Renal dysfunction in liver cirrhosis and its correlation with Child-Pugh score and MELD score

G A Siregar$^*$ and M Gurning$^1$

$^1$Division of Gastroenterology, Department of Internal Medicine, Universitas Sumatera Utara, Adam Malik Hospital, Medan, Indonesia

*Corresponding author e-mail: gontarsiregar@gmail.com

Abstract. Renal dysfunction (RD) is a serious and common complication in a patient with liver cirrhosis. It provides a poor prognosis. The aim of our study was to evaluate the renal function in liver cirrhosis, also to determine the correlation with the graduation of liver disease assessed by Child-Pugh Score (CPS) and MELD score. This was a cross-sectional study included patients with liver cirrhosis admitted to Adam Malik Hospital Medan in June – August 2016. We divided them into two groups as not having renal dysfunction (serum creatinine ≤ 1.5 mg/dL) and having renal dysfunction (serum creatinine > 1.5 mg/dL). For the processing of data, SPSS 22.0 was used. Statistical methods used: Chi-square, Fisher exact, one way ANOVA, Kruskal Wallis test and Pearson coefficient of correlation. The level of significance was p<0.05. 55 patients with presented renal dysfunction were 16 (29.1 %). There was statistically significant inverse correlation between GFR and CPS (r = -0.308), GFR and MELD score (r = -0.278). There was a statistically significant correlation between creatinine and MELD score (r = 0.359), creatinine and CPS (r = 0.382). The increase of the degree of liver damage is related to the increase of renal dysfunction.

1. Introduction
Liver cirrhosis is a major health problem worldwide and is associated with significant morbidity and mortality. According to the WHO, about 800,000 people die of cirrhosis annually.[1] Renal dysfunction (RD) is a common complication in patients with decompensated cirrhosis.[2] Acute kidney injury (AKI) occurs in approximately 19% of hospitalized patients with cirrhosis.[3] Chronic kidney disease (CKD) occurs in 1% of all patients with cirrhosis.[4]
Renal dysfunction is heavily weighted in MELD calculation as it has a strong impact on survival before transplantation.[5] Identification of renal function is important because it is associated with a high morbidity and mortality.[6] The impact of the presence of renal insufficiency at the time of transplantation on post-transplantation survival has been the focus of several studies.[7] For example, moderate elevations of creatinine up to 2 mg/dl and more severe renal insufficiency of creatinine >2 mg/dl were associated with 1.7- and 2.7-fold increases, respectively, in the risk of death.[8] Likewise, MELD estimates that a one-unit increase in loge (creatinine) is associated with a 2.6-fold increase in the risk of death.[9] Sharma et al. found that serum creatinine at the time of liver transplant is an important predictor of liver transplant survival benefit independent of MELD within MELD categories. They also found that survival varied depending on the severity of liver disease.[7]
The study was undertaken to evaluate the renal function in chronic liver disease and find out the correlation between creatinine and glomerular filtration rate (GFR) as a marker of RD with the graduation of liver disease (assessed by CPS and MELD score) and to investigate comparison of laboratory parameters between patients with and without RD.

2. Methods
The present study was a cross-sectional study on 55 consecutive liver cirrhosis patients admitted to Adam Malik General Hospital Medan in June – August 2016. Each hospital record was reviewed to verify the diagnosis and to obtain all relevant clinical and laboratory data. Inclusion criteria were inpatients and outpatients with liver cirrhosis of any etiology, age >18 years. Patients with history chronic kidney disease and had an abnormal urinalysis and renal ultrasound were excluded. Each patient gave informed consent.

Liver cirrhosis was confirmed by clinical, biochemical, and ultrasonographic findings. Renal dysfunction was defined as serum creatinine (Cr) levels more than 1.5 mg/dL. This stratification was based on the guidelines of International Ascites Club’s definition of renal failure in the setting of cirrhosis.[10] Patients with RD were grouped into two categories: group I (serum Cr more than 2.5 mg/dL or having of the creatinine clearance to less than 20 mL/min), and group II (serum Cr level more than 1.5 mg/dL but less than 2.5 mg/dL or creatinine clearance less than 40 mL/min). The severity of liver disease was assessed according to Child-Pugh and MELD score. The estimated GFR was evaluated by Cockcroft-Gault formula.

All data were analyzed with statistical software SPSS 22.0 using univariate and bivariate analysis with 95% confidence interval. Bivariate analysis was carried out using Chi-square, Fisher exact, one way ANOVA, Kruskal Wallis test and Pearson coefficient of correlation with significance level set at p<0.05.

