Correlation of Lipid Profile Levels in Sepsis Patients at the ICU H. Adam Malik Hospital Medan Associated with Sofa Score

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Abstract: *Background: Sepsis is a major cause of organ failure and death in the ICU. Septic patients may have impaired lipid profiles. This is presumably because during the infection process there is a significant change in lipid metabolism due to several mechanisms, including decreased hydrolysis of triglycerides and lipoproteins coupled with proinflammatory cytokines that stimulate the production of free fatty acids and triglycerides in the liver. Objective: Prove changes in lipid profile levels associated with SOFA scores in septic patients admitted to the ICU H. Adam Malik Hospital, Medan Methode: This research is an observational study with a cohort-prospective data collection method. This study took blood samples of patients who were treated in the ICU as many as 48 patients. Samples were checked for Lipid Profile on days 1 and 3, while SOFA scores were calculated on days 1 and 3. The study was carried out after obtaining ethical approval and informed consent. Result and Discussion: 24 men (50%) and 24 women (50%) with the youngest 18 years old and the oldest 65 years old. Using the Wilcoxon test showed that there was a difference in the mean of total cholesterol, LDL cholesterol and triglycerides between the first and third days (p<0.001). Using the Wilcoxon test showed that there was a difference in the mean of total cholesterol, LDL cholesterol and triglycerides between the first and third days (p<0.001). Conclusions and Suggesttion: Lower total cholesterol, HDL cholesterol and LDL cholesterol levels were found in septic patients but increased trigliseride levels were found in septic patients. The correlation between total cholesterol levels, LDL cholesterol with SOFA scores can be used to assess the severity of sepsis patients. Triglycerides can be used as a marker of worsening in septic patients.*

Keywords: Sepsis, Lipid Profile, SOFA score

1. Introduction

The Third International Consensus Definitions for Sepsis and Septic Shock in 2016 has issued a new definition for sepsis, which is a life-threatening organ dysfunction caused by abnormal regulation of the host response to infection. The incidence of severe sepsis is estimated at 300 cases per 100, 000 population in the United States and half of these cases occur outside the ICU. Organ failure is one of the causes of the high mortality and morbidity rates of patients in the ICU and the high costs that must be incurred. Therefore, evaluate organ dysfunction at any time during ICU care.[1]

In recent years, a decrease in lipid profile (total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides) has become a concern in patients with sepsis and septic shock. During the infectious process, significant changes occur in lipid metabolism and lipoprotein composition. In patients with infection, there is a decrease in serum levels of total cholesterol, LDL cholesterol, and an increase in serum triglycerides and a decrease in serum HDL cholesterol. These changes are mediated by cytokines such as interleukin-1 (IL-1) and tumor necrosis factor-(TNF-α) which are involved in the acute-phase response during sepsis. Cytokines stimulate the liver to increase triglyceride synthesis, reduce plasma cholesterol and apolipoproteins, especially HDL cholesterol and LDL cholesterol.[2, 3]

In addition to using lipid profile markers which are very closely related to the degree of inflammation which is the concept of sepsis, an assessment is also needed to assess the severity of sepsis patients. For this reason, in recent years several assessment models have been developed to describe the severity of disease in patients admitted to the intensive care unit or to predict the outcome of intensive care. An example is the Sepsis-related Organ Failure Assessment, which became known as the Sequential Organ Failure Assessment (SOFA).[4, 5]

2. Methods

The research was conducted at the Department of Clinical Pathology, Faculty of Medicine, University of North Sumatra / Haji Adam Malik Hospital, Medan in collaboration with the Department of Anesthesiology and Intensive Therapy, Faculty of Medicine, University of North Sumatra. This study is an observational study with a cohort study design. The study was conducted in August 2021-October 2021. The research subjects were male and female patients who were treated in the ICU of H. Adam Malik Hospital who was diagnosed with sepsis.

The sample size in this study was determined at 47 samples. The inclusion criteria in this study were patients who met the criteria for sepsis according to the Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2016 who were treated at the ICU H. Adam Malik Hospital, Medan, aged > 18 years and < 65 years, and agree to participate in the research. The exclusion criteria were liver disease, malignancy, receiving dyslipidemia drugs.

