The effect of bacterial sepsis severity on triglyceride value

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Abstract. Sepsis can increase the amount of triglyceride as well as change the functional and structural components of lipoproteins. The triglyceride level is directly proportional to the severity of sepsis and associated with a systemic inflammatory response. The study aims to determine the correlation between the severity of bacterial sepsis with triglyceride value. An observational study with case control design from January 2017 to March 2017 in 30 sepsis and 30 non-sepsis patients at H. Adam Malik General Hospital Medan. We examined Procalcitonin (PCT) and triglyceride level on the 1st, 3rd and 5th day and then analyzed using Mann-Whitney to assess their correlation. The triglyceride value in the sepsis group was 120 ± 5.1 mg/dl on day 1, non-sepsis 117.53 ± 36.37 mg/dl. However, on the fifth day, the sepsis group of triglyceride values was 124.2±50.29 mg/dl and the non-sepsis group triglyceride values 134.03±68.12 mg/dl. There was no specific connection between the severity of sepsis and triglyceride value in a patient with sepsis.

1. Introduction
Sepsis is an infection (suspicion or evidence) accompanied by SIRS (Systemic Inflammatory Response Syndrome).[1] This condition originates from the interaction between pathogenic microorganisms and the immune system that triggers an excessive and destructive irregular inflammatory response.[2,3] During the infection process, there are significant changes in lipid metabolism and lipoprotein composition. Triglyceride (TG) and very low-density lipoprotein (VLDL) increased concerning several mechanisms, including reduction of hydrolysis of triglycerides, Lipopolysaccharide (LPS) and proinflammatory cytokines induced the production of Free Fatty Acids and TG synthesis in the liver and reduced lipoprotein lipase activity resulting in VLDL clearance and increased TG levels.[4,5] Therefore we are interested in conducting a study to assess whether triglycerides have a relationship with sepsis/degree of severity and until now similar research has not been done in Indonesia.

2. Methods
The study design is case control. The study was in the inpatient ward and Intensive Care Unit (ICU) of H. Adam Malik General Hospital from January to March 2017. Inclusion criteria were sepsis patients > 17 years old. Exclusion criteria were sepsis patients with lipid-lowering drug use, chronic kidney disease or chronic liver disease or thyroid dysfunction or diabetes or malignancy, chronic inflammatory diseases such as HIV, systemic lupus erythematosus, or rheumatoid arthritis, and died within 48 hours or referred to another hospital.
There were 60 patients divided into two groups: Sepsis group (30 patients) and non-sepsis group (30 patients). Each patient was in medication according to clinical conditions, and blood sampling was on the 1st, 3rd and 5th day for PCT and TG checking, then the results are processed and analyzed using a computer program, with p<0.05 significance. Ethical clearance was from Research Committee of Medical Field Faculty of Medicine, Universitas Sumatera Utara.

3. Results
The study involved 30 subjects of sepsis and 30 non-sepsis patients, where no significant differences in baseline characteristics were between the two groups (Table 1).

