Faculty of Medicine. Universitas Airlangga / Soetomo General Hospital

ABSTRACT

Sepsis is serious medical condition with mortality rate around 25%. Sepsis cause multiorgan failure, including AKI (Acute Kidney Injury). One-hour sepsis bundle compliance is expected to prevent AKI and reduce patient mortality. **Aims:** Analyze the correlation between sepsis bundle compliance with incidence and progression of AKI and mortality in first 48 hours of treatment in the Resuscitation Room (Intensive) of RSUD Dr. Soetomo Surabaya. **Methods:** Observational retrospective study. Total sampling from medical record of adult sepsis patients who treated in Resuscitation/ Intensive Room of RSUD Dr. Soetomo in January - July 2019. Sepsis bundle compliance was assessed in first 1-hour patient was treated, then observed in first 48 hours of treatment, whether there was death or AKI. **Results:** Most of the 1-hour survival bundle sepsis compliance were classified as poor (51.6%) and very poor (26.9%). The highest component was antibiotic administration management (63.4%) and the lowest was fluid resuscitation (8.6%). There is significant correlation between sepsis bundle compliance with AKI incidence in the first 6 hours, p value= 0.048; contingency coefficient 0.280. Cumulatively, there is significant correlation between sepsis bundle compliance with mortality rates sepsis patients under 48 hours, p value: 0.000; contingency coefficient 0.614. There is significant correlation between bundle sepsis compliance to mortality under 6; 12; 42; and 48 hours. **Conclusions:** There is significant correlation between sepsis bundles compliance with AKI incidence in first 6 hours. There is significant correlation between sepsis bundle compliance to the mortality rate of sepsis patients under 48 hours of treatment.

Keywords: compliance; one-hour sepsis bundle; AKI; mortality

INTRODUCTION

Background

Sepsis bundle is the core of the Surviving Sepsis Campaign (SSC) implementation and the basis for improving the quality of sepsis management(1), from its first publication of evidence-based guidelines in 2004 to the recent edition. The bundle component is updated as considered by novel and evolving evidence. The convincing evidence in the literature, which has shown the correlation between sepsis bundle compliance and improvement of survival in patients with sepsis and septic shock, leads to the optimal application of SSC Sepsis bundle. The guidelines state that sepsis patients require immediate assessment and treatment, including initial fluid resuscitation while pursuing source of infection, obtaining further laboratory results, and obtaining more precise measurements of hemodynamic status. The newest Sepsis bundle components in 2018, which are intended to start within the first hour. Consistent with previous publications of the SSC sepsis bundle, "time zero" or "time of presentation" is defined as triage time in the emergency department.(2)

Sepsis is serious medical condition with mortality rate is still around 25%(1) In Resuscitation Room of Dr. Soetomo Hospital Surabaya throughout 2016, there were 60/900 patients who experienced sepsis and require further treatment, from all patients treated in the Resuscitation Room as many as 7197.(3) The death rate due to

sepsis was quite high, fourth out of the ten main causes of death in resuscitation rooms in 2016, as many as 40 out of 795 patients died in 2016.[4]

Sepsis is a clinical syndrome characterized by life-threatening organ dysfunction caused by dysregulation of the body's response to infection.[5] One of the organs that has the potential to experience disorders is the kidney. A previous study mentioned that of 192,980 sepsis patients in the United States, 22% develop AKI.[6] In Indonesia, study in a hospital at Bandung during the 2005-2006 observation, the most common cause of AKI (by dialysis) was sepsis (42%).

Sepsis Associated Acute Kidney Injury (SAAKI) significantly increased mortality fourfold compared with critically ill non-AKI sepsis patients. Although this intervention seems to reduce mortality rates[7], recent research seems to indicate that no further improvement on the severity of Acute Kidney Injury (AKI) is achieved by fulfilling SSC bundles when the protocol is performed.[8] In addition, several studies reported different results in the incidence of SA-AKI when the SSC bundle was conducted, with the implementation and protocol being achieved according to the target.

The purpose of this research is to **a**nalyze the correlation between sepsis bundle compliance with incidence and progression of AKI and mortality in first 48 hours of treatment in the Resuscitation Room (Intensive) of RSUD Dr. Soetomo Surabaya.