Each sample was examined for Lipid Profile on days 1 and 3. Examination of vital signs, GCS, platelets, total bilirubin,

creatinine, blood gas analysis as well as SOFA score assessment on days 1 and 3. Examination of Lipid Profile using serum was examined using an automatic device. cell counter analyzer Architect Plus C1 4100 with the principle of enzymatic examination

3. Statistic Analysis

Data analysis was performed using SPSS (Statistical Package for Social Sciences, Chicago, IL, USA) software for Windows. The description of the characteristics of the research subjects is presented in tabulated form and described. The correlation between total cholesterol and LDL cholesterol levels in septic patients used the Pearson

correlation test if the data were normally distributed. If the data is not normally distributed, Spearman's test is used. All statistical tests with p value < 0.05 were considered significant.

4. Result

This study was followed by 48 septic patients who were treated in the ICU of H. Adam Malik Hospital Medan from August 2021-October 2021. The number of male and female patients was the same, namely 24 people (50%). The mean age of the subjects was 50.63 years with the youngest 18 years old and the oldest 65 years old. The Batak tribe is the largest tribe with 30 people (62.5%).

Table 1: Demographic Characteristics of Sepsis Patients Treated in the ICU H. Adam Malik Hospital

Subject characteristics	n = 48
Sex n (%)	
Male	24 (50)
Female	24 (50)
Age	
Mean (SD)	50, 63 (14, 93)
Median (Min-Max)	55, 5 (18-65)

Table 2. shows the lipid profile on the first and third days of treatment. The mean level of procalcitonin was 46.43 ng/mL. Total cholesterol levels showed an average of 159.02 mg/dL on the first day and on the third day showed an average decrease to 110 mg/dL. Using the Wilcoxon test showed that there was a difference in the mean total

cholesterol between the first and third days (p<0.001). LDL cholesterol levels showed an average of 59.96 mg/dL on the first day and on the third day the average decreased to 57 mg/dL. Using the Wilcoxon test showed that there was a difference in the mean LDL cholesterol between the first and third days (p<0.001).

Table 2: Procalcitonin Levels and Lipid Profiles of Sepsis Patients Treated in ICU H. Adam Malik Hospital

	Day I	Day III	p
Procalcitonin, ng/mL			
Mean (SD)	46, 43 (14, 22)		
Median (Min-Max)	43, 45 (12, 74-100)		
Total Cholesterol, mg/dL			
Mean (SD)	159, 02 (6, 63)	110, 1 (13, 26)	<0, 001[a]
Median (Min-Max)	161 (150-172)	111 (98-162)	
LDL, mg/dL			
Mean (SD)	59, 96 (4, 76)	57 (3, 31)	<0, 001[a]
Median (Min-Max)	59 (54-68)	57 (51-68)	
HDL, mg/dL			
Mean (SD)	36, 88 (41, 84)	33, 44 (19, 93)	0, 251[a]
Median (Min-Max)	30 (25-319)	27 (19-78)	
Triglycerides, mg/dL			
Mean (SD)	175, 4 (9, 53)	188, 45 (12, 37)	<0, 001[a]
Median (Min-Max)	179 (147-187)	189 (159-199)	

HDL cholesterol levels showed an average of 36.88 mg/dL on the first day and on the third day the average decreased to 33.44 mg/dL. Using the Wilcoxon test showed that there was no difference in the mean HDL cholesterol between the first and third days (p=0.251). Triglyceride levels showed an average of 175.4 mg/dL on the first day and on the third day the average increased to 188.45 mg/dL. Using the Wilcoxon test showed that there was a difference in mean triglycerides between the first and third days (p<0.001).

Table 3 shows changes in the values of total cholesterol, LDL cholesterol, HDL cholesterol and triglycerides in research subjects. For parameters total cholesterol, LDL cholesterol and HDL cholesterol showed positive values, meaning that there was a decrease in the values of the three lipid profile parameters between the first and third day of examination. On the other hand, for triglycerides, it shows a negative value, which means an increase in the average value of triglycerides.

