Procalcitonin Level Differences in Patients with Liver Cirrhosis Without Bacterial Infection

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ABSTRACT

Background: *Procalcitonin level can increase in patients with liver cirrhosis without bacterial infection. The aim of this study is to identify the role of procalcitonin in patients with liver cirrhosis without bacterial infection.*

Methods: *Cross-sectional study was performed to patients with liver cirrhosis without bacterial infection. In patients, we performed procalcitonin level examination and bacterial infection identification. Further, we analysed them to know the procalcitonin level difference in patients with compensated and decompensated liver cirrhosis without bacterial infection.*

Results: *We obtained 39 patients with liver cirrhosis without bacterial infection, male 61.5% with compensated condition found in 17 patients and decompensated in 22 patients. We found significant difference in the average of procalcitonin level in decompensated patients (0.738ng/mL ± 1.185) compared to compensated (0.065ng/mL ± 0.022).*

Conclusion: *Procalcitonin level increased in patients with liver cirrhosis without bacterial infection. The level in decompensated patients were higher compared to compensated patients.*

Keywords: *procalcitonin, decompensated, compensated*

ABSTRAK

Latar belakang: *Kadar prokalsitonin dapat meningkat pada pasien sirosis hati tanpa infeksi bakteri. Tujuan penelitian ini adalah mengetahui peran prokalsitonin pada pasien sirosis hati tanpa infeksi bakteri.*

Metode: *Studi potong lintang dilakukan terhadap pasien sirosis hati tanpa infeksi bakteri. Pada pasien dilakukan pemeriksaan kadar prokalsitonin dan penentuan ada tidaknya infeksi bakteri. Lalu dianalisis untuk mengetahui perbedaan kadar prokalsitonin pada pasien sirosis hati kompensata dan dekompensata tanpa infeksi bakteri.*

Hasil: *Didapatkan 39 pasien sirosis hati tanpa infeksi bakteri, pria sebanyak 61,5%, dengan kondisi kompensata sebanyak 17 pasien dan dekompensata sebanyak 22 pasien. Terdapat perbedaan rerata kadar prokalsitonin yang bermakna antara pasien dekompensata (0,738ng/mL ± 1,185) dibandingkan dengan kompensata (0,065ng/mL ± 0,022).*

Simpulan: *Kadar prokalsitonin meningkat pada pasien sirosis hati tanpa infeksi bakteri. Kadarnya pada pasien dekompensata lebih tinggi dibandingkan dengan yang kompensata.*

Kata kunci: *prokalsitonin, dekompensata, kompensata*

INTRODUCTION

Disease progression in liver cirrhosis is divided into 2 phases, which are: compensated phase and advanced phase which consist of decompensated cirrhosis and acute-on-chronic liver failure (ACLF).[1,2] Patients with compensated liver cirrhosis has 7-10% risk to develop into decompensated. Every year 5-7% patients with compensated liver cirrhosis worsened to decompensated. Further, patients with decompensated liver cirrhosis deal with mortality risk of 20-57%.[1] Disturbance in the regulation of immune system and systemic inflammation are two main mechanisms in the natural development in pathophysiology of liver cirrhosis. The process starts with injury of liver tissue through damage-associated molecular patterns (DAMPs) which will activate immune system and cause sterile systemic inflammation. This is continued by pathogen-associated molecular patterns (PAMPs) through stimulus of bacterial translocation and their products (lipopolysaccharide and methylated DNA) which further activate immune system and worsened systemic inflammation.[3,4]

Procalcitonin (PCT) is a peptide precursor of calcitonin hormone which contains 116 amino acids. Procalcitonin is produced by various types of cells or body tissue as a response to endotoxine (lipopolysaccharide) or due to release of inflammation mediators, such as: interleukin (IL)-1β, tumour necrosis factor-alpha (TNF-α) and IL-6.[5-7] A number of studies found varied increase in PCT levels in patients with liver cirrhosis without bacterial infection, acute alcoholic and acute liver hepatitis; however, not specifically comparing procalcitonin levels based on particular compensated liver condition.[8,9]

This study aimed to know the role of PCT in liver cirrhosis without bacterial infection as a mean to increase the management quality of patients with liver cirrhosis and identify the average differences of PCT level in patients with decompensated liver cirrhosis without bacterial infection compared to compensated liver cirrhosis without bacterial infection.

