Factors associated with renal dysfunction in hepatitis C-related cirrhosis and its correlation with Child-Pugh score

Hamza Waqar Bhatti,¹ Umama Tahir,¹ Noman Ahmed Chaudhary,¹ Sania Bhatti,¹ Muhammad Hafeez,² Zuhair Ali Rizvi³

To cite: Bhatti HW, Tahir U, Chaudhary NA, *et al.* Factors associated with renal dysfunction in hepatitis C-related cirrhosis and its correlation with Child-Pugh score. *BMJ Open Gastro* 2019;6:e000286. doi:10.1136/bmjgast-2019-000286

Received 12 February 2019
Revised 5 April 2019
Accepted 19 April 2019

© Author(s) (or their employer(s)) 2019. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

¹Medicine, Rawalpindi Medical University, Rawalpindi, Pakistan

²CMH Multan Institute of Medical Sciences, Multan, Pakistan

³Medicine, Rawalpindi Medical University, Rawalpindi, Pakistan

Correspondence to

Dr Zuhair Ali Rizvi;
dr.zarizvi@gmail.com

ABSTRACT

Objectives To assess factors associated with renal dysfunction (RD) in hepatitis C virus (HCV) cirrhosis, correlate renal parameters with Child-Pugh score (CPS) and find a cut-off value of CPS to determine RD.

Materials and methods It was a cross-sectional study that included 70 cases of liver cirrhosis secondary to HCV from a period of 6 months at Combined Military Hospital, Multan. Diagnosis of HCV was confirmed by serological assay and liver cirrhosis by ultrasonography. CPS was determined and lab reports were taken. Patients were divided into two groups as not having RD (serum creatinine ≤ 1.5 mg/dL) and having RD (serum creatinine ≥ 1.5 mg/dL). Estimated glomerular filtration rate (eGFR) was calculated by chronic kidney disease epidemiology collaboration (CKD-EPI) formula. Data were analyzed using SPSS V.23.0. χ^2 , Kruskal-Wallis test and Pearson coefficient of correlation were applied. ROC curve was drawn to evaluate cut-off value of CPS for the presence of RD. Level of significance was set at $p < 0.05$. **Results** Patients with CP grade B or C develop RD as compared to patients with CP grade A ($p = 0.000$). Mean age, urea, creatinine and eGFR varies significantly among patients who develop RD and patients who do not ($p = 0.02$, $p = 0.000$, $p = 0.000$ and $p = 0.000$, respectively). eGFR negatively correlates with CPS ($r = -0.359$, $p = 0.002$). Creatinine, urea and ALBI score positively correlates with CPS ($r = +0.417$, $p = 0.000$; $r = +0.757$, $p = 0.000$; $r = +0.362$, $p = 0.002$, respectively).

Conclusion Ascites and encephalopathy are associated with RD in HCV cirrhosis.

INTRODUCTION

Hepatitis C is a liver disease that is caused by hepatitis C virus (HCV), which can cause both acute and chronic hepatitis.¹ Hepatitis C is a major health problem worldwide.^{2,3} Approximately 170 million^{2,3} to more than 185 million⁴ people are infected globally with a worldwide prevalence of 2.8%.⁴ Hepatitis C is becoming an increasing social, economic and health burden.^{2,3} In Pakistan, the prevalence of HCV is from 5%⁵ to 6.8%,⁴ which

Summary box

What is already known about this subject?

► Renal involvement in liver cirrhosis is a well-known phenomenon. Child-Pugh score (CPS) is used to predict the severity of liver dysfunction. However, creatinine levels are used to determine the severity of renal dysfunction (RD).

What are the new findings?

► The present study has highlighted a correlation between RD and severity of liver dysfunction measured by CPS in patients with hepatitis C-related liver cirrhosis. A cut-off value of 8.5 of CPS has a sensitivity of 80% and specificity of 60% to predict renal involvement in hepatitis C-related liver cirrhosis.

How might it impact on clinical practice in the foreseeable future?

