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Original Article

The association between serum liver function enzymes and the levels of serum glucose, total lipids and some vital electrolytes in patients with liver disease.

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Abstract:

The non-alcoholic fatty liver disease is a common liver disease that may progress into liver fibrosis and cirrhosis. The present study was conducted to compare between the effects of liver diseases related to hepatocyte parenchymal injury, indicated by elevated serum AST and ALT enzymes, or biliary tree related disease, indicated by the elevated serum GGT enzyme levels, on the homeostasis of some vital serum metabolites.

This cross-sectional study was conducted in Hail General Hospital, Saudi Arabia. The database of 68 (M=38, F=30) patients with abnormal liver functions and a normal control group n = 39 (M=10, F=29) were included in the study. The fasting serum glucose, total cholesterol (TC), triglycerides (TGs), serum calcium, phosphate, potassium and sodium, were assayed in the hospital laboratory. According to their biochemical data, the patients were classified into a) Group GGT (with serum GGT levels≥55IU/L), n =34(M=28, F=6); b) Group ASLT (with elevated serum Stand/or ALT levels: AST≥31I U/L and ALT ≥ 65 IU/L) n = 34 (M = 10, F = 24), and c) the normal control The results were subjected to one-way ANOVA and the regression analysis by Spearman`s Regression analysis. P values < 0.05 were considered significant.

The serum glucose concentration was significantly elevated in both GGT and ASLT groups by 69.19% and 101.8%, respectively compared to the control. The percentages of the hyperglycemic patients were raised to 47% and 53% in the GGT and ASLT groups respectively compared to controls.

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Moreover, there were significant correlations between glucose and the GGT, AST and ALT enzymes ($r = 0.27$, $P = 0.004$; $r = 0.22$, $P = 0.02$; $r = 0.54$, $P < 0.0001$), respectively. In contrast, the serum TC was significantly ($P<0.001$) reduced in the GGT and ASLT groups compared to the control, whereas, the serum TG levels exhibited significant ($P < 0.001$) increase in the ASLT, but not the GGT group. The percentage of hypertriglyceridemic patients in the ASLT group was raised to 23.5% compared to 8% in the control group, and the TG showed a significant correlation with ALT enzyme ($r =0.44$, $P < 0.0001$), whereas, the TC showed a negative correlation with GGT enzyme ($r= -0.28$, $P =0.003$). On the other hand, the serum calcium level was significantly reduced by 9.42% and 4.93% in the in the GGT and ASLT groups, respectively, compared to the control, and the calcium had a significant correlation with the GGT ($r = 0.35$, $P = 0.0002$). In contrast, the serum potassium levels were significantly elevated by 28.64% and18.52% in the GGT and ASLT groups, respectively compared to control, and it had a significant correlation with GGT ($r = 0.48$, $P = 0.0001$). The percentage of hyperkalemic patients rose from 0.00% in control to 55.0% and 35.3% in the GGT and ASLT groups, respectively. However, the serum sodium levels exhibited a significant ($P<0.05$) reduction in the ASLT group compared to the control.

These findings demonstrate the variation in the effects of liver disease on the levels of the serum vital metabolites depending on the site of liver injury. Moreover, the results highlighted the importance of healthcare providers to monitor the profiles of blood sugar, lipids and lipoproteins, and the serum electrolytes from the early days of detecting the abnormal liver functions.

Keywords:
Dyslipidemia-hypophosphatemia -hyperglycemia-hyperkalemia -Liver disease.

Introduction:

