Original Article

Electrolytes Derangements with Hepatitis C

Correlation of Electrolytes Derangements with Hepatitis C induced Liver Cirrhosis Severity Indices

Muhammad Saleem Akhter[1], Muhammad Arif Mahmood[1], Hooria Bhatti[3], Muhammad Waqar Saleem[4], Ahsanullah M Mirbahar[2] and Junaid Riaz[1]

ABSTRACT

Objective: To find Correlation of Electrolytes Derangements with Hepatitis C induced Liver Cirrhosis Severity Indices.

Study Design: A cross-sectional study

Place and Duration of Study: This study was conducted at the Study was conducted at the department of medicine, Nishtar Medical University/Hospital, Multan, from April 2020 to Dec 2020.

Materials and Methods: We studied on 54 HCV infected cirrhotic patients confirmed by presence of Anti-HCV antibodies/ HCV RNA by PCR in their serum. MELD Score, Child-Pugh Score and Child-Pugh Class were calculated. Routine serum electrolytes were measured and electrolytes abnormalities were assessed for any significant relationship with MELD Score, Child-Pugh Score and Child-Pugh Class.

Results: Linear curve estimation analysis of Child Pugh score with sodium, potassium, calcium, phosphate and magnesium showed a statistically significant relationship ($p<0.05$) with Pearson correlation coefficient (r) 0.391, 0.125, 0.460, 0.370 and 0.087 respectively. Linear curve estimation analysis of MELD score with sodium, potassium, calcium, phosphate and magnesium showed a statistically significant relationship ($p<0.05$) with Pearson correlation coefficient (r) 0.430, 0.284, 0.129, 0.296, and 0.012 respectively. Chi Square test indicated a statistically significant association between sodium, potassium, calcium, phosphate and magnesium with Child Pugh class ($p<0.05$).

Conclusion: Our data suggest moderate to strong relationship between various electrolytes abnormalities with MELD Score, Child-Pugh Score and Child-Pugh Class in Hepatitis C induced liver Cirrhosis.

Key Words: Hepatitis C induced cirrhosis, Electrolytes Abnormalities, MELD Score, Child-Pugh Score, and Child-Pugh Class.

Citation of article: Akhter MS, Mahmood MA, Bhatti H, Saleem MW, Mirbahar MA, Riaz J. Correlation of Electrolytes Derangements with Hepatitis C induced Liver Cirrhosis Severity Indices. Med Forum 2021;32(2):16-19.

INTRODUCTION

Chronic viral hepatitis C infection has more prevalence in developing countries with low to limited national per capita income [(1)]. Trickey et alreported in 2017 that, the infection of hepatitis C is more prevalent in Egyptianthan in Pakistani population [(2)].

[1.] Department of Medicine / PHRC Research Centre[2], Nishtar Medical University, Multan.
[3.] Final Year Student, CMH Institute of Medical Sciences, Multan.
[4.] Final Year Student, Bakhtawar Amin Medical & Dental College, Multan.

Correspondence: Dr. Muhammad Saleem Akhter, Associate Professor of Medicine, Nishtar Medical University, Multan.
Contact No: 03006338517
Email: asaleem913@gmail.com

Received: January, 2021
Accepted: January, 2021
Printed: February, 2021

According to this survey, 9 million Pakistanis are infected with hepatitis C which are about 4.9% of country's population[2]. Most commonly we encounter hepatitis C virus which, in most cases, progresses to chronic hepatitis disease/cirrhosis[(3,4)].The progression can be slow or rapid, consistent or inconsistent depending upon the degree of active tissue inflammation and damage[5]. It usually progresses gradually over many years[6]. Hepatitis C virus does not cause cell death directly but provoke immune inflammatory response such as chronic injury to hepatocytes causes release of IL-2 and various other cytokines to stimulate Ito cells and fibroblasts to start synthesizing collagen type-I especially that result in progressive fibrosis, hepatocellular damage and cell death[7]. Cirrhosis and its associated complications are important cause of morbidity and mortality. Chronic liver disease starts with a non-specific symptoms labelled as compensated liver cirrhosis until the development of complications like ascites, jaundice and encephalopathy when it is called as decompensated liver cirrhosis. Different parameters are used for the grading of liver cirrhosis which are grouped as MELD