Table 3: Changes in the Lipid Profile of Sepsis Patients Treated in the ICU H. Adam Malik Hospital

	Mean (SD)	Median (Min-Max)
Total Cholesterol	48, 92 (16, 87)	50 (-12-70)
LDL mg/dL	2, 96 (4, 73)	2 (-10-10)
HDL mg/dL	3, 44 (47, 82)	5 (-47-300)
Triglycerides mg/dL	- 9, 46 (14, 22)	- 10 (-40-20)

Table 4: SOFA Score of Sepsis Patients Treated in ICU H. Adam Malik Hospital

	Day I	Day III	p
SOFA Score			
Mean (SD)	3, 98 (1, 76)	5, 54 (1, 82)	<0, 001
Median (Min-Max)	3 (2-10)	5 (2-9)	

The SOFA score showed an average of 3.98 with the lowest score of 2 and the highest score of 10 on the first day and on the third day the average improvement was 5.54 with the lowest score of 2 and the highest score of 9 using the Wilcoxon test indicating that there was a difference in the mean SOFA score between the first day and the third day of treatment (p<0.001).

Table 5 shows the results of the analysis of the relationship between lipid profiles and SOFA scores on the first and third day of treatment. On the first day of treatment, total cholesterol and HDL cholesterol did not show a significant relationship with SOFA scores. On the other hand, LDL cholesterol and triglyceride levels showed a significant relationship. Using the Spearman Correlation test showed that there was a significant relationship between LDL cholesterol and SOFA score (p=0.027) with correlation value (r) =-0.320. A negative correlation value means that LDL cholesterol levels are inversely proportional to SOFA scores, an increase in LDL cholesterol levels will be followed by a decrease in SOFA scores on the first day of treatment with a weak level of strength. The triglyceride level showed a significant relationship with the SOFA score (p = 0.011) with a correlation value of 0.363, which means that the triglyceride level was directly proportional to the SOFA score. An increase in triglyceride levels will be followed by an increase in SOFA scores with a weak level of strength.

Table 5: Relationship between Lipid Profile and SOFA Score in Sepsis Patients Treated in ICU H. Adam Malik Hospital

			p	r
Day I	SOFA score	Total Cholesterol	0, 489	- 0, 102
		LDL	0, 027	- 0, 320
		HDL	0, 080	0, 255
		Triglyceride	0, 011	0, 363
Day III	SOFA score	Total Cholesterol	0, 002	- 0, 428
		LDL	0, 152	- 0, 210
		HDL	0, 036	- 0, 303
		Triglyceride	<0, 001	0, 503

On the third day of treatment, only LDL cholesterol was not associated with SOFA scores. Total cholesterol level showed a significant relationship with SOFA score (p = 0.002) with a correlation value of-0.428, which means that total cholesterol level was inversely proportional to SOFA score. A negative correlation value means that total cholesterol levels are inversely proportional to SOFA scores, an increase in total cholesterol levels will be followed by a decrease in SOFA scores on the third day of treatment with a

moderate level of strength. By using the Spearman Correlation test showed that there was a significant relationship between HDL cholesterol and SOFA score (p=0.036) with a correlation value (r) =-0.303. A negative correlation value means that HDL cholesterol levels are inversely proportional to SOFA scores, an increase in HDL cholesterol levels will be followed by a decrease in SOFA scores on the third day of treatment with a weak level of strength. Triglyceride levels showed a significant relationship with SOFA score (p < 0.001) with a correlation value of 0.503, which means that triglyceride levels were directly proportional to SOFA scores. An increase in triglyceride levels will be followed by an increase in SOFA scores with a moderate level of strength.

5. Discussion

This study was followed by 48 septic patients who were treated in the ICU of H. Adam Malik Hospital Medan from August 2021-October 2021. The number of male and female patients was the same, namely 24 people (50%). The mean age of the subjects was 50.63 years with the youngest 18 years old and the oldest 65 years old. The Batak tribe is the largest tribe with 30 people (62.5%).

In line with the research conducted by Tsui et al, 2021. Their study showed that the sepsis patients they studied were mostly male, 59.1% and the average age of the sepsis patients they studied was 69.7 years. In contrast to the research conducted by Tambajong et al, 2016. The results of their study showed that the sepsis patients they studied were mostly female as many as 19 people and male patients as many as 16 people and the lowest age of their study was under 14 years and the oldest age was 75-90 years.[6, 7]

The incidence of sepsis is not influenced by gender but is influenced by age and the type of underlying disease. Several studies conducted on the relationship between sex and sepsis found that men were more susceptible to sepsis. Men tend to have lung infections, while women tend to have urinary tract infections.[8]

In our study we saw a decrease in total cholesterol, LDL cholesterol and triglyceride levels in septic patients. Using the Wilcoxon test showed that there was a difference in the mean total cholesterol, LDL cholesterol and triglycerides between the first and third days (p<0.001). However, HDL cholesterol levels were also seen to decrease in septic patients, but using the Wilcoxon test showed that there was no difference in the mean HDL cholesterol between the first

and third days (p=0.251). This may be due to the fact that some septic patients who were admitted for 48 hours in the ICU experienced clinical improvement and also decreased SOFA scores.