METHOD

This study used cross-sectional design. This study was performed in the polyclinic and inpatient ward of Internal Medicine Department Cipto Mangunkusumo General Hospital, from March to May 2016.

Target population were all adult patients with liver cirrhosis without bacterial infection. Accessible population were all liver cirrhosis patients who came for treatment in the polyclinic or inpatient ward of Internal Medicine Department, Cipto Mangunkusumo Hospital, from March to May 2016. Research subjects were accessible population who fulfilled study criteria. Based on sample size calculation, the minimal sample needed in this study were 30 patients.

Inclusion criteria included adult liver cirrhosis without bacterial infection who were willing to participate in the study and signed informed consent. Meanwhile, exclusion criteria were patients who received antibiotics 7 days before sample collection or suffered from malignancy. Independent variable in this study was procalcitonin and dependent variables were decompensated liver cirrhosis without bacterial infection and compensated liver cirrhosis without bacterial infection.

Recruited research subjects who have been diagnosed with liver cirrhosis previously, would undergo liver cirrhosis supporting examinations to identify the Child-Turcotte-Pugh (CTP) score. After recruitment, patient underwent procalcitonin examination and bacterial infection screening based on the standard in accordance with particular suspicion of focal infection. Serum procalcitonin level was measured using immunofluorescent assay method using commercial kit (Ref. #825.050, B.R.A.H.M.S PCT *sensitive* KRYPTOR, B.R.A.H.M.S GmbH, Hennigsdorf, Germany).

Descriptive data was exhibited to comprehend characteristics of research subjects and all variables being studied, and presented in tabular and text forms. Procalcitonin level difference was tested with average difference in two groups test, which was t-test in data with normal distribution or Mann-Whitney test in data which was not normally distributed. Data analysis was performed using SPSS software version 20.0 for Windows PC (SPSS Inc., Chicago, Illinois, USA).

RESULTS

During the study period, we found 42 patients who fulfilled the inclusion criteria; however, 3 patients were later excluded with the reason as follows: 1 patient

received antibiotic and 2 patients were proven to suffer from malignancy. Finally, 39 patients were included in further analysis.

Table 1. Characteristic of research subjects (n = 39)

Characteristic	n (%)
Age, year old, average ± standard deviation	50.34 ± 1.012
Sex	
Male	24 (61.5)
Female	15 (38.5)
Liver Cirrhosis	
Compensated	17 (43.6)
Decompensated	22 (56.4)
Type of Hepatitis	
Hepatitis B	16 (41.0)
Hepatitis C	10 (25.7)
Non-hepatitis B or C	13 (33.3)
CTP Score	
Class A	26 (66.7)
Class B	9 (23.1)
Class C	4 (10.2)

Patients with liver cirrhosis without bacterial infection based on liver compensation have characteristics which can be seen in Table 2.

Table 2. Characteristics of patients with liver cirrhosis without bacterial infection

Characteristic	Compensated n = 17	Decompensated n = 22	p
Type of Hepatitis			
Hepatitis B	8 (47.1)	8 (36.4)	
Hepatitis C	4 (23.5)	6 (27.2)	0.679*
Non-hepatitis B or C	5 (29.4)	8 (36.4)	
CTP Score			
Class A	16 (94.1)	10 (45.5)	
Class B	1 (5.9)	8 (36.4)	0.001*
Class C	0 (0)	4 (18.1)	

*Chi square, $p < 0.05$

Average PCT level in the decompensated liver cirrhosis without bacterial infection group was significantly higher compared to compensated liver cirrhosis without bacterial infection group.

