Comparison of lipid profile between degrees of severity of hepatic cirrhosis in Haji Adam Malik general hospital Medan

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Abstract. Lipid metabolism disorders usually occurred in chronic liver disease. A cross-sectional study was conducted in liver cirrhosis (LC) patients who came to Central Hospital Haji Adam Malik, Medan on July-December 2016 to evaluate the comparison of total cholesterol, LDL, HDL, triglyceride in Child-Pugh class. Inclusions criteria were patient diagnosed with LC from anamnesis, physic diagnostic, laboratory, and imaging. The patients were being evaluated with Child-Pugh (CP). P-value was calculated by using univariate and bivariate analysis of variance test (ANOVA). There were 80 subjects which included 45 men (56.3%) and 35 women (43.8%). Mean age was 51.36 ± 12.6 years. There were 40% with HBsAg (+) and 12.5% with Anti-HCV (+). There was 60% patient with CP-C, 21.3% CP-B, and 18.8% CP-A. There were significant differences between LDL and HDL level among LC patient grade in CP-A, B, and C (p<0.05). HDL and LDL level significantly lower in CP-C compared with CP-A. There were significantly differences between LDL and HDL level among LC patient grade in CP-A, B, and C (p<0.05). HDL and LDL level significantly lower in CP-C compared with CP-A. There weren’t any statistically difference between total cholesterol and triglyceride level in LC patients with CP-A, B, and C.

1. Introduction
Hepatic cirrhosis is the third leading cause of death in patients aged 45-46 years (after cardiovascular disease and cancer), and ranked seventh in the cause of death worldwide. The incidence rate of Hepatic Cirrhosis in the United States is estimated to be 360 cases per 100,000 population. Causes of Hepatic Cirrhosis are mostly alcoholic and non-alcoholic steatohepatitis liver disease and hepatitis C. The incidence of Hepatic Cirrhosis in Indonesia due to Hepatitis B ranges from 21.2- 46.9% and hepatitis C ranges from 38.7-73.9%.[1]

Hepatic Cirrhosis itself is the final stage of the process of diffusing progressive liver fibrosis characterized by the distortion of the liver architecture and the formation of regenerative nodules. The occurrence of liver fibrosis is due to activation of the stellate liver cells. This activation is triggered by the release factor generated by hepatocytes and Kupffer cells. The fibrosis process causes changes in shape and triggers vascular capillarization. Sinusoid capillarization will then alter the exchange of portal venous flow with hepatocytes, so the material that should be metabolized by hepatocytes will go directly into the systemic bloodstream and inhibit the liver-produced material into the blood.[1]

Regarding of fat metabolism, the function of the liver is to produce lipoproteins, cholesterol, phospholipids and acetocetetic acids. So, in the state of cirrhosis hepatitis, lipoprotein, cholesterol, phospholipids and acetocetetic acid inhibited to enter the blood. Fat malabsorption also often occurs...
in patients with liver disease, not only because of cholestasis but also in parenchymal liver diseases.\[2\] VLDL secretion by inadequate hepatocytes has also been associated with the incidence of hypocholesterolemia, and these metabolic abnormalities are commonly found with low triglyceride levels.\[3\]

This study aims to evaluate the ratio of total cholesterol, LDL, HDL and Triglycerides between Child-Pugh A, B, and C in patients with hepatic cirrhosis who went to RSUP H. Adam Malik Medan between July - December 2016.

2. Methods

2.1. Data collection
This study is a cross-sectional study of 80 patients with hepatic cirrhosis consecutively treated at RSUP H. Adam Malik Medan from July 2015 to December 2016. Inclusion criteria were outpatients and inpatients diagnosed with hepatic cirrhosis from anamnesis, physical examination, laboratory, and imaging. Patients performed with Child Pugh’s assessment.\[1\]

2.2. Statistics
Patients performed Child-Pugh grade A, B or C assessments that would be compared with blood lipid profile levels. Statistically, univariate and bivariate analyzes were performed by ANOVA test. Data were analyzed using the statistical program. Statistically significant when p<0.05.