METHODS

This is an observational analytic study with a retrospective design, aimed to analyze the effect of bundle sepsis compliance with the outcome of AKI events and mortality in the first 48 hours of treatment of sepsis patients. The sample were obtained based on the total sampling of medical records of sepsis patients from January to July 2019. Based on previous study[4], obtained the proportion of sepsis in the Resuscitation Room Dr Soetomo Hospital Surabaya is around 12.5%. The proportion used in calculating the minimum sample size, the minimum number of samples obtained is 43

Sample Criteria

Inclusion criteria in this study included: (1) Medical records of patients who are in accordance with the diagnosis of sepsis based on the 2018 SSC criteria; (2) Medical records of sepsis patients, with a qSOFA score> 2 or SOFA score> 2; (3) Medical records of sepsis> 18 years old; (4) Medical records of patients treated in the Resuscitation Room for at least 6 hours. Exclusion criteria in this study were the medical records of certain patients such as: (1) Pregnant women; (2) Patients with a diagnosis of Chronic Kidney Disease (CKD); (3) Patients with a diagnosis of autoimmune disease or HIV; (4) Patients with trauma cases; (5) cardiac arrest less than 1 hour of treatment. Drop out criteria; samples will be excluded from the study if: (1) there is no serum creatinine laboratory data (on the first and second day care), or (2) there is no urine production data within the first 48 hours of treatment.

Sepsis Bundle Compliance

Sepsis bundle is a series of treatment directives (within the first hour) of sepsis patients consisting of (i) lactate examination, (ii) blood culture, (iii) broad-spectrum antibiotic administration, (iv) administration of resuscitation fluid in sepsis with hypoperfusion and (v)) administration of vasopressors in septic shock. Compliance with sepsis bundle management: compliance with a series of sepsis bundle in the first 1 hour sepsis / shock patients according to the 2018 SSC guideline which consists of several component (Table 1).

Table 1. Assessment of sepsis bundle compliance level

Diagnosis	Compliance			
	Good	Moderate	Bad	Very Bad
Sepsis	Fulfilled all points 1,2, and 3	Filled 2 points from the first 3 points	Filled 1 point from the first 3 points	No points have been fulfilled
Septic Shock	Fulfilled all points 1,2,3,4 and 5	Filled 4 points out of 5 points	Filled 2 or 3 points out of 5 points	Filled 1 point out of 5 points, or no points met

Explanation of points in the assessment of sepsis bundle compliance: (1) Measuring initial lactate levels; (2) Examination of blood cultures before being given antibiotics; (3) Provision of broad-spectrum antibiotics; (4) Provision of 30 ml / kg BW crystalloid fluid in patients with hypotension / hypoperfusion (MAP < 65) or

lactate> 4 mmol / L (completed within the first 3 hours); (5) Giving vasopressors if the patient is hypotensive despite having been given resuscitation fluids, to maintain MAP> 65 mmHg or lactate levels > 2 mmol / L

AKI Progressivity

AKI is defined as an increase in serum creatinine > 0.3 mg / dl (> 26.5 mmol / l) within 48 hours or an increase in serum creatinine > 1.5 from the baseline, which is known from the results available 7 days ago, or urine production less than 0.5 ml / kg body weight / hour in 6 hours. AKI progressivity can be divided into: (1) Improvement of AKI, which is a condition where after 6 hours of treatment, a decrease in serum creatinine and/ or an increase in urine production to > 0.5 ml/kg/hour; (2) Worsening AKI, which is a condition where after 6 hours of treatment, an increase in serum creatinine and / or a decrease in urine production to <0.5 ml / kg / hour.

RESULTS

A total of 116 medical records were obtained, and 23 medical records were declared drop-out, so that 93 samples were obtained. The medical record was declared drop-out because there was no laboratory data for serum creatinine (on the first and second day of treatment), and / or no urine production data was obtained within 48 hours of treatment.

Characteristics of Research Subjects

Obtained patients data of 45 men, and women as many as 48 people. The majority of subjects are Javanese (85%). This relates to the demographic environment around Dr Soetomo General Hospital, and the other regional hospital, which is largely Javanese ethnic community. Most of the study subjects were elderly, 61-70 years old with a percentage of 28%, then followed by the middle age group (51-60 years) with a percentage of 25.8%. Nutritional status of the study subjects population was measured using the Body Mass Index (BMI), which was mostly in the normal range of 67.7%, then followed by the overweight group of 20.4%.

