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Electrolytes System Disorder And Liver Enzyme Alteration In Adult Men With Hepatocellular Injury

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Abstract: Objective: The current study aimed to estimate the magnitude of liver hepatocellular damage in adult men suffering from advanced stages of liver infection considering various important variables (age, BMI, TSB, DSB, GOT, GPT, Na^+, K^+, Cl^-). Background: The main cause of hepatocellular injury is viral hepatitis C. Development of this disease leads to transformation of normal liver tissue into fibroses and nodules (cirrhosis), and it is associated with numerous complications, including gastrointestinal bleeding, ascites, renal function disorder and electrolyte disturbance. Method: The sera of all participants, including 25 patients with VHC and 15 cirrhotic patients, were collected for comparison with 23 control donors (healthy men). The present study was conducted in Baaqubah General Hospital/Diyala. Serum electrolyte concentrations were measured by spectrophotometry assay. Results: significantly decreasing sodium concentration in cirrhotic patients and statistically increasing chloride concentration in patients with liver disease compared with the control (P value < 0. 05). Furthermore, a number of disorders that effect of the liver enzymes levels, Conclusion: The essential decrease in sodium (Na^+) concentration was observed in cirrhotic men caused by reduction in renal perfusion. This result is in contrast to that of serum chloride, which increased in patients with liver diseases.

Keywords: cirrhosis, renal failure, electrolyte, gastrointestinal bleeding, alanine aminotransferase (ALT), aspartate aminotransferase (AST).

1. INTRODUCTION

Liver is a fundamental organ that plays an important role in metabolism and is a major source in body hormone synthesis **(1)**. The most common causes of chronic liver diseases include alcohol addiction, problems related to metabolic and viral hepatitis; however, early stage of liver dysfunction can be treated by lifestyle changes or by specific medications (**2**) (**3**). End-stage liver disease (ESLD) is one of the most common life-threatening diseases, but its pathogenesis remains unknown **(4)**; it is characterised by unclear symptoms with no specific test to detect liver malfunction (**5**). Thus, ESLD can be only diagnosed in late stages by several clinical complications, such as ascites, glomerular filtration rate, portal hypertension leading to acute upper gastrointestinal bleeding and jaundice; these indicators exhibit injury by cirrhosis (**6**), which replaces natural hepatic cells with fibrosis and nodules (**7**), and flow obstruction in veins causing portal hypertension **(8)**, which is considered a major cause of increased mortality or liver transplantation (LT). Electrolyte imbalance is associated with liver disorders, especially in patients with ESLD (**9**).

Sodium (Na^+), potassium (K^+) and chloride (Cl^-) act as electrolyte molecules that play a major role in body fluid balance, muscle flexibility and transfer of neural signals to the brain (**10**). Patients with cirrhosis can maintain a normal electrolyte value, but this balance is susceptible to disruption with the progression of infection affecting renal function, leading to hyponatremia, which is observed with most cases of ESLD (**11).** The direct link between renal injury and cirrhosis remains limited as a result of the lack of diagnostic tests **(12)**, renal function disorder commonly develops in patients with liver diseases and is identified in 1 out of 5 cirrhotic patients **(13).** Kidney function investigation should be conducted regularly on patients with cirrhosis, especially those who suffer from hyponatraemia and gastrointestinal bleeding **(14),** which indicate high risk of renal failure **(15).** Portal hypertension leads to circulatory dysfunction and systemic vasodilation, which result in reduced renal perfusion. As compensatory activity, kidneys excrete arginine vasopressin (antidiuretic hormone), **(16), (17)**, which will disturb the solute-free water excretion, resulting in hyponatraemia to date, studies showing the relationship of serum electrolyte disorder to liver disease progression are limited. Thus, the present study assessed the link between serum electrolyte balance and hepatic tissue damage. This work also monitored the changes that affecting liver enzymes, including alanine aminotransferase (ALT) and aspartate aminotransferase (AST), in both viral hepatitis (VHC) and cirrhotic patients and compared them with those of healthy donors.

