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Use of Non-invasive markers in Predicting the Severity of Esophageal Varices in Liver cirrhosis: A Hospital Based Descriptive Observational Study

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Abstract

Introduction: Dyselectrolytemia is frequently associated phenomenon in patients with chronic liver disease (CLD). These disorder occur due to multiple patho-physiologic mechanism and has significant impact in the morbidity, prognosis and mortality of the patient. This study aims to find out prevalence and severity of electrolytes imbalance in hospitalized patients with chronic liver diseases.

Methods: A descriptive cross-sectional study was carried out in the medical ward and ICU of Pokhara Academy of Health Sciences from 15 June 2022 to 15 May 2023. Sixty seven patients with established CLD were included in the study after ethical approval was obtained. Demographic profile, clinical features and relevant biochemical investigations were performed and recorded. Data were entered and coded in Microsoft excel and analysis was performed in Statistical Package for Social Sciences version 23.

Results: Hyponatremia 25 (37.3%) was the most common electrolyte disturbance followed by hypomagnesaemia 8 (11.94%), hypokalemia 7 (10.44%), hyperkalemia 5(7.46%) and hypocalcaemia 5(7.46%).Mild hyponatremia 15(22.89%) was predominant electrolyte imbalance.

Conclusion: Electrolytes imbalance is common in patients with CLD, most common being hyponatremia, hypokalemia, hyperkalemia, hypomagnesaemia and hypocalcaemia. These prevalence are higher in CTP class C patients.

Keywords: Chronic liver diseases, Cirrhosis, Electrolyte imbalance, Hyponatremia,, Dyselectrolytemia

Introduction

Cirrhosis of liver is defined as the fibrotic replacement of liver tissue that can result from any chronic liver disease as a result of alcohol use disorder (approximately 45%), hepatitis C (41%), nonalcoholic fatty liver disease (26%). Cirrhosis causes disturbances in fluid balance resulting in ascites, or increased fluid within the abdominal cavity. Electrolytes disturbances in chronic liver disease is a common phenomenon due to several factors like dietary restriction, poor appetite, nausea, vomiting, neuro-humoral renal angiotensin aldosterone activation system (RAAS) activation, use of drugs like diuretics and malabsorption. Though, hyponatremia has been found to be the most common electrolyte disturbance, other electrolyte disturbances varies differently depending on the etiology and disease severity[1].

Despite the established fact, there is lack of data focusing in the electrolyte disturbance among the chronic liver disease patients in Nepal. This study was conducted with the aim to identify the prevalence of electrolyte disturbance among the chronic liver disease patients admitted in the hospital.

Methods

This is a hospital-based cross-sectional observational study which was conducted among 67 CLD patients who were admitted to the medical ward & intensive care unit (ICU) of Pokhara Academy of Health Sciences in period of one 12 months (15 June 2022 to 15 May 2023). Ethical clearance was obtained from institutional review board (Ref no 89/079). The aim of the study was to identify the prevalence of electrolyte imbalances in admitted patients with chronic liver disease.

For calculation of sample size, prevalence of hyponatremia was taken as 5.25% with 95% confidence interval and margin of error 5.5 %. The calculated sample is 64, there were 67 patients admitted in the period of one year so additional three patients

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were included.

Written consent was taken from all of the patients prior to the enrollment. Detailed history and physical examination were carried out, biochemical tests; complete blood count (CBC), Liver function tests (LFT), renal function tests (RFT), Prothrombin time and International normalize ratio (PT/INR), serum calcium, serum magnesium, random blood glucose, Hepatitis B surface antigen (HBsAg) and Anti hepatitis C virus (HCV) antibodies were performed and data was collected. Automated electrolytes analyzer (Integraded Mindray system M1000 with ISE module biochemistry 2800 M) was used for determining electrolytes.

Patients with chronic kidney disease, any malignancies and heart failure and taking drugs like selective serotonin intake inhibitors, tricyclic antidepressants calcium, magnesium or sodium supplements were excluded.

The collected data were entered and coded in Microsoft Excel 2010 and then exported to Statistical Package for the Social Sciences version 23 for statistical analysis. The frequency, percentages, and mean (SD) were estimated.Unpaired ttest, oneway analysis of variance (ANOVA), and Chisquare test were applied. P value of <0.05 consider as statistically significant.

Results

Sixty seven patients with chronic liver disease were include in the study. Mean age of the patients were 53±12.58 years (Range: 22-80 years).Two patients (2.98%) were under nutrition (BMI <18.5kg/m2) and 3 (4.77%) had grade II (BMI≥ 30kg/m2) obesity, however 28 patients (41.79%) patients have normal BMI (18.5-22.9 kg/m2). Hyponatremia 25(37.31%) was the most common electrolyte disturbance followed by hypomagnesaemia 8(11.94%), hypokalemia in 7 (10.44%), hyperkalemia occurs in 5(7.46%).