Diagnosis of Sepsis and Comorbidity

All samples that have been sorted by inclusion and exclusion criteria are then declared as patients experiencing sepsis-related conditions. A total of 93 samples were divided into two diagnoses according to severity namely: sepsis; and sepsis shock. The majority of research subjects were classified as septic shock, with a percentage of 58.1%. The highest source of infection in this study was caused by pneumonia (51.6%), followed by infections originating from intraabdominal or peritonitis (15.1%) as well as infections from the skin and tissues, such as cellulite (4.3%) and pedic ulcers (4.3%). Most of the subjects had comorbid diabetes mellitus (37.6%), then anemia (12.9%), and hypertension (17.2%)

Compliance with the Sepsis Bundle

Compliance with the overall implementation of the sepsis bundle done within 1 hour (hour-1 bundle sepsis). Based on data tracing, it was found that most of the compliance rates for the implementation of the sepsis bundle were classified as poor (51.6%) and very poor (26.9%). In this study it was found that the highest compliance to sepsis bundle component, is antibiotic management (63.4%) and the lowest adherence to fluid resuscitation (8.6%).

Table 2. The level of compliance of the sepsis bundle

Level of Compliance	Frequency	Percentage
Good	7	7.5
Moderate	13	14
Poor	48	51.6
Very Poor	25	26.9
Compliance of Sepsis Bundle Component		
Lactate assessment	26	28
Culture	23	24.7
Antibiotic management	59	63.4
Fluid Resuscitation	8	8.6
Vasopressor	52	55.9

***Outcome* Related to Acute Kidney Injury (AKI) and Mortality**

In this study, the diagnosis of AKI was stated at 6 hours after admission in the resuscitation room. There were found 51 patients (54.8%) with AKI, and 42 patients (45.2%) with Non-AKI. These findings were then followed for the next 48 hours, resulting in 19.4% worsening (from Non AKI to AKI), and 14% improved (from AKI to Non-AKI), and most of the subjects remained Non-AKI from initial admission to treatment 48 hours (38.7%). In this study, it was found that 58% of subjects died during the 48-hour treatment period, 33.3% died more than 48 hours of treatment, and 8.7% of the research subjects survived.

Table 3. Status of acute kidney injury (AKI) in research subjects

AKI Status	Frequency	Percentage
AKI	51	54.8
Non AKI	42	45.2
Progressivity of AKI		
Worsening	18	19.4
Remained as AKI	26	28
Remained as Non AKI	36	38.7
Improving	13	14

Analysis of Research Results

In this study, sepsis bundles implementation were assessed regarding its compliance into four categories: good, moderate, poor, and very poor. Compliance to bundle sepsis was further analyzed in correlation to the incidence of acute kidney injury (AKI), progression of AKI, and mortality of patients under 48 hours of treatment

Table 4. Correlation between the sepsis compliance with AKI

	Sepsis bundle compliance	
	p-value	Contingency coefficient
AKI in 6 hours	0.048	0.280
AKI in 12 hours	0.692	0.152
AKI in 18 hours	0.905	0.103
AKI in 24 hours	0.497	0.222
AKI in 30 hours	0.809	0.150
AKI in 36 hours	0.258	0.299
AKI in 42 hours	0.364	0.268
AKI in 48 hours	0.583	0.218
Progressivity of AKI	0.026	0.411

The incidence of AKI stated after 6 hours after the patient's admission. Based on statistical results (Table 4), significant correlation was found between bundle sepsis compliance and the incidence of AKI in the first 6 hours with a p value of 0.048 (<0.050), which has a contingency coefficient of 0.280 (degree of weak correlation). Meanwhile, the AKI incident at 12; 18; 24; 30; 36; 42; and 48 hours, did not show a significant correlation with sepsis bundle compliance. Progression of AKI status in sepsis patients was also assessed, where patients who were initially non-AKI would be seen as remained non-AKI, or became AKI. Statistical test results showed a significant correlation between compliance to the sepsis bundle with AKI progressivity, with a p value of 0.026 (<0.050), and a contingency coefficient of 0.411 (moderate degree of correlation).