► The cut-off value of 8.5 of CPS can be used to predict the need for diuretic prescription and to monitor the extent of RD.

is the second highest in the entire world.⁶ About 15%–30% of patients with hepatitis C progress to cirrhosis after 20 years of disease.¹ Approximately, 399 000 people die from liver cirrhosis or hepatocellular carcinoma caused by hepatitis C.¹ About 15%–45% patients infected with HCV recover within 6 months without any treatment whereas the rest 60%–80% become chronically infected.¹

Renal failure is a common complication of decompensated liver cirrhosis.^{7–14} About 40%–49% of patients with liver cirrhosis requiring intensive care eventually develop renal failure.^{7,13} However, 24% of outpatients with liver cirrhosis develop renal failure within 1 year of developing ascites.^{11–14} According to healthcare personnel, the development of renal failure in patients with liver cirrhosis is associated with significant morbidity and mortality and hence, the diagnosis of renal

failure in liver cirrhosis should be early and accurate so that specific treatment be initiated to improve the outcome.^{12 15 16}

There is a spectrum of factors causing acute kidney injury (AKI) in liver cirrhosis including (1) prerenal AKI, which is caused by hypovolaemia due to gastrointestinal bleeding, aggressive diuretic treatment and lactulose-induced diarrhoea or infections, (2) the hepatorenal syndrome-type AKI (HRS-AKI), which is a potentially reversible decline in renal function unresponsive to volume resuscitation, (3) intrinsic causes, such as acute tubular necrosis, and (4) postrenal causes.^{15 17–20} In short, the mechanism of HRS has been explained by increased formation of vasoconstrictors and decreased formation of vasodilators and significant decline in glomerular filtration rate (GFR).^{21 22}

Child and Turcotte first gave a scoring system to predict operative risk in patients undergoing portosystemic shunt surgery for variceal bleeding. Initially, it included ascites, hepatic encephalopathy (HE), nutritional status, total bilirubin and albumin but later, it was modified by Pugh *et al* who added prothrombin time or international normalised ratio and removing nutritional status. Child-Pugh score (CPS) has been useful to find the severity of liver dysfunction in the clinical setting.^{23 24}

The objectives of this study were to determine:

- ▶ the factors associated with renal dysfunction (RD),
- ▶ the correlation between the severity of RD and extent of liver damage and
- ▶ the cut-off value of CPS to predict RD in patients with HCV-induced liver cirrhosis.

MATERIALS AND METHODS

This cross-sectional study included 70 cases of liver cirrhosis secondary to hepatitis C infection from a period of January 2018 to June 2018 at Combined Military Hospital, Multan on patients recruited using consecutive non-randomized sampling technique. We included all the patients from inpatient and outpatient department having hepatitis C-induced liver cirrhosis who were aged ≥ 18 years. Patients having a history of diabetes, diuretic use, hypertension, chronic kidney disease, an abnormal urinalysis, abnormal renal ultrasound and liver cirrhosis secondary to other causes were excluded. There was no patient with alcoholic hepatitis in our study, so no difficulty was encountered in measuring serum creatinine in patients with high bilirubin levels. Diagnosis of HCV was confirmed by serological assay and liver cirrhosis was confirmed by ultrasonography. CPS was determined and lab reports were taken on the same day. RD associated with HCV-induced liver cirrhosis was detected in the patients on study inclusion by serum creatinine at the time of admission. Guidelines of the International Ascites Club's definition were used to define patients having RD on the basis of serum creatinine.²⁵ Patients were divided into two groups as having RD (serum creatinine ≥ 1.5 mg/dL) and not having RD (serum creatinine < 1.5 mg/dL). Estimated GFR (eGFR) was calculated by CKD-EPI

Table 1 Demographic details (n=70)

Variable	N=70
Gender*	
Male	56 (80%)
Female	14 (20%)
Renal dysfunction*	
Yes	30 (43%)
No	40 (57%)
Ascites*	
Yes	40 (57%)
No	30 (43%)
Child-Pugh score*	
A	18 (26%)
B and C	52 (74%)
Hepatic encephalopathy*	
Yes	30 (43%)
No	40 (57%)
Age, years†	55 (IQR=15)

*Categorical variable: n%.

†Numerical data, asymmetric distribution, median (IQR).

collaboration formula.²⁶ HE was diagnosed clinically by an experienced consultant. Grading of HE was done according to grades mentioned in Davidson's Principles and Practice of Medicine.²⁷ Ascites was detected by clinical examination and confirmed by ultrasonography.