Table 3. Comparison of average procalcitonin level in decompensated liver cirrhosis without bacterial infection group compared to compensated liver cirrhosis without bacterial infection group

Variable	Decompensated (n = 22)	Compensated (n = 17)	p
Procalcitonin, ng/mL, average ± standard deviation	0.738 ± 1.185	0.065 ± 0.022	0.000

*Mann Whitney test

DISCUSSION

Liver cirrhosis is the last phase in the progression of chronic liver disease. Natural progression of liver cirrhosis occurs in two phases, which are: asymptomatic phase which is known as compensated cirrhosis and advanced phase which include decompensated cirrhosis and acute-on-chronic liver failure (ACLF).[1,10] In this study, there were no significant difference in the average age, proportion of sex, or proportion of hepatitis type in decompensated liver cirrhosis and compensated liver cirrhosis without bacterial infection. Severity of liver cirrhosis was determined through calculation of Child-Turcotte-Pugh (CTP) score. Globally, this score is the most common being used by clinicians due to its simple calculation, can be used as a short-term predictor of liver cirrhosis patient's survival (1 to 2 years), and help clinicians to identify priority of treatment in liver cirrhosis patients.[1] In this study, statistically there were difference of CTP score between compensated liver cirrhosis group compared to decompensated liver cirrhosis without bacterial infection group. CTP score class A was most frequently found in compensated liver cirrhosis patients; however, the number was not of much difference with CTP score class A in decompensated patients.

Pathophysiological pathway of liver cirrhosis is influenced by various factors including oxidative stress, systemic inflammation and organ dysfunction; therefore, the appeared clinical manifestations and prognosis may vary. Advanced liver cirrhosis is differentiated based on disease progression and severity of worsening. Decompensated liver cirrhosis is slow lane which is marked by several phases of cirrhosis associated complications. Meanwhile, ACLF is a shortcut marked by acute alterations of liver function which is usually provoked by particular precipitating factors resulting in failure of one or more organs and increase short-term risk of mortality.[1,10]

In this study, we found significant difference in the average PCT levels in patients with liver cirrhosis without bacterial infection in decompensated group (0.738ng/mL ± 1.1850) compared to compensated (0.065 ng/mL ± 0.022), analysis results p *value* 0.000 ($p < 0.05$). Average of PCT level in patients with decompensated liver cirrhosis without bacterial infection was 11.4x higher compared to patients with compensated liver cirrhosis without bacterial infection. Study conducted by Attar et al found significant difference of PCT levels in severe liver cirrhosis patients with massive ascites (0.42ng/mL ± 0.19) compared to those without ascites (0.10 ng/mL ± 0.01).[9] Feng et al obtained positive PCT (which was set to be more than 0.5ng/mL in their study) only in patients with decompensated liver cirrhosis with CTP class B and C.[30] This data revealed that in liver cirrhosis, decompensated liver condition was the component which could increase PCT level. Guide of increased PCT level in patients with liver cirrhosis without bacterial infection could help clinicians ensure

decompensation condition and restrict monitoring of worsening liver compensation progression; thus, quality of optimal management of liver cirrhosis could be improved.

Generally, liver cirrhosis patients who came for treatment to Cipto Mangunkusumo Hospital might represent characteristics of liver cirrhosis patient in Indonesia, which one of the reason was most of those patients were referral patients from other parts in Indonesia. It means that sample which was used in this diagnostic study represent wide spectrum. This kind of study has never been performed in Indonesia.

On the other hand, there were several limitations, which included this study did not monitor the development of patients who participated as subjects to know their prognosis. This study only collected PCT sample one time in each patient; therefore, changes of PCT value as evaluation of management which had been given was unknown.

CONCLUSION

Average of PCT level in patients with decompensated liver cirrhosis without bacterial infection was significantly higher compared to compensated liver cirrhosis without bacterial infection. Further study is needed to identify the development of liver cirrhosis patients in association with changes of PCT values and severity degree of liver cirrhosis (compensated to decompensated); thus, we could further understand the morbidity and mortality of those patients.

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