The highest incidence of mortality occurred at the 18th hour of care, with a total of 31 patients dying, then the mortality rate increased but at a frequency of ≤10 per treatment period up to 48 hours. Cumulatively, the results of statistical analysis show significant correlation between sepsis bundle compliance to the mortality rate of sepsis patients under 48 hours of care, with a p value: 0,000 (<0.05), and a contingency coefficient of 0.614 (degree of strong correlation). Other findings also show a significant correlation between sepsis bundle compliance to the mortality of sepsis patients under 6 hours; 12 hours; 42 hours; and 48 hours (p value <0.050).

Table 5. Correlataion between bundle sepsis compliance with mortality

	Sepsis bundle compliance	
	p-value	Contingency coefficient
6 hours mortality	0.000	0.422
12 hours mortality	0.000	0.403
18 hours mortality	0.315	0.233
24 hours mortality	0.400	0.231
30 hours mortality	0.842	0.133
36 hours mortality	0.838	0.141
42 hours mortality	0.000	0.562
48 hours mortality	0.007	0.480
> 48 hours mortality	0.100	0.371
Cummulative mortality	0.000	0.614

DISCUSSION

The majority of subjects experienced septic shock, with a percentage of 58.1%. This finding is in accordance with the latest literature which states that nearly 50% of sepsis patients continue in the severe stage of sepsis / shock sepsis.[9] The respiratory system is the most common factor in sepsis and sepsis shock. The highest source of infection in this study was caused by pneumonia (51.6%). The data obtained in this study is in accordance with the latest available literature, which states that the respiratory system as the focus of infection which most often causes sepsis.[10]

Comorbid diseases represent the conditions that there are other diseases experienced by research subjects other than the main disease. Most of the research subjects had comorbid diabetes mellitus (37.6%). Based on studies by Whiles et al. (2016) comorbidity could be a positive correlative factor with mortality related to sepsis, if 4 or more comorbidities are found. Elderly patients tend to have multiple comorbidities, which are at high risk of experiencing and worsening the condition of sepsis. Elderly patients according to research by Sehgal et al (2015), tend to have several types of diseases such as severe congestive heart failure (CHF) (especially right heart failure), dementia, increased incidence of urinary tract infection (UTI) associated with urinary catheter insertion, pneumonia, and trauma, which complicates the clinical scenario. Pneumonia and sepsis are one of the most common associations, the most common cause of secondary bacteremia. Diabetes, due to its high prevalence in elderly patients, is the most common risk factor for sepsis. Diabetes mellitus is also associated with an increased risk of nosocomial sepsis, related to the patient's immunosuppressed condition. Pneumonia can predispose to severe sepsis in about half of patients and about 5% experience septic shock.

Nutritional status of the study subjects population was measured using the Body Mass Index (BMI), which was mostly in the normal range of 67.7%, then followed by the overweight nutritional status group of 20.4%. Obesity is associated with the occurrence of AKI in critically ill patients with sepsis; however, despite not directly related to hospital mortality.[11] Recent data has highlighted organ-specific abnormalities in obesity, with changes seen in the kidney and heart organs. Obesity causes glomerular hypertrophy and renal hyperfiltration which can potentially contribute to kidney vulnerability. Recently, the "adipose-renal" hormonal axis theory has emerged. Adiponectin, an insulin sensitizing hormone that regulates glucose and lipid metabolism, and which actually decreases visceral obesity, has a protective effect on several models of renal ischemia reperfusion injury. Leptin, an adipocyte-derived cytokine that is metabolized in the kidneys and controls energy metabolism and appetite, modulates susceptibility to endotoxin-mediated kidney failure and stimulates proliferation and fibrosis. Thus, kidney-specific changes associated with obesity contribute to the incidence of AKI, especially in critical illness patient.[12]

Compliance of 1-hour bundle implementation in this study were classified as poor (51.6%) and very poor (26.9%). This finding is certainly still far from the compliance standard of 1-hour sepsis in developed countries, which reaches a range of 60% optimal compliance.[13] In this study, the highest adherence to antibiotic management (63.4%) and the lowest adherence to fluid resuscitation (8.6%), with only 31% of medical records documenting Central Venous Catheter (CVC) insertion. This finding is similar to the results of previous studies by Raj et al. (2019) which showed the highest level of adherence found in antibiotic management at 88.88% and lactate examination (77.78%). The low compliance to the component of fluid resuscitation needs to be studied further, despite the limitations of this study in analyzing the causal factors associated with these findings.[14]