| Characteristics       | Group          | Total | P value  |
|-----------------------|----------------|-------|----------|
| Age group (years)     | Sepsis         | Non Sepsis |       |
| 25 – 35               | 3 (10.0%)      | 3 (10.0%)  | 6 (10.0%) | 0.987<sup>a</sup> |
| 36 – 45               | 7 (23.3%)      | 6 (20.0%)  | 13 (21.7%)|
| 46 – 55               | 7 (23.3%)      | 9 (30.0%)  | 16 (26.7%)|
| 56 – 65               | 9 (30.0%)      | 8 (26.7%)  | 17 (28.3%)|
| > 65                  | 4 (13.3%)      | 4 (13.3%)  | 8 (13.3%) |
| Sex                   | Male           | Female     |         |
|                       | 14 (46.7%)     | 19 (63.3%) | 33 (55.0%)| 0.194<sup>b</sup> |
|                       | 16 (53.3%)     | 11 (36.7%) | 27 (45.0%)|
| Bacteria type         | Gram Positive  | Gram Negative | 5 (8.3%) | 0.146<sup>a</sup> |
|                       | 2 (6.7%)       | 3 (10.0%)  | 5 (8.3%) |
|                       | 15 (50.0%)     | 18 (60.0%) | 33 (55.0%)|
| Polymicrobial         | 5 (16.7%)      | 0 (0%)     | 5 (8.3%) |
|                       | 8 (26.7%)      | 9 (30.0%)  | 15 (25.0%)|
| Source of infection   | Lung           | Abdomen    | 17 (28.3%)|
|                       | 14 (46.7%)     | 10 (33.3%) | 17 (28.3%)|
|                       | 5 (16.7%)      | 7 (23.3%)  | 10 (16.7%)|
|                       | 1 (3.3%)       | 2 (6.7%)   | 3 (5.0%)  |

<sup>a</sup>Fisher exact test
<sup>b</sup>Chi-square test

In this study, a Chi-square test showed that there was no significant relation between group sepsis and non-sepsis with age (p=0.194). Fisher exact test showed that there was no specific relationship between group sepsis and non-sepsis with age (p=0.987), bacterial type (p=0.146) and source of infection (p=0.791).

Table 2. Values of procalcitonin (PCT) and TG of the study subjects.

| Laboratory Characteristics | N  | Mean | Std. Deviation | Median | p Value<sup>*</sup> |
|----------------------------|----|------|----------------|--------|--------------------|
| 1st day PCT                |    |      |                |        |                    |
| Sepsis                     | 30 | 20.02| 51.11          | 18.12  | 0.0001             |
| Non Sepsis                 | 30 | 0.74 | 1.24           | 0.25   |                    |
| 3rd day PCT                |    |      |                |        |                    |
| Sepsis                     | 30 | 15.97| 18.03          | 8.64   | 0.0001             |
| Non Sepsis                 | 30 | 0.48 | 0.81           | 0.17   |                    |
| 5th day PCT                |    |      |                |        |                    |
| Sepsis                     | 30 | 16.82| 20.73          | 8.85   | 0.0001             |
| Non Sepsis                 | 30 | 0.36 | 0.84           | 0.04   |                    |
| 1st day TG                 |    |      |                |        |                    |
In this study, a Mann-Whitney test showed that there were significant differences in PCT value on day 1 to 5 between the sepsis and non-sepsis groups (p<0.05), but there were no significant differences in triglyceride value on day 1-5 between sepsis and non-sepsis group (p>0.05).

4. Discussion

The results of this study found that the Triglycerides value in the sepsis group at baseline examination was 120.83±51.11mg/dl and increased on days 3 and 5 treatments to 124.20±50.29mg/dl. In the non-sepsis group, the mean value of Triglycerides at the initial examination was within normal limits of 117.53±36.37mg/dl and increased on day 3 and five treatment to 134.03±68.12mg/dl. Statistically, there was no significant difference in Triglyceride levels between sepsis and non-sepsis group on the first day of medication, day 3 and day 5 of medication (p>0.05).

Sepsis is the culmination of a complex interaction between infectious organisms and immune hosts. Both host responses and the characteristics of infectious organisms affect the outcome of sepsis. In sepsis begins with the activation of the innate immune system, in response to infection, through the introduction of a foreign object of bacterial lipopolysaccharide (endotoxin or LPS). These mechanisms include cytokine release, neutrophil activation, monocytes, macrophages and endothelial cells and complement activation, coagulation, fibrinolytic, and contact systems.[6,7,8]

Increased levels of Triglycerides in cases of sepsis can be explained based on the literature that during the infection process, significant changes in lipid metabolism and lipoprotein composition occur. Triglycerides (TG) and Very Low-Density Lipoprotein (VLDL) increased concerning several mechanisms, including reduction of hydrolysis of TG, Lipopolysaccharide (LPS) and proinflammatory cytokines induced free fatty acid production and TG synthesis in the liver and reduced lipoprotein lipase activity resulting in VLDL clearance and increasing TG levels.[5,9] However, the results of this study found that there was no significant correlation between Triglycerides with sepsis degree.