Table 1: Electrolytes imbalance

SN	Electrolytes imbalance	n(%)
1	Hyponatremia	25 (37.31)
2	Hypomagnesaemia	8 (11.94)
3	Hypokalemia	7 (10.44)
4	Hyperkalemia	5 (7.46)
5	Hypocalcaemia	5 (7.46)
6	Hypernatremia	3 (4.47)

Mild hyponatremia 15(22.89%) was the most common finding followed by moderate hyponatremia 9(13.43%), mild hypomagnesaemia 7(10.44%) and mild hypokalemia 7(10.44%).

Table 2: Severity of different electrolytes imwbalance

SN	Electrolyte imbalance	Severity	n (%)
1	Hyponatremia	Mild (130-134 mEq/L)	15 (22.89)
		Moderate (125-129 mEq/L)	9 (13.43)
		Severe(<125 mEq/L)	1 (1.49)
2	Hypokalemia	Mild (3.0- 3.4 mEq/L)	7 (10.44)
		Moderate(2.5-2.9 mEq/L)	0
		Severe(<2.5 mEq/L)	0
3	Hyperkalemia	Mild (5.6 – 6.5 mEq/L)	5 (7.46)
		Moderate (6.5-7.5 MEq/L)	0
		Severe (> 7.5 mEq/L)	0
4	Hypocalcemia	Mild(8.4-7.5 mg/dl)	5 (7.46)
		Severe (< 7.5 mg/dl)	0
5	Hypomagnesemia	Mild (1.2- 2.0 mg/dl)	7 (10.44)
		Severe(<1.2 mg/dl)	1 (1.49)

Most common presentation was abdominal distension 60(89.55%) followed by jaundice 49(73.13), fatigue 17 (25.37%), gastrointestinal bleeding 14 (20.89%), altered sensorium 11(16.4%) and drowsiness 10 (10.44%).

Table 3: Presenting complain

SN	Symptoms	n (%)
1	Abdominal Distention	60(89.55)
2	Jaundice	49 (73.13)
3	Fatigue	17 (25.37)
4	GI bleeding	14 (20.89)
5	Alcohol craving	11 (16.41)
6	Altered sensorium	11 (16.41)
7	Drowsiness	10 (14.92)
8	Nausea/Vomiting	7 (10.44)
9	Itching	6 (8.95)
10	Abnormal behavior	6 (8.95)
11	Tremor	5 (7.46)
12	Muscle cramps	5 (7.46)
13	Seizure	1 (0.01)

Biochemical investigation of the participants were as follows:

Table 4: Lab investigations

SN	Tests	Mean±SD
1	Total serum bilirubin (mg/dl)	6.24 ±5.83
2	ALT (IU/L)	81.69 ±166.62
3	AST (IU/L)	177.65 ±454.00
4	ALP (U/L)	194.22 ±123.63
5	Serum albumin (mg/dl)	2.73 ±0.67
6	PT (sec)	22.70 ±11.09
7	INR	1.92 ±1.04
8	RBS (mg/dl)	122.94 ±54.22
9	Blood urea (mg/dl)	45.75 ±41.58
10	Serum creatinine (mg/dl)	1.20 ±0.84
11	Serum sodium (mEq/L)	135.66 ±5.66
12	Serum potassium (mEq/L)	4.23 ±0.67
13	Corrected Calcium(mg/dl)	9.62 ±0.77
14	Serum magnesium(mg/dl)	1.91 ±0.44
15	Total blood count ($mm^{3)}$)	10133.8 ±6687.9
16	Mean corpuscular volume (fl)	96.6±11.07

Among these patients Child Turcotte Pugh (CTP) class A 5 (7.5%), CTP B 18(26.9%) and CTP C 44 (65.7). The commonest cause of CLD was alcohol 63(94.3%) followed by chronic hepatitis B viral infection 3 (4.5%) and nonalcoholic fatty liver diseases 1 (1.5%).

Discussion

In this study, mean age of the patient was 53±12.58 years which is comparable to study conducted by Poudel SC et al where mean age was 49.69±10.94. Minimum age was 22 years and maximum age 80 years. These variation was possibly due to young patients who consumes alcohol higher amount than elderly one. Male gender was predominant (71.6%) which is similar to study conducted by Poudel SC12[13].Gender preponderance is possibly due to male dominant society and higher BMI than female.Most (41.72%) of the patients had BMI of (18.5-22.9 kg/m2) which is similar to study conducted by Khadka D et al showing median BMI of 23.64 kg/m2.