3. Results
Fifty-five patients (31 males, 24 females, mean age 51.51 ± 12.6 years) with the diagnosis of liver cirrhotic were enrolled. The demographic parameters are described in Table 1. Based on criteria described earlier 16 (29.1%) patients had RD, which RD group I 9 (16.6%) and RD group II 6 (12.7%).

| Variables                             | n = 55 |
|---------------------------------------|--------|
| Gender                                |        |
| Male                                  | 31 (56.4%)^a |
| Female                                | 24 (43.6%) |
| Age                                   | 51.51 ± 12.6^b |
| Renal dysfunction (RD)                |        |
| Absence of RD                         | 39 (70.9%)^a |
| Presence of RD                        | 16 (29.1%) |
| Grup I                                | 9 (16.4%) |
| Grup II                               | 7 (12.7%) |

^aCategoric data : n(%)  
^bNumeric data, normal distribution : mean± SD

Table 2 shows ascites was found to be the common presentation, 38 (69%) of the patients. Hepatic encephalopathy (HE) was found in 8 (14%) patients. There was a statistically significant association between HE and reduction of kidney function which RD more frequent in patients with HE (OR: 5.45; p<0.038).
Table 2. Association between renal dysfunction with gender, ascites, hepatic encephalopathy and Child-Pugh score.

| Variable       | Renal dysfunction | Total | P    | OR (95%CI) |
|----------------|-------------------|-------|------|------------|
|                | Yes               | No    |      |            |
| Gender         |                   |       |      |            |
| Male           | 9(29%)            | 22(71%) | 31(100%) | 0.991      | 1.00 |
| Female         | 7(29.2%)          | 17(70.8%) | 24(100%) | 0.336      | 1.28 |
| Ascites        |                   |       |      |            |
| Yes            | 13(34.2%)         | 25(65.8%) | 38(100%) | 0.038a     | 5.45 |
| No             | 3(17.6%)          | 14(82.4%) | 17(100%) | 0.012a     | 1.593 |
| Hepatic Encephalopathy |         |       |      |            |
| Yes            | 5(62.5%)          | 3(37.5%) | 8(100%) | 0.038a     | 3.11-7.25 |
| No             | 11(23.4%)         | 36(76.6%) | 47(100%) |            | 1.265-2.005 |
| Child-Pugh Score |         |       |      |            |
| Class A        | 0(0%)             | 12(100%) | 12(100%) |            | 1.569 |
| Class B-C      | 16(37.2%)         | 27(62.8%) | 43(100%) |            | 1.265-2.005 |

*P<0.05

Table 3. Correlation of GFR and creatinine with the Child-Pugh score.

| Variable | Correlation Coefficient | P   |
|----------|-------------------------|-----|
| GFR      | -0.308                  | 0.022 |
| Creatinine | 0.359                  | 0.007 |

Table 4. Correlation of GFR and creatinine with MELD score.

| Variable | Correlation Coefficient | P   |
|----------|-------------------------|-----|
| GFR      | -0.278                  | 0.040 |
| Creatinine | 0.382                  | 0.004 |

Figure 1. Correlation plot is comparing GFR with Child-Pugh and MELD score.
Figure 2. Correlation plot is comparing creatinine with Child-Pugh and MELD score.

Table 5. Comparison of laboratory parameters among absence of RD, RD group II, RD group I.

| Variables         | Absence of RD (n = 39) | RD Group I (n = 9) | RD Group II (n = 7) | P     |
|-------------------|------------------------|-------------------|--------------------|-------|
| Hemoglobin \(^a\) | 10.54 ± 2.52           | 9.81 ± 2.85       | 10.36 ± 2.75       | 0.78  |
| WBC \(^b\)        | 7.52 (1.86-35.19)      | 10.01 (5.59 - 23) | 7.4 (5.96 - 10.7)  | 0.15  |
| Platelet \(^b\)   | 195.500 (22.000-)      | 145.000 (12.000-) | 130.000(12.000-)   | 0.78  |
| Albumin \(^a\)    | 2.7 ± 0.64             | 1.92 ± 0.84       | 2.43 ± 0.61        | 0.01\(^d\) |
| INR \(^b\)        | 1.22 (0.89 - 3.71)     | 1.2 (0.96 - 2)    | 1.1 (0.94 - 1.61)  | 0.31  |
| Total Bilirubin \(^b\) | 2.25 (0.3 - 17.7)   | 1.3 (0.5 - 12.2)  | 0.6 (0.2 - 3.4)    | 0.09  |
| Direct Bilirubin \(^b\) | 1.1 (0.1 - 13.1)       | 0.9 (0.3 - 8.9)   | 0.3 (0.1 - 2.1)    | 0.10  |
| AST \(^b\)        | 61 (18 - 377)          | 41 (31 - 79)      | 42 (15 - 90)       | 0.05  |
| ALT \(^b\)        | 56.5 (18 - 253)        | 28 (11 - 58)      | 25(12 - 146)       | 0.10  |
| ALP \(^b\)        | 121.5 (40 - 331)       | 148 (58 - 304)    | 83 (50 - 148)      | 0.15  |
| GGT \(^b\)        | 98.5 (16 - 346)        | 48 (31 - 102)     | 56 (13 - 78)       | 0.12  |
| RBG \(^b\)        | 105.5 (53 - 258)       | 102 (62 - 204)    | 95 (72 - 137)      | 0.37  |
| Ureum \(^b\)      | 39.21 ± 19.91          | 103.78 ± 88.64\(^c\) | 102.14 ± 59.13\(^c\) | 0.0001\(^d\) |
| Creatinin \(^b\)  | 0.8 (0.45 - 1.4)       | 4.9(2.76 - 7)\(^c\)  | 1.73(1.51 - 2.49)\(^c\) | 0.0001\(^d\) |
| GFR \(^a\)        | 83.16 ± 27.03          | 13.98 ± 4.53\(^c\) | 33.4 ± 10.72\(^c\) | 0.0001\(^d\) |
| MELD Score \(^b\) | 21 (7 - 36)            | 29 (7-34)\(^c\)  | 27 (18 - 29)       | 0.01\(^d\) |