The non-alcoholic fatty liver disease (NAFLD) is the most common liver disease in adults and children worldwide [1]. It is a progressive disease that can further develop into steatohepatitis, liver fibrosis, cirrhosis, and hepatocellular carcinoma. Moreover, the disease was shown to be accompanied by diabetes, cardiovascular disease, metabolic syndrome and chronic kidney disease [2, 3]. All types of the NAFLD are associated with elevations of serum liver enzymes and the condition is believed as a risk factor for the development of cardiovascular defects, oxidative stress, endothelial dysfunction, as well as metabolic syndrome [4]. The aspartate aminotransferase (AST) enzyme is known to occur in higher concentrations in tissues of liver, cardiac and skeletal muscles and at lower concentrations in kidneys, brain, pancreas and lungs. whereas, the alanine aminotransferase (ALT) enzyme exists primarily in the liver, thus its elevation in serum is considered a more specific indicator of liver injury [5]. On the other hand, liver diseases such as lymphoma, amyloidosis or liver metastasis cause cholestasis (marked reduction in bile secretion and flow). The cholestasis that involves biliary obstruction or hepatic infiltration is known to induce synthesis of alkaline phosphatase (ALP) and gamma-glutamyl transpeptidase (GGT). These two enzymes are released into the blood circulation in greater concentrations as a result of cellular damage in the biliary region. The GGT is a microsomal enzyme present mainly in the liver, and to some extent in kidney and pancreas, thus, elevated serum GGT level is considered to be related to the biliary canaliculi injury [6]. Therefore, measurements of the serum levels of AST, ALT and GGT are used as liver function parameters and to distinguish between cholestasis and other hepatocellular injury. Moreover, the ratio of AST to ALT(termed DeRitis Ratio) was used to evaluate the levels of liver injury and lower values were found to be associated with abnormal glucose metabolism and metabolic syndrome [7]. Several investigators have also used the AST/ALT ratio to interpret the status severity of liver diseases, its related cardiovascular disease and metabolic syndrome [8-10].

The aim of the present study was to investigate whether there are differences between the liver diseases associated with the parenchymal hepatocellular injury, as indicated by the abnormally elevated serum AST and ALT levels, and the cholestasis, shown by the elevated serum GGT levels, on the homeostasis of the serum glucose, total lipids and some serum electrolytes profiles.

Patients and Methods:

Sample frame:

This study was carried out at Hail General hospital, Hail, Saudi Arabia, as a cross sectional study between May 2018 and August 2018. The project was in compliance with the Helsinki Declaration and was approved by the Research Ethical Committee, Faculty of Applied Medical Sciences, and University of Hail. Saudi Arabia. The electronic database was searched for 68 patients with abnormal liver function parameters attending the outpatient clinic of the hospital who`s laboratory request included liver function tests. The records of patients with overt diabetes mellitus on medication, or patients who were not fasting were excluded from the study. The patient`s blood samples were received in the laboratory for their liver function tests (AST, ALT and GGT). Fasting normal individuals visiting the clinic for routine check- up (n= 39) were selected and used as control.

Following the release of results, a copy of the data was entered in our records and the residual serum samples were stored at-20°C for the assay of the glucose, total cholesterol (TC), triglycerides (TGs), calcium, phosphate, potassium and sodium.

According to their serum levels of the liver function enzyme, the patients were distributed into two groups:

a) Group GGT, patients with serum GGT enzyme levels ≥ 55IU/L, n=34(M=28, F=6) ;

b) Group ASLT, with elevated serum AST and/or ALT levels (AST ≥ 31 IU/L and ALT ≥ 65 IU/L) n = 34 (M = 10, F = 24), and

c) Control group n = 39 (M = 10, F = 29).

Biochemical analysis:

All the biochemical measurements of serum AST, ALT, GGT, glucose, TC, TG, calcium, phosphate, sodium and potassium were carried out with The Dimension Spectrophotometer (RxL XPAD- Germany), utilizing commercial kits.

Statistical analysis:

Results are expressed as means ± SD. The differences between the means were computed by one-way ANOVA using Statistical Package for Social Sciences version 16.0 (SPSS Inc, Chicago, IL, USA).

The significance of differences between the means was carried out by Unpaired Student`s T-test. P values<0.05 were considered significant. The regression analysis between the various parameters was carried out by Spearman`s Regression analysis. P values < 0.05 were considered significant.

Results:

As shown in Table 1, The overall mean age was 50.29 ± 8.77 years (range, 19 – 85 years). The mean ages in the GGT and AST groups were significantly higher than that of control (P<0.001). The mean serum GGT levels in the GGT group was 81.64± 14.50 compared to31.45 ±8.69 and 24.23±7.74 in the control and the ASLT groups, respectively. Whereas, the mean AST levels in the ASLT group was 65.38±18.67 compared to 28.88±5.04 and 28.12±4.62 in the GGT and control groups, respectively. Similarly, the mean serum ALT level in the ASLT group was 47.41 ± 12.37 compared to 16.02 ± 6.59 and13.33±4.88 in the GGT and control groups, respectively.

Table 1: The mean ages, serum Gamma Glutamyl transpeptidase (GGT), A spartate transpeptidase (AST) and Alanine Transpeptidase (ALT) enzymes of patients in group (GGT) with elevated serum GGT enzyme; group (ASLT) with elevated AST and/or ALT and Control group.