In line with the study conducted by Guirgis et al, 2021. They conducted a study of 104 postoperative patients with sepsis who were admitted to the ICU. And all patients were examined for lipid profile and calculated SOFA score. The results of their study showed that all septic patients admitted to the ICU experienced a decrease in total cholesterol, LDL cholesterol, HDL cholesterol and an increase in triglycerides and in all septic patients with a decrease in the lipid profile with an increase in SOFA scores (SOFA scores ranging from 5 to 10).[9]

Study conducted by Irene et al, 2020 They conducted a prospective study of 82 septic patients. After the patient was admitted to the ICU, the levels of Total Cholesterol, HDL cholesterol and LDL cholesterol were significantly lower and Triglycerides were significantly higher in patients compared to controls (p<0.001). Total cholesterol and LDL cholesterol increased one week after the onset of sepsis (21% and 30% increase compared to baseline, respectively) while HDL cholesterol and triglycerides did not change significantly. Initial triglycerides were significantly higher in patients with septic shock (N=30) compared with patients with sepsis (N=52) (221±109mg/dL vs 166±97mg/dL, p=0.03), whereas total cholesterol and Initial LDL cholesterol was significantly higher in survivors (N=58) than nonsurvivors at 28 days (N=24) (122±36mg/dL vs 97±41mg/dL, p=0.015 and 61±38mg/dL vs 38±23mg/dL, p=0.002, respectively).[10]

During the infectious process, there are some significant changes in lipid metabolism and lipoprotein composition. In patients with infection, total cholesterol levels, LDL cholesterol are decreased, and serum triglycerides are increased, while serum HDL cholesterol levels are decreased which has been reported in several studies. This is associated with several mechanisms, including reduced triglyceride hydrolysis, LPS and proinflammatory cytokines inducing free fatty acid production and triglyceride synthesis in the liver. LDL cholesterol and HDL cholesterol receptors are important steps in the clearance of lipid pathogens from circulating sepsis, severe sepsis, and septic shock.[11]

Sepsis is defined as life-threatening organ dysfunction caused by dysregulation of the host's response to infection. Despite many advances in antibiotics and intensive care, sepsis is a serious infectious complication that is a leading cause of mortality. The product of the cell wall of gram-negative bacteria, namely lipopolysaccharide (LPS) can trigger severe immune reactions, leading to sepsis and organ failure. In gram-negative bacteremia, the inflammatory response is triggered by LPS components and acts as pathogen associated molecular patterns (PAMPs). After LPS binds to CD14, the inflammatory cascade begins.[12]

For the total cholesterol parameter, LDL cholesterol and HDL cholesterol showed a decrease in the values of the three lipid profile parameters between the first and third day

of examination. On the other hand, for triglycerides, it shows an increase in the average value of triglycerides.

Several studies have investigated lipoprotein changes in sepsis in relation to the type of organism that causes sepsis. The study by Guoying et al 2020 followed changes in the lipid profile of patients starting from the local infection stage, SIRS and progressing to sepsis. The research of Guoying et al 2020 showed that levels of Total Cholesterol, LDL cholesterol, and HDL cholesterol tend to decrease when patients have sepsis and this decrease is more significant in gram-negative sepsis patients when compared to gram-positive sepsis.[13]

Lipid Profile is a pattern of blood lipids consisting of total cholesterol, triglycerides, low-density lipoprotein (LDL) and high-density lipoprotein (HDL). Changes in the concentration and composition of plasma lipids and lipoproteins occur in acute infection, inflammation, sepsis and septic shock. In sepsis, neuroendocrine and metabolic changes occur such as increased serum cortisol concentrations, low thyroid hormone, insulin resistance, increased glucose, lactate, free fatty acid levels, triglycerides and decreased HDL cholesterol. These changes are mediated by cytokines such as interleukin-1 (IL-1) and tumor necrosis factor-(TNF-α) which are involved in the acute-phase response during sepsis. Cytokines stimulate the liver to increase triglyceride synthesis, reducing plasma cholesterol, especially HDL cholesterol.[14]