In our study commonest presenting complain of these patients were abdominal distension (89.55%), jaundice (73.13%), fatigue (25.37%), GI bleeding (20.89%) and alcohol craving. Clinical features like jaundice (79.1 %), pedal edema (79.1%), pallor (59.7%), fetor hepaticus (16.4%) and ascites (88.1%). These findings were similar to study conducted by Bhattarai S where jaundice was (74.2%), pedal edema (60.5%), pallor (72.2%) and ascites (92.5%).Lab investigations showed mean serum bilirubin 6.24±5.83 mg/dl with maximum level 28.5 mg% which may be due to alcoholic hepatitis or herbal induced liver injury. Mean AST was higher than ALT (177.65±454.0 IU/L versus 81.69±166.62 IU/L) suggestive of alcohol abuser of underlying alcoholic hepatitis. These finding were similar to Maskey R colleague's studies where mean ALT 63.34±97.59 IU/L, mean AST 127±98.37 IU/L. Mean Albumin in our study was 2.3±0.67 mg/dl, while in Maskey R[17] study was higher 2.73±0.50 mg/dl. Likewise in this study mean serum urea was 45.75±41.58 mg/dl, creatinine 1.2±0.84mg/dl which is comparable to Maskey R[17] study.

In our study hyponatremia was noted in 37.15% (Mild 14%, moderate 9% and severe 1%) likewise in similar study conducted by Bhandari A and coworker in year 2021 observed hyponatremia 41.77% ((32.18-50.25 at 95% Confidence Interval)

Similarly,hypernatremia was seen in 3(4.47%) patients which was possibly by using lactulose use causing diarrhea or due to UGI bleeding. Mild hypokalemia was seen in 7(10.44%) patients was possibly due to diuretics.In a study entitled prevalence of hypokalemia in 120 patients conducted by Izhar S where prevalence of hypokalemia was 20(16.7%). Prevalence of hypokalemia was lower in our study possibly due to etiology of cirrhosis (Ethanol versus Hepatitis B and hepatitis C). Potassium status of cirrhotic patients is affected adversely by many factors including diet, diuretic use or gastrointestinal losses

In our study prevalence of hyperkalemia was 7.46% which is low in compare to study done by Singh Y et alwhere prevalence was 13%.Likewise prevalence of hypocalcaemia in our study was 7.46% which is again low in compare to study conducted by Singh Y et al[20] which shows 16%. Hypocalcaemia occurs in cirrhosis due to poor nutrition, vitamin D deficiency, blood transfusion or use of diuretics.Similarly, hypomagnesaemia was found in 8(11.94%) which is lower than study conducted by Gandhi N et al where prevalence was 42.8%. Most common causes of hypomagnesaemia was diuretic use, vomiting, poor absorption or alcohol abuser.

Diagnosis of dyselectrolytemia and its correction in patients with CLD has paramount importance as many patients had hepatic encephalopathy due to hypokalemia. Model for end stage liver disease (MELD) is mathematical model where we can determine the short term mortality (within 90 days) When sodium incorporated with MELD which is popularly known as MELD Na which had similar sensitivity and predicts for short term mortality or need for liver transplant or liver related mortality in alcoholic hepatitis, acute liver failure. Seizure may be manifestations of severe hyponatremia. Severe hyponatremia usually managed by fluid restriction, stoppage of diuretics (if any) and occasionally with hypertonic saline.

European association of study of liver (EASL) clinical practice guidelines 2018suggestions in decompensated CLD are A) Frequent clinical and biochemical monitoring should undergo in patients with cirrhosis during first week of treatment.B) Electrolytes imbalances (Hyponatremia, hypokalemia) should be corrected prior to initiation of diuretics therapy in patients with hepatic encephalopathy, renal impairment. C) Diuretics should be discontinued if severe hyponatraemia(serum sodium concentration <125 mmol/L) acute kidney injury. D) Furosemide should be stopped if severe hypokalemia occurs (<3 mmol/L) and anti-mineralocorticoids should be stopped if severe hyperkalemia occurs (>6 mmol/L).

Regarding symptoms of electrolytes imbalance jaundice (p= 0.017) and itching (p=0.042) were significant in calcium group. Likewise calcium group was significant in CTP class A (p=0.03). Most of the other symptoms are insignificant.

Conclusion

Electrolytes imbalance were frequently occurs in patients with decompensated chronic liver diseases. Commonest electrolytes abnormalities were hyponatremia, hypokalemia, hypocalcaemia and hypomagnesaemia and most of the symptoms of dyselectrolytemia were insignificant.

Conflict of interest: None

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