Variable	Control	GGT	ASLT
Sex	M=10, F=29	M=28, F=6	M=10, F=24
Age (Year)	36.10 ± 12.25	59.65± 15.33 a*	59.70± 16.68 a*
GGT(IU/L)	24.23 ± 7.74	84.11± 25.29 a*	31.45± 8.69 a* b**
AST (IU/L)	28.12 ± 4.62	28.88 ± 5.04	65.38± 18.67 a* b**
ALT(IU/L)	13.33 ± 4.88	16.02 ± 6.59	40.92± 12.12 a* b**
Presented values are mean±SD *a:significantly different from Control; **b:significantly different from GGT. ^P < 0,05; ¥P< 0.01; ₸P < 0.001.			

As depicted in Fig.1, the serum glucose concentration was significantly elevated in the GGT and AST groups by 69.19% and 101.8%, respectively compared to the control. Moreover, the percentage of the hyperglycemic patients in the GGT and ASLT groups were 47% and 53% respectively, compared to 0.00% in the control group. In contrast, the serum total cholesterol was significantly reduced in the GGT and ASLT groups by 27.17% and 18.04%, respectively compared to the control, whereas, the serum triglyceride levels exhibited significant (P < 0.001) increase in the ASLT, but not the GGT group, compared to control (Fig. 2). The percentage of the hyper triglyceridemic individuals in the ASLT group was raised to 23.5% compared to 8% in the control group. Whereas, the percentage of the hyper cholesterolemic individuals in the control group was 20.5% which dropped to 0.00% in both

GGT and ASLT groups (Table 2).

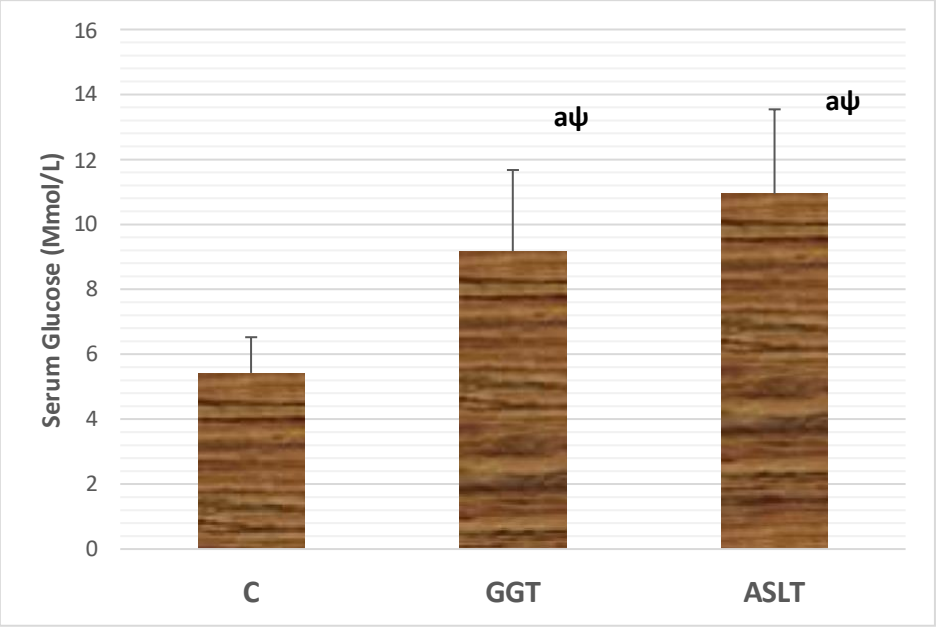

Figure 1: The serum glucose concentrations in liver disease patients with elevated serum GGT enzyme levels (GGT). Patients with elevated serum AST and/or ALT enzymes (ASLT) and control(C). The columns and vertical bars represent mean ± SD. ψ P < 0.001, a: significantly different from C, b: significantly different from GGT group.