The different results were by Ali Cetinkaya et al in Turkey where there was a significant increase in triglycerides in septic patients compared with non-sepsis patients.[10] In a Korean study by Sang Hoon Lee et al stated that elevated triglyceride levels associated with mortality in cases of sepsis.[11] As well as research by Khovidhunkit W et al in San Francisco who found that there was an increase in triglyceride values in infected hosts and inflammation.[9] The differences in our study compared with previous studies are likely due to the limitations of this study. The limitations are not to consider the nutritional status of patients, do not check the levels of albumin and transferrin levels. The sampling
time may have affected the duration of the infection to the occurrence of sepsis in each patient. The value of triglycerides in Asian race is equal to the value of triglycerides in NCEP ATP III given the presence of genetic, dietary and geographic differences. However, we have reexamined patients who survive and get the results of triglycerides within normal limits. Large-scale studies are important to ensure the role of lipids and lipoproteins in patients with sepsis.

5. Conclusion
There was no significant correlation between the severity of sepsis and triglyceride value in a patient with sepsis.

References
[1] Guntur A H 2014 Sepsis Buku ajar ilmu penyakit dalam vol 3, ed S Setiati (Jakarta: Interna Publishing FK UI) pp 692-9
[2] Dellinger P R, Levy M M, Rhodes A, Annane D, Gerlach H and Opal S M 2012 Surviving sepsis campaign: International guidelines for management of severe sepsis and septic shock Crit. Care Med. 41 580–637
[3] Ertel W, Kremer P J, Kenney J, Steckholzer U, Jarrar D and Trentz O 1995 Down regulation of proinflammatory cytokine release in whole blood from septic patients Blood 85(5) 1341–7
[4] Anthony M, Barcia H W and Harris 2005 Triglyceride-rich lipoproteins as agent of innate immunity CID 2005 498-503
[5] Kenneth R F, et al. 1992 Endotoxin rapidly induces changes in lipid metabolism that produce hypertriglyceridemia: low doses stimulate hepatic triglyceride production while high dose inhibit clearance J. Lipid Res. 1992 1756-76
[6] Pittet D, Rangel F S, Li N and Tarara D C 1995 Systemic inflammatory response syndrome, sepsis, severe sepsis and septic shock; incidence, morbidities and outcomes in surgical ICU patients Intensive Care Med. 21 302-9
[7] Reinhart K, Brunckhorst F M, Bone H G, Bardutzky J and Dempfle C E 2010 Prevention, diagnosis, therapy and follow-up care of sepsis: 1st revision of S-2k guidelines of the German sepsis society (Deutsche Sepsis-Gesellschaft e.V (DSG)) and the German Interdisziplinare Vereinigung für Intensiv- und Nothallmedizin (DIVI) Ger. Med. Sci. 8 1-86
[8] Balk R A 2008 Pathogenesis and management of multiple organ dysfunction or failure in severe sepsis and septic shock Crit. Care Clin. 16(2) 1-10
[9] Khovidhunkit W, Kim M S, Memon R A 2004 Effects of infection and inflammation on lipid and lipoprotein metabolism: mechanisms and consequences to the host J. Lipid Res. 45 1169–96
[10] Ali C, et al. 2014 Is hypertriglyceridemia a prognostic factor in sepsis Dovepress 2014 147-50
[11] Sang H L, et al. 2015 Prognostic implications of serum lipid metabolism over time during sepsis Hindawi Publishing Corporation 2015 1-8
[12] Scott M, Diane B and Luther T 2001 National cholesterol education program expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel III) National Inst. Health 1 3670