Score, Child-Pugh Score and Child-Pugh Class. Child-Pugh is simple and convenient prognostic measure to judge prognosis of liver cirrhosis. In Child-Pugh Class A& B, one year survival is about 70% and Child-Pugh Class C survival is poor. There is a connection between liver disease and Electrolyte imbalance and this imbalance has been observed in many studies[8]. Major electrolytes imbalance associated with cirrhosis is sodium concentration, and hyponatremia is commonly observed in30-48% cases of cirrhosisin different studies[9,10,11]. Chronic hyponatremia is labelled when sodium concentration is below 130 mEq/L and is present in about 22% of patients of cirrhosis[12]. These patients are usually asymptomatic when sodium concentration is above 120 mEq/L[9]. The hyponatremia is as a result of excessive water retention in comparison to sodium and other solutes. Resultant less amount of water excreted in urine as compared to water ingested leads to dilutional hyponatremia. Hyponatremic patients have less survival as compared to the patients who do not have hyponatremia[13]. According to different studies, hyponatremia is an important prognostic factor in cirrhotic patients and its weightage key factor in MELD score[14]. On other hand hypernatremia is also associated with higher mortality in cirrhotic, although it is uncommon. Increased renin release by kidney leads to secondary hyperaldosteronism and in cirrhotic patient's comparative solute free water retention causes dilutional hyponatremia. Hepatic dysfunction leads to potassium depletion to extent that potassium supplements and correction should be considered in the management. At any stage of liver disease, electrolyte imbalance can occur but cirrhosis is main culprit. Cirrhosis and hepatitis are the cause of serum and urinary electrolyte imbalance[15]. The aim of our study was to observe correlation of electrolytes derangements with hepatitis C induced liver cirrhosis severity indices.

MATERIALS AND METHODS

This study was carried out at department of medicine, Nishtar Medical University/Hospital, Multan. Before data collection we shared protocol of our study to all participants for the clarification of patient's concepts about our study, then Informed consent was obtained from those patients who were willing for participation in this research. This study was carried out from 28 April 2020 to 29 Dec 2020. Only infected with hepatitis C patients having chronic history were identified among the patients who were visiting medical ward and OPD of Nishtar hospital, Multan, and they were positive for HCV antibodies/detected positive HCV RNA by Polymerase Chain Reaction (PCR). Patient who had history of co-infection i.e; HBV/HCV and HCV/HIV and known patient of liver cancer were not included in the study. Total 54 patients were engaged over this period. Quantitative determination of the baseline viral load obtained by PCR and biomarkers (liver function tests (LFTs), albumin, bilirubin, prothrombin time and Complete Blood Count (CBC) were done. MELD Score, Child-Pugh Score and Child-Pugh Class were calculated. Routine serum electrolytes were measured and electrolytes abnormalities were assessed for any significant relationship with MELD Score, Child-Pugh Score and Child-Pugh Class.

RESULTS

We studied 54 patients, out of which 32(59.3%) were males and 22(40.7%) females. Twenty (37%) were government employee, 18(33.4%) laborer and 16 (29.6%) housewives by profession. Thirty (55.6%) were of Child-Pugh class B, 18(33.4%) were in class C. Patients with normal serum sodium were 36 (66.7%), hyponatremia 16 (29.6%) and hypernatremia 2 (3.7%). There was normal potassium in 36(66.7%), hypokalemia in 8 (14.8%), hyperkalemia in 10 (18.5%) subjects. Patients with normal serum calcium were 10(18.5%) and hypocalcemic were 44(81.5%). Subjects with normal serum phosphate levels were 42(77.8%) and hypophosphatemia were 12(22.2%). Patients with normal serum magnesium 44 (81.5%), hypomagnesemia 6 (11.1%) and hypermagnesemia were observed in 4 (7.4%). Electrolytes abnormalities distribution is given in table no.1.