Data were analysed using SPSS V.23.0. Normality of quantitative variables was checked by Kolmogorov-Smirnov and Shapiro-Wilk tests. Quantitative variables were described by means in case of normal distribution and medians in case of asymmetric distribution. Qualitative variables were described by their frequencies. χ^2 , Kruskal-Wallis test and Pearson coefficient of correlation was applied. ROC curve was drawn to evaluate cut-off value of CPS for presence of RD. Level of significance was set at $p < 0.05$.

RESULTS

Out of 70 patients with liver cirrhosis, 56 (80%) were males while 14 (20%) were females. The median age was 55 years (IQR=15 years). A total of 40 out of 70 (57%) had ascites while the rest 30 (43%) did not develop ascites. About 30/70 (43%) had HE while the rest 40 (57%) did not. Out of 70 patients, 30 (43%) patients developed RD and 40 (57%) did not develop RD. Demographic details of the patients are presented in [table 1](#). The distribution of patients having HE into the four grades is presented in [table 2](#).

Patients with ascites and encephalopathy are prone to develop RD ($p < 0.000$, OR=32.6; $p = 0.012$, OR=3.5, respectively). Frequency of RD is significantly higher in CP grade B or C patients as compared with patients with CP grade A ($p < 0.000$). RD showed no significant association

Table 2 Distribution of grades of hepatic encephalopathy in patients with HCV-induced liver cirrhosis (n=30)

Grades of hepatic encephalopathy	N (%)
Grade 1	4 (13.33%)
Grade 2	14 (46.67%)
Grade 3	12 (40%)
Grade 4	0 (0%)
Total	30 (100%)

HCV, hepatitis C virus.

with gender ($p \geq 1.00$). These associations are presented in table 3.

Quantitative variables presented in table 4 were asymmetrically distributed, and their medians are reported and compared by Kruskal-Wallis test. The difference in medians of urea, creatinine, eGFR, age and CPS between patients who had developed RD and patients who did not was significant ($p < 0.000$, $p < 0.000$, $p < 0.000$, $p = 0.02$ and $p = 0.001$, respectively), whereas the difference in serum total bilirubin and albumin was insignificant ($p = 0.064$ and $p = 0.18$, respectively).

There was a strong positive correlation between serum creatinine and CPS ($r = +0.757$, $p < 0.000$) (table 5) and inverse correlation between eGFR and CPS ($r = -0.359$, $p = 0.002$) as shown in figure 1.

ROC curve was constructed for finding cut-off value of CPS at which RD develops. Area under ROC curve was 0.730 ($p = 0.001$) for 95% CI. Cut-off value of 8.5 shows 80% sensitivity and 60% specificity as shown in figure 2.

DISCUSSION

In countries where viral hepatitis is a health burden, liver cirrhosis has become an important health problem.²⁸ Liver cirrhosis is accompanied by RD, especially in advanced liver disease. Reduced effective arterial blood volume and peripheral vasodilation cause haemodynamic alterations, which are followed by activation of vasoconstrictors, such as renin, aldosterone, vasopressin, endothelin and increased activity of neurohormonal systems.²⁵

Table 3 Factors associated with renal dysfunction

Variables		Renal dysfunction		Total	P value	OR
Gender	Male	24	32	56	1.000	1.00
	Female	6	8	14		
Ascites	Yes	12	28	40	<0.000*	32.6
	No	18	12	30		
Hepatic encephalopathy	Yes	18	12	30	0.012*	3.5
	No	12	28	40		
Child-Pugh score	A	0	18	18	<0.000*	
	B and C	30	22	52		

* $p < 0.05$ was considered statistically significant**Table 4** Comparison of quantitative variables according to renal dysfunction

Variable	Renal dysfunction		P value
	Yes	No	
Total bilirubin	35.91	23.47	0.064
Albumin	3.2	3.3	0.180
Urea	13.7	3.9	<0.000
Creatinine	150	93.5	<0.000
eGFR	37	83.5	<0.000
Child-Pugh score	10	7	0.001
Age	60	55	0.02

a. All variables are asymmetrically distributed; medians are reported and compared.

b. Significance is calculated by non-parametric Kruskal-Wallis test.