In this study, the diagnosis of AKI was stated at 6 hours after admission in the resuscitation room, found 51 patients (54.8%) with AKI. This finding is in accordance with previous research which states that AKI associated with sepsis ranges from 26% to 50% of cases of sepsis.[15] Sepsis is the main cause of AKI, contributing to 30 to 50% of AKI cases in critical patients. The mortality rate of critically ill patients with AKI due to sepsis is also higher than patients with AKI which are not caused by sepsis.[16] Based on the study results,

a significant correlation between sepsis bundle compliance and the incidence of AKI in the first 6 hours. Sepsis Associated AKI is a hallmark of severe sepsis and septic shock and is associated with worse outcomes including long hospital stays, and increased mortality when compared to patients with non-septic AKI.[17]

The previous theory state that AKI induced sepsis is due to acute tubular necrosis is controversial. The pathogenesis of AKI in sepsis is complex and involves many mechanisms. The main processes include disorders of the macrocirculation and microcirculation in the kidney, inflammation, activation of the coagulation pathway, the adaptive response of tubular cells to injury by mitochondria, and the release of microvesicles.[18] New evidence suggests that the inflammatory response during sepsis causes an adaptive response to tubular epithelial cells. These changes induce downregulation of cell function to minimize energy demand and to ensure cell survival. The result is reduced kidney function. Simultaneous occurrence of kidney inflammation and microvascular dysfunction exacerbates the adaptive response of tubular epithelial cells to adverse signals. Targeting tubular epithelial cells and microcirculation components can be an effective strategy in preventing and / or treating AKI induced by sepsis.

Statistical test results showed a significant correlation between compliance to sepsis bundles with AKI progressivity. The findings in this study were more encouraging compared to previous studies by Mehta et al.[19] who studied 611 patients with sepsis status during hospitalization, 174 (28%) were sepsis with a diagnosis of AKI from baseline, 194 (32%) patients remained free of AKI related to sepsis, and 243 (40%) sepsis patients without AKI who then appear AKI within 5 days of treatment. This difference might be because the differences in the time of observation, where in our study observations of up to 48 hours.

Cumulatively, the results of statistical analysis show a significant correlation between sepsis bundle adherence to the mortality rate of sepsis patients under 48 hours of treatment. This finding is in line with other previous studies[20], mortality in hospitals for secondary hospitalization due to sepsis has decreased from 24.1% in 2010 to 14.8% in 2015, along with increasing levels of compliance to the management of sepsis and decrease inpatient mortality in the hospital.

Our study is limited due to the absence of exceptions and the sorting out of possible outcomes, and the potential for bias due to heterogeneity in mixed cases or secondary disease. Another limitation of this study is the workload of medical and paramedical personnel, as well as the medical record component which previously had to be ascertained the quality and completeness. A good medical record, should fulfill all of the requirements: correct, complete, clear, accurate, legible, and written in a scientific manner.[21]

CONCLUSION

Most of the levels of compliance with the implementation of the 1-hour survival bundle sepsis campagin were classified as poor (51.6%) and very poor (26.9%). The highest compliance was the management component of antibiotic administration (63.4%) and the lowest adherence to fluid resuscitation (8.6%). There is a significant correlation between sepsis bundle adherence with the incidence of AKI in the first 6 hours, AKI progressivity, and the mortality rate of sepsis patients under 48 hours of treatment. Eventually, compliance with the sepsis campaign bundle survival can be used as a reliable management guideline for sepsis/septic shock to reduce the incidence of AKI related to sepsis and mortality rates of sepsis patients at Dr. Soetomo General Hospital Surabaya. Further research, including the prospective / cohort design, needs to be done in reference to the limitations of the study.