Table No.1: Distribution of electrolytes abnormalities among study cases

Electrolytes	N/Percentage	p value*
Sodium 1. Normal 2. Hyponatremia 3. Hypernatremia	 36 (66.7%) 16 (29.6%) 2 (3.7%)	 0.020
Potassium 1. Normal potassium 2. Hypokalemia 3. Hyperkalemia	 36 (66.7%) 8 (14.8%) 10 (18.5%)	 0.012
Calcium 1. Normal calcium 2. Hypocalcemia 3. Hypercalcemia	 10 (18.5%) 44 (81.5%) NIL (0%)	 0.023
Phosphate 1. Normal phosphate 2. Hypophosphatemia 3. Hyperphosphatemia	 42 (77.8%) 12 (22.2%) NIL (0%)	 0.010
Magnesium 1. Normal magnesium 2. Hypomagnesemia 3. Hypermagnesemia	 44 (81.5%) 6 (11.1%) 4 (7.4%)	 0.040

*Chi Square Test results with Child Pugh Class and various electrolytes levels.

Table No.2: Descriptive statistics of our study population.

Variables	Mean	Std. Deviation
Age	41.33	11.11
Height	168.40	5.51
Weight	72.03	25.09
CHILD-Pough SCORE	9.29	1.21
MELD Score	15.52	3.03
Hb	9.51	1.43
T. Bilirubin	1.51	0.28
AST	58.59	56.02
ALT	82.44	49.55
ALP	160.08	93.25

Linear curve estimation analysis of Child Pugh score with sodium, potassium, calcium, phosphate and magnesium showed a statistically significant relationship ($p<0.05$) with Pearson correlation coefficient (r) 0.391, 0.125, 0.460, 0.370 and 0.087 respectively.

Linear curve estimation analysis of MELD score with sodium, potassium, calcium, phosphate and magnesium showed a statistically significant relationship ($p<0.05$) with Pearson correlation coefficient (r) 0.430, 0.284, 0.129, 0.296, and 0.012 respectively.

Table No.3: Pearson correlation coefficients (r) values of Child Pugh score and MELD Score with various electrolytes

Electrolytes	MELD Score (r) value	Child-Pugh Score (r) value
Sodium	0.430	0.391
Potassium	0.284	0.125
Calcium	0.129	0.460
Phosphate	0.296	0.370
Magnesium	0.012	0.087

*Chi Square test indicated a statistically significant association between sodium, potassium, calcium, phosphate and magnesium with Child Pugh class ($p<0.05$)