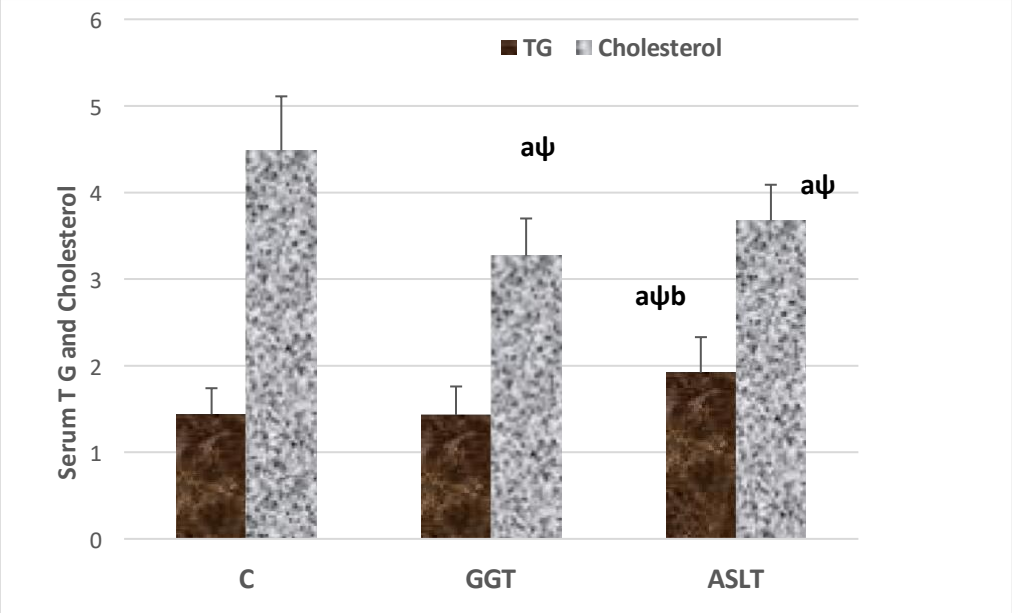

Figure 2: The serum triglycerides and total cholesterol levels in patients with abnormal liver function. Group GGT; patients with elevated serum GGT enzyme levels, Group ASLT; Patients with elevated serum AST and/or ALT enzymes and control (C). The columns and vertical bars represent mean ± SD. ψ P < 0.001, a: significantly different from C, b: significantly different from GGT group.

Table2: Comparison between the percentages of patients with hyper, hypo-or normal levels of the various serum glucose, triglycerides and total cholesterol of patients in group (GGT) with elevated serum GGT enzyme; group (ASLT) with elevated AST and/or ALT and Control group. Presented data are the numbers and percentages of patients from the total number in each group.

Variables	Status	Control(n = 39)	GGT(n =34)	ASLT(n=34)
Glucose (Mmol/L)	Hyper	0.0 (0%)	16(47%)	18(53%)
	Normal	39(100%)	16(47%)	16(47%)
	hypo	0.0 (0%)	2(6%)	0.0(.0%)
Triglyceride (Mmol/L)	Hyper	7(8%)	2(6%)	8(23.5%)
	Normal	32(82%)	32(94%)	26(76.5%)
Cholesterol(Mmol/L)	Hyper	8(20.5%)	0(0%)	0(0%)
	Normal	31(79.5%)	34(100%)	34(100%)

As shown in Table 3, the serum calcium level was significantly reduced in the GGT group by 9.42% and by 4.93% in the ASLT group, compared to the control. Whereas, the serum phosphate levels showed a trend of reduction in both GGT and ASLT groups, but were not statistically significant. In contrast, the serum potassium levels were significantly elevated by 28.64% in the GGT group and by 18.52% in the ASLT group compared to the control group.

Whereas, the serum sodium levels exhibited a slight but significant ($P < 0.05$) reduction in the ASLT group compared to the control. On the other hand, the percentage of patients with hypocalcemia increased from 2.6% in control to 82.4% and 47% in GGT and ASLT groups, respectively, whereas, those with hypophosphatemia raised from2.6% in control to 17.7% in both GGT and ASLT groups. In contrast, the percentage of patients with hyper kalemia increased from 0.00% in control to 55.0% and 35.3% in the GGT and ASLT groups, respectively. Whereas, the percentages of those with hyponatremia increased from 2.60% in control to 29.6% and 14.7% in the GGT and ASLT groups, respectively (Table 4).

Table3: The profiles of serum glucose, total lipids, and some minerals of patients in group (GGT) with elevated serum GGT enzyme; group (ASLT) with elevated AST and/or ALT and Control group. Presented values are mean ± SD. a: significantly different from Control; b: significantly different from GGT.* P < 0,05; ¥P< 0.01; ₸P < 0.001.