6. Conclusion

There were differences in the mean total cholesterol, LDL cholesterol and triglycerides between the first and third days (p<0.001). There was no difference in mean HDL cholesterol between the first day and the third day (p=0, 251). Total cholesterol level showed a significant relationship with SOFA score (p = 0.002) with a correlation value of-0.428, which means that total cholesterol level was inversely proportional to SOFA score. There was a significant relationship between LDL cholesterol and SOFA score (p = 0.027) with correlation value (r) =-0.320. There is a significant relationship between HDL cholesterol and SOFA score (p = 0.036) with a correlation value (r) =-0.303. Triglyceride levels show a significant relationship with SOFA score (p < 0.001) with a correlation value of 0.503, which means that triglyceride levels directly proportional to the SOFA score.

References

[1] Hall MJ, Williams SN,, DeFrances CJ, Golosinskiy A Inpatient care for septicemia or sepsis: a challenge for patients and hospitals. NCHS Data Brief 2011; (62): 1 8. pmid: 22142805

[2] Levy MM, Rhodes A, Phillips GS, et al Surviving Sepsis Campaign: association between performance metrics and outcomes in a 7.5-year study. Crit Care Med 2015; 43 (1): 3-12.

[3] Singer M, Deutschman CS, Seymour CW, et al The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA 2016; 315 (8): 801 810. doi: 10.1001/jama.2016.0287

[4] Lagrost L, Girard C, Grosjean S, et al. Low preoperative cholesterol level is a risk factor of sepsis and poor clinical outcome in patients undergoing cardiac surgery with cardiopulmonary bypass. *Crit Care Med*.2014; 42 (5): 1065-1073. doi: 10.1097/CCM.0000000000000165.

[5] Chien Y-F, Chen C-Y, Hsu C-L, Chen K-Y, Yu C-J. Decreased serum level of lipoprotein cholesterol is a poor prognostic factor for patients with severe community-acquired pneumonia that required intensive care unit admission. *J Crit Care*.2015; 30 (3): 506-510. doi: 10.1016/j. jcrc.2015.01.001.

[6] Tsui T-L, Huang Y-T, Kan W-C, Huang MS, Lai M-Y, Ueng K-C, et al. (2021) A novel procalcitonin-based score for detecting sepsis among critically ill patients. PLoS ONE 16 (1): e0245748.

[7] Tambajong RN, Lalenoh CD. Profil penderita sepsis di ICU RSUP Prof. Dr. R. D. Kandou Manadoperiode Desember 2014-November 2015. *Jurnal e-Clinic (eCl), Volume 4, Nomor 1, Januari-Juni 2016*

[8] Tambajong RN, Lalenoh CD. Profil penderita sepsis di ICU RSUP Prof. Dr. R. D. Kandou Manadoperiode Desember 2014-November 2015. *Jurnal e-Clinic (eCl), Volume 4, Nomor 1, Januari-Juni 2016*

[9] Guirgis, F. W., Leeuwenburgh, C., Moldawer, L. *et al.* Lipid and lipoprotein predictors of functional outcomes and long-term mortality after surgical sepsis. *Ann. Intensive Care* 11, 82 (2021). https: //doi. org/10.1186/s13613-021-00865-x

[10] Irene Karampela, Evangelia Chrysanthopoulou, George Skyllas, Panagiotis Simitsis, Gerasimos Socrates Christodoulatos, Evangelia Kandri, George Antonakos, Apostolos Armaganidis, Maria Dalamaga European Respiratory Journal Sep 2020, 56 (suppl 64) 2753; DOI: 10.1183/13993003. congress-2020.2753

[11] Yang Y, Xie J, Guo F, Longhini F, Gao Z, Huang Y, et al.*2016. Combination of C-reactive protein, procalcitonin and sepsis-related organ failure score for the diagnosis of sepsis in critical patients.* Ann Intensive Care, 6: 51.

[12] Farhana A, Khan YS. Biochemistry, Lipopolysaccharide. [Updated 2021 Apr 29]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https: //www.ncbi. nlm. nih. gov/books/ NBK554414/

[13] Guoying et al.2016. The delta high density lipoporotein cholesterol ratio, a novel parameter from gram negative sepsis. Springer plus 5 (1), pp 1-12.