DISCUSSION

Chronic viral infection causes multiple waves of inflammation and tissue repair which involves deposition of extracellular matrix resulting in scarring or progressive fibrosis over time and ultimately liver cirrhosis occurs[6]. Most commonly we encounter hepatitis C virus which, in most cases, progresses to chronic hepatitis disease/cirrhosis. Chronic liver disease starts with a non-specific symptoms labelled as compensated liver cirrhosis until the development of complications like ascites, jaundice and encephalopathy when it is called as decompensated liver cirrhosis. Cirrhosis and its associated complications are important cause of morbidity and mortality. Different parameters are used for the grading of liver cirrhosis which are grouped as MELD Score, Child-Pugh Score and Child-Pugh Class. Child-Pugh is simple and convenient prognostic measure to judge prognosis of liver cirrhosis. In Child-Pugh Class A & B, one-year survival is about 70% and Child-Pugh Class C survival is poor [(16)]. Actually, liver failure, in most cases, develops gradually over the years. One of the feared complication of cirrhosis is electrolytes abnormalities. Kim et al. showed that 3.9% of the hyponatremic patients were likely to develop hepatorenal syndrome and its associated complications which are one of the most deadly outcomes associated with cirrhotic patients[9]. In cirrhotic patients there is dilutional type of hyponatremia. Fluid intake restriction half or less than output can correct false hyponatremia. Severity of hepatic disease also result in hypokalemia. Major electrolytes imbalance associated with cirrhosis is sodium concentration and hyponatremia is commonly observed in more than 57% of hospitalized cirrhotic patients[17]. Chronic hyponatremia is labelled when sodium concentration is below 130 mEq/L and is present in about 22% of patients of cirrhosis[12]. The hyponatremia is as a result of excessive water retention in comparison to sodium and other solutes. Resultant less amount of water excreted in urine as compared to water ingested leads to dilutional hyponatremia. Hyponatremic patients have less survival as compared to the patients who do not have hyponatremia. According to different studies, hyponatremia resulted due to reduced solute-free water clearance was a prognostic factor in hyponatremic patients in cirrhosis when sodium was incorporated into the MELD score[13].

In our study 29.6% patients were hyponatremic. Borroni et al[11] reported same result 29.8%, while higher level of hyponatremia which may be due to different demographic and large study population are reported by Angeli[10] et al and Kim et al[9] that is 49.4% and 47.9%. While near to our finding 35% of hyponatremia in cirrhotic patients was also reported in Bangladesh by Mamun et al[14] which is also closed to our study results.

Hypokalemia was observed in 14.8% cases in our study. Ahmed et al[18] reported similar results 14% and Alam et al[19] also reported 18% which is near to our study result. Diet, GIT loss and diuretic treatment can change potassium levels. Cirrhotic patients without edema or ascites may have total low body potassium level in presence of normal serum potassium. Potassium supplementation should be given orally or intravenously.

Our study showed that linear curve estimation analysis of Child Pugh score with sodium, potassium, calcium, phosphate and magnesium showed a statistically significant relationship ($p<0.05$) with Pearson correlation coefficient (r) 0.391, 0.125, 0.460, 0.370 and 0.087 respectively. Linear curve estimation analysis of MELD score with sodium, potassium, calcium, phosphate and magnesium showed a statistically significant relationship ($p<0.05$) with Pearson correlation coefficient (r) 0.430, 0.284, 0.129, 0.296, and 0.012 respectively. Chi Square test indicated a statistically significant association between sodium, potassium, calcium, phosphate and magnesium with

Child Pugh class ($p<0.05$). Hence hyponatremia and hypokalemia needs to be corrected immediately and electrolytes should be kept in check. This can improve prognosis. Our study also reported same results which were demonstrated by Borroni et al[11], Ahmed et al[18] and Alam et al [(19)] about frequency of hyponatremia and development of various complications due to cirrhosis and its associated electrolytes derangements. We also recommend control other confounding factors for various electrolytes. Hepatic dysfunction leads to potassium depletion to the extent that potassium supplements are necessary. At any stage of liver disease, electrolyte imbalance can occur but cirrhosis is main culprit. Our data suggested moderate to strong relationship between various electrolytes abnormalities with MELD Score, Child-Pugh Score and Child-Pugh Class in Hepatitis C induced liver Cirrhosis. So, we recommend that Hepatitis C patients should be treated as early as possible and meanwhile their electrolyte should be kept in check to avoid any associated complication like arrhythmias, hypotension, peripheral edema and CVS complications.

CONCLUSION

Our data suggest moderate to strong relationship between various electrolytes abnormalities with MELD Score, Child-Pugh Score and Child-Pugh Class in Hepatitis C induced liver Cirrhosis.