3. Result
There were 80 subjects consisting of 45 men (56.3%) and 35 women (43.8%). With average age 51.36 ± 12.60 years. 40% patients with HBsAg (+) and 12.5% with Anti HCV (+). 60% of patients with Child-Pugh C, followed by 21.3% Child-Pugh B and 18.8% Child-Pugh A.

| Variable                  | n = 80 |
|---------------------------|--------|
| Gender                    |        |
| Man                       | 45 (56.3%) a |
| Woman                     | 35 (43.8%) |
| Age                       | 51.36 ± 12.60 b |
| Educational status        |        |
| Elementary School         | 8 (10%) a |
| Junior High School        | 22 (27.5%) |
| Senior High School and higher degrees | 50 (62.5%) |
| Ethnicity                 |        |
| Batakese                  | 45 (56.3%) a |
| Javanese                  | 28 (35.0%) |
| etc.                      | 7 (8.8%) |
| Virus Serology            |        |
| HBsAg (+)                 | 32 (40%) a |
| Anti HCV (+)              | 10 (12.5%) |
| Child Pugh Class          |        |
| A                         | 15 (18.8%) |
| B                         | 17 (21.3%) |
| C                         | 48 (60%)  |

\[a\] Categorical Data: n (%)  
\[b\] Numerical data, normal distribution: mean ± SD

From Demographic Data can be seen, from 80 subjects with highest education status of high school and higher degree (62.5%), Ethnic most is Batak ethnic with 45%, from Child-Pugh score calculation
got the most subject at Child- Pugh C as much as 60%. From the above data, we also see, on the subject, there are 40% with HBs Ag (+) and 12.5% Anti HCV (+).

**Table 2.** Comparison of lipid profile content between Child-Pugh A, B, and C in hepaticcirrhosis patients.

| Lipid Profile | Child-Pugh A n=15 | Child-Pugh B n=17 | Child-Pugh C n=48 | P     |
|---------------|-------------------|-------------------|-------------------|-------|
| Total Cholesterol | 165.4 ± 32      | 162.3 ± 42.8      | 134 ± 13.6        | 0.093 |
| LDL           | 112 ± 34         | 100 ± 16.3        | 82.9 ± 28+        | 0.001b|
| HDL           | 47.4 ± 10.4      | 42.3 ± 5.7        | 40.7 ± 6.3+       | 0.009b|
| Triglyceride  | 119.4 ± 36.7     | 88.9 ± 40.1       | 91 ± 45.3         | 0.354 |

*a numerical data, normal distribution: mean ± SD  
b*p<0.05, The results of this category differed significantly with Child-Pugh A results (p <0.05)

In table 2 we can see in LDL and HDL profiles, there are significant differences in patients with Child-Pugh A, B, and C, whereas for Total Cholesterol and Triglycerides we cannot find a significant difference.

In the LDL and HDL profiles, we can see a decrease as Child-Pugh's score changes, the higher the Child Pugh score, the lower the LDL and HDL profile of the patient.

**Figure 1.** Boxplot diagram of LDL level between the patients with hepatic cirrhosis and Child-Pugh A, B, and C.
There were significant differences in LDL and HDL levels between cirrhotic hepatic patients with Child-Pugh A, B, and C (p<0.05). HDL and LDL levels were significantly lower in Child-Pugh C than in Child-Pugh A. There was no statistically significant difference in total cholesterol and triglyceride levels between patients with hepatic cirrhosis with Child-Pugh A, B, and C.

4. Discussion
The liver has a very important function especially regarding metabolism. The liver is largest metabolic center in the human body. The liver plays important function for the regulation of lipid metabolism and lipoprotein.[1] Liver not only synthesizes and secretes endogenous lipoproteins, enzyme synthesis is also important for LDL metabolisms such as Lecithin cholesterol acyltransferase (LCAT), hepatic lipase and apolipoprotein, but also regulates catabolism of some plasma lipoproteins via lipoprotein receptors cellularity on the cell surface, which will maintain the relative balance of plasma lipids and in vivo lipoproteins. This process can be impaired when hepatic cell damage occurs, leading to changes in plasma lipids and lipoprotein patterns, and cholesterol, triglyceride, APOAI, Apo-B and Lp(a) synthesis may change, and plasma concentrations can be impaired.[10] Therefore, progressive lipid with severity of liver disease and plasma lipid assessment and lipoprotein levels may be helpful in evaluating the increased liver damage.