Variable	Control	GGT	ASLT
Calcium (Mmol/L)	2.23 ± 0.11	2.02 ± 0.29 a*	2.12 ± 0.22 a*
Phosphate (Mmol/L)	1.28 ± 0.30	1.20 ± 0.33	1.14 ± 0.32
Potassium (Mmol/L)	4.05 ± 0.40	5.21± 1.03 a***	4.80± 0.83 a***
Sodium (Mmol/L)	136.78 ± 3.34	134.78 ± 4.65	133.94 ± 7.43 a*

Table 4: Comparison between the percentages of patients with hyper, hypo- or normal levels of the various serum metabolites of patients in group (GGT) with elevated serum GGT enzyme; group (ASLT) with elevated AST and/or ALT and Control group. Presented data are the number s and percentages of patients from the total number in each group.

Variables	Status	Control(39)	GGT(34)	ASLT(34)
Calcium	Hyper	0(00.0%)	2(5.9%)	0(00.0%)
	Normal	38(97.4%)	4(11.7%)	18(53%)
	Hypo	1(2.6%)	28(82.4%)	16(47%)
Phosphate	Hyper	0(00.0%)	4(11.7%)	6(17.7%)
	Normal	38(97.4%)	24(70.6%)	22(64.6%)
	Hypo	1(2.6%)	6(17.7%)	6(17.7%)
Potassium	Hyper	0(00.0%)	18(55.0%)	12(35.3%)
	Normal	39 (100.0%)	16(45.0%)	22(64.7%)
	Hypo	0(00.0%)	0(00.0%)	0(00.0%)
Sodium	Hyper	0(00.0%)	0(00.0%)	0(00.0%)
	Normal	38(97.4%)	24(70.6%)	29(85.3%)
	Hypo	1(2.6%)	10(29.4%)	5(14.7%)

Table 5 depicts the correlation of the three live enzymes, as independent parameters, and the various analytes as dependent variables. The serum glucose showed significant correlations with the GGT, AST and ALT enzymes (r=0.27, P=0.004; r=0.22, P=0.02; r=0.54, P<0.0001), respectively. Whereas, the triglyceride did not show any significant correlations with GGT or AST enzymes, but showed a significant correlation with ALT enzyme (r = 0.44, P < 0.0001). However, the serum cholesterol showed a significant negative correlation with the GGT enzyme (r= -0.28, P=0.003), but not with the AST or ALT enzymes. Similarly, the serum calcium showed a significant correlation with the GGT (r=0.35, P=0.0002), but not with AST or ALT enzymes. Moreover, the serum potassium also showed a significant positive correlation with the GGT (r=0.48, P=0.0001), but not with AST or ALT. In contrast, the serum phosphate and sodium

did not exhibit any significant correlations with any of the three liver enzymes.

Table5: The regression analysis between the liver enzymes (GGT, AST and ALT) as independent variables and the various serum metabolites as dependent variables.

Dependent variable (Mmol/L)	Independent variable(IU/L)	Rvalue	P value	Significance	
				S	NS
Glucose	GGT	0.27	0.004		
	AST	0.22	0.02		
	ALT	0.54	< 0.0001		
Triglyceride	GGT	0.17	0.08		
	AST	0.11	0.26		
	ALT	0.44	< 0.0001		
Cholesterol	GGT	- 0.28	0.003		
	AST	- 0.12	0.23		
	ALT	- 0.10	0.30		
Calcium	GGT	0.35	0.0002		
	AST	- 0.10	0.28		
	ALT	- 0.07	0.50		
Phosphate	GGT	0.07	0.45		
	AST	0.11	0.23		
	ALT	0.13	0.18		
Potassium	GGT	0.48	0.0001		
	AST	0.14	0.15		
	ALT	0.003	0.97		
Sodium	GGT	0.03	0.74		
	AST	0.12	0.23		
	ALT	0.15	0.11		

Discussion:

The NAFLD can progress into advanced liver diseases which may involve cholestasis and hepatocyte parenchymal injury [3]. In the present study we investigated the possible influences of the two main types of liver dysfunction (homeostasis and parenchymal hepatocyte injury) on the main serum metabolites regulations. Since the liver enzymes AST and