Author's Contribution:

Concept & Design of Study:	Muhammad Saleem Akhter
Drafting:	Muhammad Arif Mahmood, Hooria Bhatti
Data Analysis:	Muhammad Waqar Saleem, Ahsanullah M Mirbahar and Junaid Riaz
Revisiting Critically:	Muhammad Saleem Akhter, Muhammad Waqar Saleem, Ahsanullah M Mirbahar and Junaid Riaz
Final Approval of version:	Muhammad Saleem Akhter

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Liaw YF. Antiviral therapy of chronic hepatitis B: opportunities and challenges in Asia. J Hepatol 2009;51(2):403-10.
2. Trickey A, May MT, Davies C, Qureshi H, Hamid S, Mahmood H, et al. Importance and contribution of community, social, and healthcare risk factors for hepatitis C infection in Pakistan. Am J Tropical Med Hygiene 2017;97(6):1920-8.
3. Al Kanaani Z, Mahmud S, Kouyoumjian SP, Abu-Raddad LJ. The epidemiology of hepatitis C virus in Pakistan: systematic review and meta-analyses. Royal Society Open Sci 2018;5(4):180257.
4. Vegnente A, Larcher VF, Mowat AP .Duration of chronic active hepatitis and the development of cirrhosis. Arch Dis Child 1984;59(4):34.
5. Tsochatzis EA, Bosch J, Burroughs AK. Liver cirrhosis. Lancet 2014;383:1749-61.
6. Iredale JP. Models of liver fibrosis: exploring the dynamic nature of inflammation and repair in a solid organ. J Clin Invest 2007;117(3):539.
7. Keltch B, Lin Y, Bayrak C. Comparison of AI techniques for prediction of liver fibrosis in hepatitis patients. J Med Syst 2014;38(8):60.
8. Baldus WP, Feichter RN, Summerskilll WH, Hunt JC, Wakim KG. The kidney in cirrhosis Disorders of renal function. Annn Int Med 1964;60:366-77.
9. Kim WR, Biggins SW, Kremers WK, Wiesner RH, Kamath PS, Benson JT, et al. Hyponatremia and mortality among patients on the liver-transplant waiting list. N Engl J Med 2008;359(10):1018–1026.
10. Angeli P, Wong F, Watson H, Gines P. Hyponatremia in cirrhosis: results of a patient population survey. Hepatol 2006;44:1535-42.
11. Borroni G, Maggi A, Sangiovanni A, Cazzaniga M, Salerno F. Clinical relevance of hyponatremia for the hospital outcome of cirrhotic patients. Dig Liver Dis 2000; 32:605-10.
12. Ginès P, Guevara M. Hyponatremia in cirrhosis: pathogenesis, clinical significance, and management. Hepatol 2008;48(3):1002–10.
13. Moreau R. Hyponatremia in cirrhosis: Pathophysiology, prevalence, prognostic value & treatment. Acta Gastroenterol Belg 2008;71(4): 379–85.
14. Mamun AA, Mridha MJ, Alam K, Asraf MS, Ferdoushi S, Majid F. Correlation between the serum sodium and the severity of liver disease in cirrhotic patients. Bangladesh Med J 2013;42(3): 73-7.
15. Epstein M. Deranged sodium hemostasis in cirrhosis. Gastroentrol 1979;76(3):622-35.
16. Usman M, Anjum AH, Ahmed SM, Rafiq S, Mahmood MA, Akhtar MS, et al. Assessment of Severity of Cirrhosis in Hospitalized Patients. Esculapio 2005;1(3):5-10.
17. Kumar VS, Ashok A. Study of Correlation between Serum Sodium and Severity in Chronic Liver Disease. Int J Sci Stud 2020;8(4):122-6.
18. Ahmed I, Amin ZA, Ashraf HM. Determination of factors precipitating encephalopathy in patients with liver cirrhosis. Pak Armed Forces Med J 2006;56(3): 284-8.
19. Alam I, Razaullah, Haider I, Humayun M, Taqweem MA, Nisar M. Spectrum of precipitating factors of hepatic encephalopathy in liver cirrhosis. Pak J Med Res 2005;44(2): 96-100.