In the condition of Hepatic Cirrhosis, there is diffuse liver fibrosis so that the body's metabolic processes will be disrupted. The course of Cirrhosis Hepatitis is slow, asymptomatic and cannot be predicted until the complications of liver disease occur.[1] Patients with Hepatic Cirrhosis are often found to be in a decompensated condition, under these conditions the prognosis is worse than other.

Some scoring systems can be used to assess the severity of Hepatic Cirrhosis and determine its prognosis. One of the scoring systems is Child-Pugh scores, used for the evaluation of patients with a liver transplant plan. Over the years Child Pugh's scoring system has been used in many studies of patients with hepatic cirrhosis. In 1997, the Child-Pugh scoring system was used by experts at the American Society of Transplant Physicians and The American Association for the Study of the Liver, as a criteria for a liver transplantation queue system at UNOS (the United Network for Organ Sharing). This criterion was used as a "minimum criteria" for liver transplant candidates.[5]
George V Papatheodoridis et al. in his study comparing the scoring system in patients with Hepatic Cirrhosis Decompensated states that both MELD and Child-Pugh can accurately predict short-term survival (3-6 months) in patients Decompensated Hepatic Cirrhosis, with MELD is more accurate in the prediction of survival of term patients (12-24 months). Child-Pugh Modification with an addition of serum creatinine as a parameter proved to be more accurate in the prediction of survival of medium-term patients compared to conventional Child-Pugh.[12] This can be considered in subsequent research.

D’Arienzo et al. in his study said the lower serum cholesterol associated with mortality rates in patients with Hepatic Cirrhosis.[6] Same with D’Arienzo et al. study, Selcuk et al. analyzed the deaths of 99 patients with Hepatic Cirrhosis and found that the total cholesterol level was lower than normal. From this study, there was a possibility of serum cholesterol levels correlated with the severity of the Hepatic Cirrhosis disease. Subhan et al. also investigated that patients with chronic liver disease parenchyma without cholestasis, HDL levels decreased and worsened in line with the progression of the disease.[4]

AmanullahAbbasi et al. 2010 study questioned whether the Lipid profile could be used as an additional parameter in Child-Pugh on Cirrhosis caused by Hepatitis Virus. From this study, found significant results about the relations of Lipid Profile with Child-Pugh scoring. Serum Total cholesterol and Triglycerides have a significant relation with Child-Pugh scores, the increased severity of hepatic dysfunction in Hepatic Cirrhosis, serum cholesterol, and triglyceride levels decreased.[7]

From the study of Sanjay Kumar Mandal et al. in 2012 about Lipid Profiles on Chronic Heart Disease, dyslipidemia was found in patients with Hepatic Cirrhosis, and Lipid Profile screening for therapeutic interventions to prevent the incidence of cardiovascular disease. Four lipid profile variables (LDL, HDL, VLDL and total cholesterol) were significantly lower in patients with Hepatic Cirrhosis compared with controls. For the association with the severity of the Hepatic Cirrhosis assessed by the Child-Pugh scoring system, no significant results were found in the four variables.[8]

From the results of this study, there were significant differences in LDL and HDL levels between cirrhotic hepatic patients with Child-Pugh A, B, and C (p<0.05). HDL and LDL levels were significantly lower in Child-Pugh C than in Child-Pugh A. There was no statistically significant difference in total cholesterol and triglyceride levels between patients with hepatic cirrhosis with Child-Pugh A, B, and C. This was analogous with Lech Krosteck et al. in 2013 writing about the serum HDL and LDL values can be considered as a marker of degrees of liver damage in NASH, but in alcoholic cirrhosis, TG is considered a marker. There is elevated TG in NASH and NAFLD seen in Paschos P, Paletas K research on NAFLD metabolic syndrome.[13]

In this study, the cause of cirrhosis of the hepatitis is not separated, but there is a possibility that there is no significant difference in TG value because the patient of the object is NAFLD or NASH. More detailed and specific research is needed to compare the severity of Hepatic Cirrhosis with serum lipid profile levels by comparing with the causes of Hepatic Cirrhosis in patients.

5. Conclusion
There are significant differences in patients with Child-Pugh A, B, and C, whereas for Total Cholesterol and Triglycerides we are not significantly different. In the LDL and HDL profiles, we can see changes as Child-Pugh’s score increases, the higher the Child-Pugh score, the lower the LDL and HDL profile of the patient.

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