In our study, liver cirrhosis was more frequent in males (80%) than in females (20%). This was consistent with the study conducted by Siregar and Gurning, where 56.4% of males developed liver cirrhosis as compared with 43.6% females.²⁹ However, according to another study, males with liver cirrhosis comprised 68.8% of total patients.³⁰ This may be due to the fact that men are two times more likely to die from chronic liver disease as compared with women³¹ and women clear HCV infection more readily as compared with men.³² There is also a decreased risk of decompensated liver cirrhosis due to HCV in women as compared with men.³³ However, there were only 14 females in our study as compared with 56 males so there may be a lack of sufficient power to strongly support this outcome. Hence, more studies should be conducted with an equal number of cases from both genders to support this.

The median age of cirrhotic patients in our study was 55 years. This is comparable to Siregar and Gurning, where the mean age was 51.51 years.²⁹ However, according to another study, the mean age was 56.12 years.³⁰ It has been shown in several studies that ageing increases the risk of liver fibrosis in hepatitis C infections.^{34–36}

In our study, 43% of patients with liver cirrhosis developed RD, whereas in case of Siregar and Gurning,²⁹ 29.1% of patients developed RD and Mohan *et al*³⁷ reported 22% of patients with RD in liver cirrhosis. Another study by Cheyron *et al*³⁸ showed that AKI occurs in approximately 19% of hospitalised patients with cirrhosis.

Our study shows that patients with ascites and encephalopathy are prone to develop RD ($p = 0.000$, OR=32.6; $p = 0.012$, OR=3.5, respectively). About 30% of the patients

Table 5 Correlation of eGFR and creatinine levels with Child-Pugh score

Variable	Correlation coefficient (r)	P value
eGFR	-0.359	0.002
Creatinine	+0.757	<0.000

eGFR, estimated glomerular filtration rate.

Figure 1 Correlation between eGFR and Child-Pugh score. eGFR, estimated glomerular filtration rate.

with ascites and 60% of the patients with the encephalopathy developed RD. In the study by Siregar and Gurning,²⁹ 34.2% of the patients with ascites and 62.5% of the patients with HE developed RD (OR=1.28 and OR=5.45, respectively). These results are quite comparable to ours. Presence of ascites and encephalopathy are strong indicators of liver cirrhosis, which leads to kidney failure due to HRS. The activation of RAAS and sympathetic nervous system in the kidney causes sodium retention, which, in turn, causes ascites.²⁵ Thus, both decrease synthesis of albumin by the liver in decompensated liver disease and development of HRS converge to produce fluid retention and thus, causing ascites.

Figure 2 ROC for cut-off point for Child-Pugh score for renal dysfunction (AUC=0.730).

RD showed no significant difference among gender because RD was equally prevalent in both males and females (43% in both genders). This was confirmed by Siregar and Gurning,²⁹ where 29% males and 29.2% females with liver cirrhosis developed RD and gender was insignificantly associated with RD in liver cirrhosis. The difference in serum bilirubin (median=35.91 in RD and 23.47 in patients with no RD) and albumin (median=3.2 in RD group and 3.3 in non-RD group) between the patients who developed RD and those who did not develop it was also statistically insignificant in our study. However, Siregar and Gurning²⁹ reported that mean serum bilirubin was insignificant among patients with and without RD (median=2.25 and 1.3, respectively) but the distribution of serum albumin (mean=2.7 and 1.92, respectively) was statistically significant between two groups. Our study shows that median levels of urea, creatinine, eGFR, age and CPS between patients who had developed RD and patients who did not was significant. Siregar and Gurning²⁹ also showed that mean urea, creatinine and eGFR were significantly different among the patients with and without RD.

Our study showed a significant relationship between CPS and RD. RD was significant in patients with CP grade B and C (58%) as compared with those with grade A (0%). Siregar and Gurning²⁹ also found that no one (0%) in grade A of liver cirrhosis developed RD whereas 37.2% of patients with grade B or C developed renal failure. This shows that higher the severity of cirrhosis greater will be the risk of renal injury. To prove this, we correlated the CPS with serum creatinine and eGFR and found a significant direct correlation between serum creatinine with CPS ($r=0.757$, $p=0.000$) and an inverse correlation with eGFR ($r=-0.359$, $p=0.002$). Siregar and Gurning²⁹ also reported a positive correlation between serum creatinine and CPS ($r=0.359$, $p=0.007$) and an inverse correlation between eGFR and CPS ($r=-0.308$, $p=0.022$). This proves that higher the CPS greater will be the kidney injury, so greater will be the serum creatinine and lower will be the eGFR. Das *et al*³⁹ also found that CPS and serum creatinine are significantly correlated with each other. Choi *et al*⁴⁰ also showed that RD was much more common in patients with higher severity of liver cirrhosis.