ALT originate from the hepatocellular parenchymal cells, whereas the GGT enzyme is confined to the hepatic biliary region, their release into the blood stream in abnormally elevated concentrations would indicate the location of the injured cells within the liver. To elucidate the possible effects of each hepatic site involved in the metabolic homeostasis, we compared the serum metabolites levels in the group with high serum GGT levels (GGT) with those of high serum AST and/or ALT levels (ASLT) and the control group with normal serum enzyme levels. Moreover, the correlations of the various serum metabolites with the three enzymes were also studied. Our data showed significant elevation in the serum glucose levels in both GGT and the ASLT groups. Moreover, the glucose showed significant correlations with the serum GGT, AST and ALT enzymes. This was consistent with the findings of several investigators who reported that elevated serum ALT levels and low AST/ALT ratios are associated with insulin resistance [11-13]. The mechanism was shown to involve impairment of insulin signaling that opposes the insulin-related suppression of gluconeogenesis pathway resulting in the development of hyperglycemia [14]. Furthermore, the enhanced gluconeogenesis caused by the insulin resistance was shown to trigger the accelerated hepatic uptake of glucose that ends up in increased hepaticlipogenesis [15] and consequently the development of fatty liver [16]. On the other hand, both intra hepatic and post-hepatic cholestasis demonstrated by the elevated serum GGT levels have also been shown to cause insulin resistance. This was demonstrated by investigators who reported that both serum ALT and GGT levels linearly correlated with the insulin resistance [17], and that the elevation of both ALT and GGT showed a combined effect in predicting the development of insulin resistance [18]. Moreover, the elevated levels of serum ALT and GGT are believed as predictive markers for the development of oxidative stress [19] that may contribute to the development and progression of diabetes mellitus and cardiovascular disease [20]. Therefore, some authors have suggested that measurement of these serum enzymes could serve as predictive tools for screening and monitoring the incidence and prevalence of insulin resistance in the

population [21]. Furthermore, measurement of these enzymes may be an index for the development of the cardiovascular diseases [22] and to assess the progression of liver fibrosis [23]. However, since the two enzymes are used to differentiate between cholestasis and the parenchymal hepatocellular injury as a cause of the liver disease, our results suggest that injury of both sites within the liver can suppress the insulin signaling and initiate insulin resistance. On the other hand, our results revealed that the serum triglyceride levels showed a significant elevation in the ASLT group, but not the GGT group with a highly significant correlation with the ALT enzyme. Moreover, the percentage of patients with hyper triglyceridemia increased from 8% in the control to 23.5% in the ASLT group. On the other hand, the serum cholesterol levels showed significant ($P < 0.001$) reductions in both GGT and ASLL groups with a significant negative ($r = - 0.28$, $P=0.003$) correlation with the GGT enzyme but not with AST or ALT, whereas, the percentage of hypercholesterolemic patients dropped from 20.5% in control to 0.00% in both GGT and ASLT groups. Our findings were consistent with several reports. It has been reported that dyslipidemia frequently exists in patients with NAFLD. The disorder may be characterized by hypertriglyceridemia, increased LDL particle size, and decreased HDL levels [24]. Consequently, some investigators demonstrated accumulation of lipids in the hepatocytes as a result of dyslipidemia and insulin resistance leading to hepatic inflammation and fibrosis [25]. The hepatic influx of fatty acids and the intrahepatic lipogenesis, triggered by the accelerated gluconeogenesis, was shown to cause hepatic lipotoxicity that may end up in the development of fibrosis [26]. The patients with primary biliary cholangitis were also shown to exhibit increased serum triglyceride levels accompanied with variable levels of HDL [27]. In patients with chronic liver disease, the serum cholesterol levels are known to vary between mildly elevated levels to reduced concentrations. In line with our findings, several authors have reported that patients with cirrhotic liver diseases exhibit lower total cholesterol, HDL and LDL levels compared to normal individuals, and showed positive correlations with the severity of liver damage [28]. Similar results were also reported by other investigators who showed significant declines in the serum total cholesterol and triglyceride levels with variable lipoprotein levels in the chronic liver disease patients [29]. Moreover, patients infected with hepatitis C virus were also shown to have lower serum total cholesterol levels compared to the control group [30]. The reduction of serum cholesterol levels in the liver disease patients was related to the reduced synthesis of the hepatic apoprotein-A

which caused variation in the HDL levels depending on the extent of liver damage [31]. It was therefore concluded that the extent of decrements measured in the levels of serum total cholesterol and lipoproteins in cirrhotic patients may reflect the progression of the liver cirrhosis. Our results have revealed that the serum glucose and triglycerides had significant correlations with the ALT enzyme, whereas, the cholesterol correlated with the GGT. This suggests that the developed insulin resistance in these liver disease patients was more strongly related to the parenchymal hepatocyte injury that resulted in the development of hyperglycemia and hypertriglyceridemia. Whereas, alteration of the serum cholesterol levels was related to hepatic or extra- hepatic cholestasis that may have influenced the mechanism of cholesterol transport and excretion.