\(^a\) Numeric data, normal distribution : mean ± SD
\(^b\) Numeric data, abnormal distribution : median (min-max)
\(^c\) the result of this category was significant differences with the absence of RD (p<0.05)
\(^d\) p< 0.05

The liver insufficiency degree, determined by generally accepted Child-Pugh classification, was divided into three stages but in this study, we divided to become two groups 12 patients with CPS class A and 43 patients with CPS class B-C. There was a statistically significant difference of the presented of RD between patients with different stages of liver cirrhosis according to Child-Pugh. In the cirrhotic patients with higher severity of cirrhosis (Child-Pugh class B and C), renal dysfunction was developed much more (OR: 1.59; P<0.012). Gender and the presented of ascites had no significant effect on impairment of renal function (p = 0.991 and p = 0.336 respectively).

Table 3 and figure 1 shows there were statistically significant inverse correlation between GFR and CPS (p = 0.991; r = - 0.308). There were statistically significant correlation between creatinine and CPS (p = 0.007; r = 0.382).
Table 4 and figure 2 shows there were statistically significant inverse correlation between GFR and MELD score (p = 0.04; r = -0.278). There were statistically significant correlation between creatinine and MELD score (p = 0.004; r = 0.359).

Table 5 shows laboratory parameters among this three groups of patient. A simple analysis of variance, ANOVA, revealed there were statistically significant differences in parameters of renal function. Ureum, serum Cr, and GFR were significantly higher in RD patients (p<0.0001) while albumin and MELD score were only significantly higher in RD group I (p<0.01).

4. DISCUSSION

In countries where the brunt of viral hepatitis affected a significant percentage of its population, cirrhosis and its complications continue to be a health problem.[11] Cirrhosis of the liver is often accompanied by functional renal failure particularly in advanced stages of liver disease. Hemodynamic alterations with reduced effective arterial blood volume and peripheral vasodilation are followed by activation of vasoconstrictive hormones (rennin-aldosterone, vasopressin, endothelin) and neurohumoral systems (including increased activity of nervous system).[10] Furthermore, infections, aggressive use of diuretics, repeated large volume paracenteses and gastrointestinal hemorrhage often contributes to RD in these patients cause the pronounced reduction in glomerular filtration rate (GFR).[12]

We found that 29.1% of hospitalized patients with cirrhosis was diagnosed as having RD. Mohan et al. observed RD in 22% of cirrhosis case.[13] We found that liver cirrhosis was more frequent in male than female (56.4%) with mean age is 51.5± 12.6 it is similar with Ira IY who also found that male was the majority (68.8%) with mean age 56.12 years.[14]

This study found a statistically significant relationship between CPS and presented of RD. This finding was similar to Nupur Das et al. who also found a statistically significant relationship between CPS and serum Cr as a parameter of RD.[15] Yun Jung Choi, et al. found in the cirrhosis patients with higher severity of cirrhosis, RD was developed much more.[16]

The MELD score was significantly different from RD group I and patient with normal renal function. Both the CPS and the MELD score correlated positively with serum Cr. These results are confirmed by the research done by Amin et al. (CPS and serum Cr r = 0.556; p< 0.0001, MELD scores and serum Cr r = 0.849; p<0.0001).[11] Habib et al. found serum Cr at transplantation rose progressively from low MELD to high MELD groups with a statistically significant positive correlation (R = 0.44, p = 0.0001).[17] Qureshi et al. found Child-Pugh and MELD scores were significantly higher in RD patients (11±2 vs. 9.4±2; p<0.001 and 19.6±5.7 vs. 16.3±4; p<0.001).[18] Both scores also showed a negative correlation with GFR. These contrast with Culavic D at al which detected no significant correlation between creatinine and MELD score (p = 0.091) and also no significant correlation between GFR and MELD score (p = 0.460).[19]

The laboratory parameters of the patients with decompensated cirrhosis showed abnormal values particularly those related to the synthetic capacity of the liver. The CPS and MELD scores are partially based on some of these parameters. In the present study, there were no statistically significant differences in complete blood count (Hemoglobin, WBC, platelets) and liver function parameter (INR, total bilirubin, direct bilirubin, AST, ALT, ALP, GGT).

5. Conclusions

Significant correlations were observed between renal dysfunction with both Child-Pugh and MELD score. The increase of the degree of liver damage is related to the increase of renal dysfunction. The study emphasizes that we should be more vigilant when treating cirrhotic patients, regarding their renal function, as proper screening, prevention, and treatment of renal dysfunction can decrease morbidity and mortality.

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