In our study, we made an ROC curve to find the cut-off point of CPS at which RD can be predicted at maximum sensitivity and specificity and found that CPS of 8.5 shows 80% sensitivity and 60% specificity for detecting a disturbance in kidney function in patients with liver cirrhosis.

CONCLUSION

Ascites and encephalopathy are associated with RD in HCV cirrhosis. Patients with CP B and C are more prone to have RD as compared with CP A. Greater the CPS greater is the extent of renal injury. A cut-off value of CPS 8.5 is highly sensitive to predict RD in HCV-related liver cirrhosis and can be used as screening test due to high

sensitivity. This may help in diuretic prescription for the patients and monitoring the extent of RD.

Contributors HWB planned and designed the study, and contributed in manuscript writing as well. UT contributed in data collection, entry and manuscript writing. NAC analysed the data, contributed in manuscript writing and reviewing the paper. SB contributed in data collection and quality assurance. MH contributed in data collection, technical supervision and patient selection. ZAR submitted the manuscript and did final review of the paper.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval The study is approved by the Institutional Research Forum of Rawalpindi Medical University.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement No additional data are available.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

REFERENCES

1. WHO. Hepatitis C [Internet], 2019. Available: <https://www.who.int/news-room/fact-sheets/detail/hepatitis-c> [Accessed 20 Jan 2019].
2. Lavanchy D. Evolving epidemiology of hepatitis C virus. *Clin Microbiol Infect* 2011;17:107–15.
3. Hajarizadeh B, Grebely J, Dore GJ. Epidemiology and natural history of HCV infection. *Nat Rev Gastroenterol Hepatol* 2013;10:553–62.
4. Naseer A, Ambreen S, Faheem M, et al. Treatment efficacy of sofosbuvir and ribavirin combination at two weeks in chronic hepatitis C. *JRMC* 2017;21:313–6.
5. Al Kanaani Z, Mahmud S, Kouyoumjian SP, et al. The epidemiology of hepatitis C virus in Pakistan: systematic review and meta-analyses. *R Soc Open Sci* 2018;5.
6. WHO. Fighting hepatitis in Pakistan [Internet], 2019. Available: <https://www.who.int/news-room/feature-stories/detail/pakistan-tackles-high-rates-of-hepatitis-from-many-angles> [Accessed 20 Jan 2019].
7. Cárdenas A, Ginès P, Uriz J, et al. Renal failure after upper gastrointestinal bleeding in cirrhosis: incidence, clinical course, predictive factors, and short-term prognosis. *Hepatology* 2001;34:671–6.
8. Sort P, Navasa M, Arroyo V, et al. Effect of intravenous albumin on renal impairment and mortality in patients with cirrhosis and spontaneous bacterial peritonitis. *N Engl J Med* 1999;341:403–9.
9. Follo A, Llovet JM, Navasa M, et al. Renal impairment after spontaneous bacterial peritonitis in cirrhosis: incidence, clinical course, predictive factors and prognosis. *Hepatology* 1994;20:1495–501.
10. Terra C, Guevara M, Torre A, et al. Renal failure in patients with cirrhosis and sepsis unrelated to spontaneous bacterial peritonitis: value of MELD score. *Gastroenterology* 2005;129:1944–53.
11. Martín-Llahí M, Guevara M, Torre A, et al. Prognostic importance of the cause of renal failure in patients with cirrhosis. *Gastroenterology* 2011;140:488–96.
12. Cholongitas E, Senzolo M, Patch D, et al. Cirrhotics admitted to intensive care unit: the impact of acute renal failure on mortality. *Eur J Gastroenterol Hepatol* 2009;21:744–50.
13. Carvalho GCde, Regis CdeA, Kalil JR, et al. Causes of renal failure in patients with decompensated cirrhosis and its impact in hospital mortality. *Ann Hepatol* 2012;11:90–5.