[14] Qasim A, Kousa O, Andukuri VG. Hypo lipidemia contributing to the severity of sepsis triggered by influenza a virus: A case report. *J Clin Transl Res*.2020; 6 (6): 198-202. Published 2020 Dec 11.

[15] Singer, M, Deutschman SC, Seymour WC, Hari SM, Annane D.2016. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA*, 315 (February), pp.801-810.

[16] Surviving Sepsis Campaign, International Guidelines For Management Of Sepsis And Septic Shock, 2016. *Intensive Care Med (2017) 43: 304-377*

[17] Liu Z, Meng Z, Li Y, Zhao J, Wu S, Gou S and Wu H. Prognostic accuracy of the serum lactate level, the SOFA score and the qSOFA score for mortality among adults with Sepsis. Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine (2019) 27: 51

[18] Seo MH, Choa2 M, You JS, Lee HS, Hong JH. Hypoalbuminemia, low base excess values, and tachypnea predict 28-day mortality in severe sepsis and septic shock patients in the emergency department. Yonsei Medical Journal. November 2016; 57 (6): 1361-9.

[19] Kendall H, Abreu E, An-Lin Cheng. Serum Albumin Trend Is a Predictor of Mortality in ICU Patients With Sepsis. Biol Res Nurs 2019 May; 21 (3): 237-244

[20] Sanderson M, Chikhani M, Blyth E, Wood S, Moppett IK, McKeever T, *et al.* Predicting 30-day mortality in patients with sepsis: an exploratory analysis of process of care and patient characteristics. Journal Of The Intensive Care Society. November 2018; 19 (4): 299-304.

[21] Kim HM, Ahn JY, Song JE, Choi H, Ann HW.2015. The C-Reaktive Protein / Albumin Ratio as an Independent Predictor of Mortality in Patients with Severe Sepsis or Septic Shock Treated with Early Goal Directed Theraphy. PLOS ONE.10 (7). pp.1-13.

[22] Aftab H, Sachin P, Alexis LP, Ronald SC.2013. The Simplified Acute Physiology Score III Is Superior to the Simplified Acute Physiology Score II and Acute Physiology and Chronic Health Evaluation II in Predicting Surgical and ICU Mortality in the ''Oldest Old''. Hindawi Publishing Corporation Current Gerontology and Geriatrics Research Volume 2014. pp.1-9

[23] Yang Y, Xie J, Guo F, Longhini F, Gao Z, Huang Y, et al.*2016. Combination of C-reactive protein, procalcitonin and sepsis-related organ failure score for the diagnosis of sepsis in critical patients.* Ann Intensive Care, 6: 51.

[24] Takegawa R, Kabata D, Kentaro Shimizu, Saya Hisanob, Hiroshi Ogura, Ayumi Shintanit, Takeshi Shimazu. Serum albumin as a risk factor for death in patients with prolonged sepsis: An observational study. Journal of Critical Care 51 (2019) 139-144

[25] Sun J, Sun F, Wang X, Yuan S, Zeng S, Mu X. Risk factors and prognosis of hypoalbuminemia in surgical septic patients. Peerj.2015; 3: E1267

[26] Safari S, Shojaee M, Rahmati F, Barartloo A, Hashhemi B, Forouzanfar MM, Mohammadi E.2016. Turkish Journal of Emergency Medicine 16 (2016) 146-150.

[27] Grissom CK, Brown SM, Kuttler KG, Boltax JP, Jones J, Jephson AR, et al. A modified sequential organ failure assessment score for critical caretriage. Disaster medicine and public health preparedness.2010; 4 (04): 277-284.

[28] Pandharipande PP, Shintani AK, Hagerman HE, St Jacques PJ, Rice TW, Sanders NW, et al. Derivation and validation of SpO2/FiO2 ratio to impute for PaO2/FiO2 ratio in the respiratory component of the Sequential Organ Failure Assessment (SOFA) Score. Critical care medicine.2009; 37 (4): 1317.

[29] Yoon JC, Kim Y-J, Lee Y-J, Ryoo SM, Sohn CH, Seo D-W, et al. (2018) Serial evaluation of SOFA and APACHE II scores to predict neurologic outcomes of out-of-hospital cardiac arrest survivors with targeted temperature management. PLoS ONE 13 (4):