REFERENCES

1. Dellinger RP, Levy MM, Rhodes A, et al. Surviving sepsis campaign: International guidelines for management of severe sepsis and septic shock. Crit Care Med. 2013;41:580–637.
2. Dellinger RP, Levy MM, Rhodes A, AnnaneD, Gerlach H, Opal SM. Surviving Sepsis Campaign international guidelines for management of severe sepsis and septic shock. Crit Care Med. 2012;41(2):580–637.
3. Faozi A, Rahardjo P, Utariani. Faktor Pengaruh Keterlambatan Perpindahan Pasien Dari Ruang Resusitasi ke Ruang Perawatan Intensif Atau Ruang Tindakan RSUD Dr. Soetomo Surabaya. Thesis. Surabaya: Universitas Airlangga; 2015.
4. Anestesia R, Utariani A, Semedi, BP. Analisis Penanganan Pasien Sepsis Dan Syok Sepsis Tiga Jam Dan Enam Jam Pertamadi Ruang Resusitasi RSUD Dr. Soetomo Surabaya. Thesis. Surabaya: Universitas Airlangga; 2018.
5. Ramsdell, Taylor H. et.al. Comlpiance with Updated Sepsis Bundles to Meet New Sepsis Core Measure in a Tertiary Care Hospital. 2017:177-186.
6. Bellomo R, John A. Kellum, Claudio Ronco, Ron Wald, Johan Martensson, Matthew Maiden. Acute kidney injury in sepsis. Intensive Care Med. 2017;43:816–828

7. Miller RR III, Dong L, Nelson NC, Brown SM,Kuttler KG, Probst DR, Allen TL, Clemmer TP. Intermountain Healthcare Intensive MedicineClinical Program. Multicenter implementation ofa severe sepsis and septic shock treatment bundle. Am J Respir Crit Care Med; 2013;188:77-82.
8. Mouncey PR, Osborn TM, Power GS, HarrisonDA, Sadique MZ, Grieve RD, Jahan R, HarveySE, Bell D, Bion JF, Coats TJ, Singer M, YoungJD, Rowan KM. ProMISe Trial Investigators.Trial of early, goal-directed resuscitation for septicshock. N Engl J Med. 2015;372:1301-1311.
9. Mayr FB, Yende S, Angus DC. Epidemiology of severe sepsis. Virulence; 2014;5(1):4–11.
10. Chen C. Age May Not Influence the Outcome of Patients with Severe Sepsis in Intensive Care Units q, International Journal of Gerontology. 2014;8(1):22–26.
11. Gameiro J, Gonc M, Neves M. Obesity, acute kidney injury and mortality in patients with sepsis: a cohort analysis. Renal Failure. 2018;40(1):120–126.
12. Danziger J, Ken Chen, Joon Lee, Mengling Feng, Roger G. Mark, Leo Anthony Celi, & Kenneth J. Mukamal. Obesity, Acute Kidney Injury, and Mortality in Critical Illness. Crit Care Med. 2016;44(2):328–334.
13. Milano PK. Sepsis Bundle Adherence Is Associated with Improved Survival in Severe Sepsis or Septic Shock. Western Journal of Emergency Medicine. 2018;19(September):774–781.
14. Raj SK. et al. Compliance with 6 h-Sepsis Resuscitation Bundle of Surviving Sepsis Campaign before and after Resident Physicians 'Training : A Quality Improvement Interventional Study among Indian Patients Full Text Introduction. Journal of Emergencies. Trauma, and Shock. 2019;12(1):3–9.
15. Alobaidi R. et al. Sepsis-Associated Acute Kidney Injury Rashid. Semin Nephrol. 2015;35(1):2–11.
16. Bilgili B, Haliloğlu M, Cinel İ. Sepsis and Acute Kidney Injury. Turk J Anaesth Reanim. 2014;(9):294-301
17. Murray P. et al. Clinical Approach to the Patient with AKI and Sepsis. Semin Nephrol. 2017;35(1):12–22.
18. Doradla LPS, Prasad, N. (2016). Pathophysiology of sepsis-associated AKI [SA-AKI]. Clinical Queries: Nephrology. Elsevier, a division of Reed Elsevier India, Pvt. Ltd, 5(1), pp. 21–25.
19. Mehta RL, Soroko SB, Ikizler TA (2011). Sepsis as a cause and consequence of acute kidney injury : Program to Improve Care in Acute Renal Disease. Intensive Care Med. 2011;2011;37:241–248.
20. Farrell C, Casserl, B. Sepsis, the earlier the better, 3 to 1-hour bundle. J Emerg Crit Care Med. 2018: 3–5.
21. Mathioudakis A, Rousalova I, Gagnat AA, Saad N, Hardavella G. How to keep good clinical records. Breathe (Sheff). 2016;12(4):369–373.