The serum minerals levels are also known to be disturbed by the abnormal liver functions. In the present study the serum calcium levels showed significant ($P < 0.05$) reductions in both GGT and ASLT groups with significant correlation with the GGT enzyme, ($r = 0.35$, $P = 0.0002$). In contrast, the serum phosphate levels showed a trend of reduction, but was not significant in any of the groups, and did not show any significant correlations with any of the liver enzymes, with a slight increase in the percentage of hypophosphatemic patients in both groups. In normal individuals, reductions in the serum ionized calcium are sensed by the calcium-sensing receptor (CaSR) in the parathyroid glands resulting in increased parathyroid hormone (PTH) secretion. The released PTH enhances bone resorption that releases calcium and phosphate into circulation, stimulates urinary calcium reabsorption and stimulates the 1α-hydroxylase enzyme enhancing formation of the active1, 25(OH)2D and down-regulating the 24-hydroxylase enzyme responsible for its degradation. Consequently, the active 1,25(OH)2D enhances the intestinal calcium absorption and ameliorate the hypocalcemia. However, in the chronic liver disease patients, hypocalcemia is a common complication which ranges from mild asymptomatic to severe life-threatening disorder. Acute hypocalcemia may cause tetany, seizures, and heart failure, whereas, chronic hypocalcemia may lead to osteoporosis, dental caries, basal ganglia calcification, cataracts, and other ophthalmological manifestations [32]. In line with our findings, authors have reported that patients with advanced liver disease had lower calcium levels and there was a strong correlation between the low serum calcium levels and albumin deficiency [33].

Moreover, patients with cholestatic liver disease were shown to have hypocalcemia accompanied with poor intestinal absorption of vitamin D leading to diminished levels of active 1, 25-

vitamin D levels that may explain the persistent hypocalcemia in these patients [34]. Therefore, patients with liver cirrhosis are known to develop bone loss and fractures, and the physicians were advised to monitor the bone density in these patients and supplement the patients with vitamin D and calcium if needed to prevent osteoporosis [35]. Beside the lower serum calcium levels, our results also indicated that the patients had a trend of lower serum phosphate levels, with the percentage hypophosphatemic patients raised in the patients compared to the controls. This was in line with the finding of several investigators who reported prevalence of hypophosphatemia in cirrhotic patients. The hypophosphatemia in acute liver failure was related to enhanced renal tubular phosphate wasting with no evidence for proximal tubular damage [36]. The calcium and phosphate are known to share a common pathway of regulation. The steps regulating the process involve PTH, fibroblast growth factor 23 (FGF-23), and 1, 25-dihydroxyvitamin D. The PTH regulates the serum ionized calcium levels, and the FGF-23 governs phosphate homeostasis by stimulating its urinary excretion, whereas +the 1, 25(OH) 2D is responsible for the intestinal absorption of both calcium and phosphate. In patients with liver disease the impaired intestinal absorption of vitamin D would diminish the intestinal absorption of calcium and phosphate along with the FGF-23 related urinary phosphate loss, and possibly other unforeseen factors, may explain the observed reductions in the serum levels of both calcium and phosphate.

Another finding in our study was the significantly ($P<0.001$) elevated serum potassium levels in both GGT and ASLT groups with a strong correlation with the GGT enzyme. This was in line with the reports of Mohsin et al. who reported that patients with chronic liver disease had a higher incidence of hyperkalemia as compared to their healthy counterparts [37]. In these patients the fluid and electrolyte imbalances may include hyperkalemia, hyponatremia, respiratory alkalosis, and metabolic acidosis [38]. Moreover, the prevalence of hyperkalemia in patients with advanced cirrhosis was about 14% compared to 2.1% in the population [39]. However, our results showed that as high as 55% of the GGT group and 26.7% of the ASLT patients had hyperkalemia compared to the 0.00% in control group. In normal individuals, liver and muscles play a buffering role in the distribution of potassium between the intracellular and extracellular compartments. This process is known to be aided by insulin. Following the binding of potassium ions to the cellular receptors, insulin causes the cellular glucose uptake and stimulates the uptake of potassium ions by increasing the activity of the sodium/potassium-ATPase [40]. Therefore, during the development of insulin resistance in chronic liver disease, the cellular uptake of potassium is

hindered causing increased levels of the extracellular potassium concentration. Moreover, another contributor for hyperkalemia in the cirrhotic patients is the increased outflow of potassium ions from the intracellular matrix to the extracellular fluid due to metabolic acidosis, hyperglycemia, and inpatients on beta-blockers medication [41]. The management of the developed hyperkalemia in these patients is based on discontinuing potassium-sparing diuretics, restriction of dietary potassium intake, and correction of any underlying acid-base disturbances [41].