14. Montoliu S, Ballesté B, Planas R, et al. Incidence and prognosis of different types of functional renal failure in cirrhotic patients with ascites. *Clin Gastroenterol Hepatol* 2010;8:616–22.
15. Garcia-Tsao G, Parikh CR, Viola A. Acute kidney injury in cirrhosis. *Hepatology* 2008;48:2064–77.
16. Ginès P, Schrier RW. Renal failure in cirrhosis. *N Engl J Med* 2009;361:1279–90.
17. Hartleb M, Gutkowski K. Kidneys in chronic liver diseases. *World J Gastroenterol* 2012;18:3035–49.
18. Ginès A, Escorsell A, Ginès P, et al. Incidence, predictive factors, and prognosis of the hepatorenal syndrome in cirrhosis with ascites. *Gastroenterology* 1993;105:229–36.
19. Nadim MK, Kellum JA, Davenport A, et al. Hepatorenal syndrome: the 8th International consensus Conference of the acute dialysis quality Initiative (ADQI) group. *Crit Care* 2012;16.
20. Kellum JA, Levin N, Bouman C, et al. Developing a consensus classification system for acute renal failure. *Curr Opin Crit Care* 2002;8:509–14.
21. Gerbes AL. Liver cirrhosis and kidney. *Dig Dis* 2016;34:387–90.
22. Lenz K. Hepatorenal syndrome—is it central hypovolemia, a cardiac disease, or part of gradually developing multiorgan dysfunction? *Hepatology* 2005;42:263–5.
23. Pugh RN, Murray-Lyon IM, Dawson JL, et al. Transection of the oesophagus for bleeding oesophageal varices. *Br J Surg* 1973;60:646–9.
24. Peng Y, Qi X, Guo X. Child–Pugh versus MELD score for the assessment of prognosis in liver cirrhosis. *Medicine* 2016;95:e2877.
25. Salerno F, Gerbes A, Ginès P, et al. Diagnosis, prevention and treatment of hepatorenal syndrome in cirrhosis. *Gut* 2007;56:1310–8.
26. Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. *Ann Intern Med* 2009;150:604–12.
27. Ralston S. *Davidson's principles and practice of medicine*. 857. 23rd ed. Elsevier, 2018.
28. Amin MA, Fawzi M, Sabri D, et al. Liver specific serum micro RNA122as a prognostic marker in Egyptian patients with liver cirrhosis. *Arch Hepat Res* 2017;3:004–9.
29. Siregar GA, Gurning M. Renal dysfunction in liver cirrhosis and its correlation with Child–Pugh score and MELD score. *IOP Conf Ser Earth Environ Sci* 2018;125.
30. Yu I, Abola L. Predicting prognosis among cirrhotic patients: Child–Pugh versus APACHE III versus MELD scoring systems. *Phil. J Gastroenterol* 2006;2:19–24.
31. Rogers RG, Everett BG, Onge JMS, et al. Social, behavioral, and biological factors, and sex differences in mortality. *Demography* 2010;47:555–78.
32. Kenny-Walsh E. Clinical outcomes after hepatitis C infection from contaminated anti-D immune globulin. Irish Hepatology Research Group. *N Engl J Med* 1999;340:1228–33.
33. Guy J, Peters MG. Liver disease in women: the influence of gender on epidemiology, natural history, and patient outcomes. *Gastroenterol Hepatol* 2013;9:633–9.
34. Poynard T, Ratzu V, Charlotte F, et al. Rates and risk factors of liver fibrosis progression in patients with chronic hepatitis C. *J Hepatol* 2001;34:730–9.
35. Forrest EH, Evans CDJ, Stewart S, et al. Analysis of factors predictive of mortality in alcoholic hepatitis and derivation and validation of the Glasgow alcoholic hepatitis score. *Gut* 2005;54:1174–9.
36. Kim IH, Kisseleva T, Brenner DA. Aging and liver disease. *Curr Opin Gastroenterol* 2015;31:184–91.
37. Mohan Jet al. Clinical profile of renal dysfunction in cirrhotic liver. *Int J Biomed Res* 2016;7:73–6.
38. du Cheyron D, Bouchet B, Parienti J-J, et al. The attributable mortality of acute renal failure in critically ill patients with liver cirrhosis. *Intensive Care Med* 2005;31:1693–9.
39. Das N, Bhattacharyya A, Paria B, et al. Study on assessment of renal function in chronic liver disease. *J Clin Diagn Res* 2015;9:OC09–OC12.
40. Choi YJ, Kim JH, Koo JK, et al. Prevalence of renal dysfunction in patients with cirrhosis according to ADQI-IAC Working Party proposal. *Clin Mol Hepatol* 2014;20:185–91.