2. MATERIALS AND METHODS

The current study focused on 40 adult men patients suffering from liver diseases in Baqubah General Hospital (from October 2017 to June 2018. The participants were divided into two groups according to the stage of illness: 25 subclinical VHC ***(B)*** and 15 with cirrhosis ***(C)***. The main cause of cirrhosis. in this study, was VHC, and it has been histologically diagnosed and identified by clinical signs, which were matched to those of 23 healthy men, as control ***(A),*** which were selected according to absence of any chronic history. All participants were aged 17–42 years old (mean ± SE) of (31.03 ± 1.366) years. A total of 5 mL blood was collected from each donor after overnight fasting and was dispensed to vacuum serum separator gel tubes as per protocol to obtain serum for routine biochemical analysis. Sera samples were kept at −20 °C until use for measurement of indicators, such as TSB, ALT and AST, Na^+, Cl^- and K^+, which have been studied to elucidate the development of liver disease stages. The current study required the collection of physical measurements as baseline characteristics of each volunteer; these measurements included BMI, which is a simple scale depending on weight and height **(18)** its representing global criteria for general health; age and type with duration of disease (for patients only). The World Health Organization divides the Asian community into three groups according to BMI: normal (18–24.9 kg/m^2), overweight (25–29.9 kg/m2) and obese (≥30 kg/m^2). The normal values for electrolytes Na^+, Cl^- and K^+ are 136–145, 3.5–5 and 98–106 mmol/L, respectively.

All results in the current study were analysed by using SPSS software version 20. They were analysed using analysis of variance (P-value ≤ 0.05). The correlation among electrolytes was analysed using Pearson correlation (r) assuming significance at the 0.05 level (two-tailed).

3. RESULTS AND DISCUSSION

Table (1) presents the effect of liver diseases evolution on BMI, the observation was a significant difference between groups A and C, (≥23) kg/m^2 and (<18) kg/m^2, respectively, excessive decrease in BMI (<18 kg/m^2) in group (C) due to protein and calorie malnutrition also occurred in patients with ESLD or with LT, leading to increased mortality. Such results deals with individuals according to global nutrition that marker for healthy body **(19),** on the

other hand, BMI raised in patients suffering from VHC (26 kg/m^2), but it isn't represented a significant difference, however increasing of BMI was used as an indicator to treatment response **(20).** The outcome classification of most previous studies depending on standard markers were more influential in terms of age such as the present findings which showed no significant difference in the mean of age between patients with VHC (B) and cirrhosis group (C), which yielded values of (30.1 ± 8.29) and (34.7 ± 5.57) years, respectively, comparison with the control (28.5±7.9) year; *P value (≥ 0.05)* **(21).** Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) are considered the most important liver enzymes that aid in predicting and monitoring hepatocellular injury **(22)**. The present findings indicated the increased AST (GOT) levels in HCV patients group (B): (52.24 ± 66.72 U/L), continually increased and peaked in cirrhotic patients group (C): (90 ± 147.9 U/L), revealing significant differences compared with control group (A): (25.92 ± 9.78 U/L); ***P value < 0. 05)***, increasing value of AST with damaging effects on hepatocellular injury leads to AST leakage in circulating blood, which is in line with the present study **(23)**. The present findings also show the increase in ALT in patients with HCV (49.16 ± 37.43 U/L) compared with the other donors, with values of (23.44 ± 11.28) and (13.84 ± 5.47 U/L) observed for A and C groups, respectively ***(P value < 0. 05)***. GPT value will decline with tissue disturbance (fibroses or tissue models), as commonly observed in patients suffering from cirrhosis. This result deals with the current study **(24).** Jaundice refers to abnormal haemoglobin breakdown, indicating an increase in bilirubin serum (≥35 µmol/l), which is often observed with non-alcoholic fatty liver disease (NAFLD), which agrees with all cases of this current study, that is, NAFLD significantly increased (41.00 ± 38.26 µmol/L) in C compared with A (5.79 ± 2.18 µmol/l) ***(P value < 0. 05).*** Moreover, in the present study, moderate levels of serum bilirubin were in patients with VHC (9.6 ± 6.38 µmol/L) **(25)**. Bilirubin features two forms: the indirectly reacting unconjugated form and the directly reacting conjugated bilirubin, with the latter form being predominantly observed among patients with acute liver disease **(26)** as shown in our findings. Table (1) shows the significantly increasing serum bilirubin levels in cirrhotic patients (26.09 ± 32.03 µmol/L) compared with A (2.32 ± 1.02 µmol/L). Further studies must to be carried out in this field in the future.

Table (1) Mean differences in general characteristics by mean ± SD

Variable	groups	N	Mean ± SD	Significant < 0.05
Age (year)	Control (A)	23	28.5± 7.9	non-significant
	VHC (B)	25	30.1±8.29	
	Cirrhosis (C)	15	34.7±5.57	
BMI (kg/m^2)	Control (A)	23	23.05± 9.71	(A, C)
	VHC (B)	25	26.7±8.45	(B, C)
	Cirrhosis (C)	15	15.36±10.7	
TSB (µmol/L)	Control (A)	23	5.79± 2.18	(A, C)
	VHC (B)	25	9.6±6.38	(B, C)
	Cirrhosis (C)	15	41.00±38.26 l	
DSB (µmol/L)	Control (A)	23	2.32±1.02	(A, C)
	VHC (B)	25	5.99±6. 26	
	Cirrhosis (C)	15	09±32	
AST (µ/L)	Control (A)	23	25.92±9.78	(A, C)
	VHC (B)	25	52.24±66.72	
	Cirrhosis (C)	15	90.68±147.9	
ALT (µ/L)	Control (A)	23	23.44±11.28	(A, C)
	VHC (B)	25	49.16± 37.43	(B, C)
	Cirrhosis (C)	15	13.84±5.47	

P value> 0.05 is considered statistically significant.

As shown in Table (2), the relation of electrolytes disturbances with hepatocellular injury, significantly decreased with Na^+ serum concentration (hyponatraemia) in (B) group (131.5 ± 3.63 mmol/L) and C group (127.35±4.54 mmol/L) compared with A group (145.52±6.3 mmol/L); the deficiency in Na^+ serum concentration (hyponatraemia) decreased at a value of less than 130 mmol/L (asymptotic characteristic) **(27) (28)**. This result relates to predominance of antidiuretic hormone secretion resulting from impairment in perfusion of renal solute-free water **(29)** and decline in effectiveness of arterial blood volume **(30).** The fluid path turns into splanchnic circulation, which explains the formation of ascites in most cirrhotic patients **(31).** Furthermore, Table (2) reveals non-significant increase in K^+ serum concentration in C group (5.09±0.95 mmol/L) compared with A group (4.23±0.75 mmol/L) **(P value > 0.05)**. Most patients with liver disease suffer from disorder in K^+ levels, as a similar event occurs during treatment by medication intake or extracellular shift, impairing glomerular filtration owing to kidney injury in ESLD, leading to hyperalkalism, parallel with the current study **(32)**.

Conversely, Table (2) shows a statistical significant increase in Cl^- serum concentration (hyperchloraemic) in C group (106.9 ± 3.5 mmol/L) when compared with A (98.90 ± 7.8 mmol/L) **(P value < 0. 05)**; this finding is mostly observed among patients suffering from liver disease (as hepatocytes aid in regulating inorganic electrolyte to maintain homeostasis inside and outside of cells) **(33)**. Increased secretion of Cl^- (hyperchloraemia) compensates for the loss in negatively charged carbonate ion (CO_3^-) **(34)**, which occurs due to various complications, including gastrointestinal bleeding and diarrhoea, as result of a portal hypertension in cirrhosis **(35).**

Table (2): Effect of hepatocellular injury development with electrolyte disorders

Variable	groups	N	Mean ± SD	Sig
Na^+ (mmol/L)	Control	23	145.52±6.3	(A, B)
	VHC	25	131.5±3.63	
	Cirrhosis	15	127.35±4.54	(A, C)
Cl^-(mmol/L)	Control	23	98.90±7.8	(A, C)
	VHC	25	102.9±2.62	
	Cirrhosis	15	106.9±3.5	
K^+ (mmol/L)	Control	23	4.23±0.75	Non Sig
	VHC	25	4.64±0.56	
	Cirrhosis	15	5.09±0.95	

P value> 0.05 is considered statistically significant.

Correlation test was conducted among electrolytes (K^+, Na^+ and Cl^-) in patients with liver diseases only as shown in Table (3). Na^+ featured a positive correlation (r = 0.485) with Cl^-, which increased with increasing in serum Na^+ concentration. The serum Cl^- concentration will significantly increase also to maintain the ionic gap balance and to compensate for the loss of CO_3^- resulting from gastrointestinal bleeding (P value ≤ (0.05) **(36)**, whereas K^+ showed a non-correlation with Na^+ and Cl^- (r = 0.31, 0.138) respectively.

Table (3) Electrolyte correlations with each other (Pearson correlation test).

		Na	Cl	K
Na	Pearson Correlation	1	.485*	.041
	Sig. (two-tailed)		.030	.864
	N	40	40	40

	Pearson Correlation	.485*	1	.138
Cl	Sig. (two-tailed)	.030		.561
	N	40	40	40
	Pearson Correlation	.031	.138	1
K	Sig. (two-tailed)	.864	.561	
	N	40	40	40

*. Correlation is significant at the 0.05 level (two-tailed).

4. CONCLUSION:

Electrolytes system disturbance is very common and associated with hepatocellular injury, decreasing in sodium concentration (hyponatremia) especially in cirrhotic patient and increasing in chloride concentration (hyperchloraemia) in patients who have end stage of liver disease. Liver enzymes are considered as an indicator to monitor the condition of the liver that increasing in GOT and GPT pointing to hepatocellular injury. For future studies. Kidney tests are recommended as a future study for liver patients to reduce disease progression.

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