On the other hand, the present results exhibited that the serum sodium levels were slightly but significantly reduced in the ASLT group, and the percentage of hyponatremic patients rose to 14.7%. This was in congruence with the findings of several authors who reported the prevalence of hyponatremia as one of the electrolyte disturbances in chronic liver disease patients. This was more prevalent in patients with advanced cirrhosis causing increased risk of mortality [42]. The cause of hyponasty remain in these patients was related to enhanced secretion of the ant diuretic hormone, triggered by the decreased circulating blood volume, caused by arterial splanchnic vasodilatation and decreased delivery of sodium to the distal convoluted tubules [43].

Conclusion:

The liver disease, involving the parenchymal hepatocellular injury, indicated by the elevated serum ALT and AST enzyme levels, exhibited hyperglycemia, hypertriglyceridemia and reduction in the total cholesterol level. Whereas, the cholestasis, as indicated by the elevated serum GGT enzyme levels, caused hyperglycemia with a significant reduction in the serum cholesterol levels. Moreover, Elevated levels of serum potassium and reductions in the levels of both calcium and sodium and a trend of lower phosphate levels were evident in both parenchymal hepatocyte related disease and cholestatic patients. The serum glucose had significant correlations with the three liver enzymes, whereas, cholesterol, potassium and calcium showed correlations with the GGT and the triglyceride correlated with the ALT enzyme.

These findings demonstrate the variation in the effects of liver diseases on the levels of the serum vital metabolites depending on the site of liver injury. Moreover, the results highlight the importance of monitoring the profiles of blood sugar, lipids and lipoproteins, and the serum electrolytes from the early days of detecting the abnormal liver functions and management if required.

More elaborated study is warranted to address, in more details, the metabolic disturbances related to the various classes of liver disease and their correlation with the extent of the disease progression.

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References:

1. ForlanoR, Mullish BH, Nathwani R, Dhar A, Thursz MR, etal. Non-alcoholic fatty liver disease and vascular disease. Curr Vasc Pharmacol. 2021; 19(3):269–279.
2. PouwelsS,SakranN,GrahamY,LealA,PintarT.etal.Non-alcoholic fatty liver disease (NAFLD): a review of path physiology, clinical management and effects of weight loss. BMC Endocr Disord 2022; 22 (1): 63.
3. CorradiniE, BuzzittiE, DongiovanniP, ScarliniS, CaleffiA.etal. Ceruloplasm in gene variants are associated with hyperferritinemia and increased liver iron in patients with NAFLD.J Hepatol.2021; 75(3): 506–513.
4. Onat A, Can G, Ornek E, Cicek G, Ayhan E, Dogan Y. Serum γ-glutamyltransferase: independent predictor of risk of diabetes, hypertension, metabolicsyndrome, and coronary disease. Obesity (Silver Spring) 2012; 20:842–848.
5. Pratt DS, Kaplan MM. Evaluation of abnormal liver enzyme results in asymptomatic patients. N Engl J Med 2000; 342:1266-1271.
6. Neuman MG, Malnick S, ChertinL.Gamma glut amyl transferase-an under estimated marker for cardiovascular disease and the metabolic syndrome. J Pharm Pharm Sci. 2020; 23(1): 65-74.
7. Niu H, Zhou Y. Non linear relationship between AST-to-ALT ratio and the incidence of type2 diabetes mellitus: a follow-up study. Int J Gen Med. 2021; 14: 8373-8382.
8. Parmar KS, Singh GK, Gupta GP, Pathak T, Nayak S. Evaluation of DeRitis ratio in liver-associated diseases. International Journal of Medical Science and Public Health 2016; 5 (9): 1783 – 1788.
9. Ndrepepa G.DeRitis ratio and cardiovascular disease: evidence and underlying Simental-Mendia LE, Rodriguez-Moran M, Gomez-Diaz R,

Wacher NH, Rodriguez-Hernandez H, et al. Insulin resistance is associated with elevated transaminases and low aspartate aminotransferase/alanine aminotransferase ratio in young adults with normal weight. Eur J Gastroenterol Hepatol. 2017; 29 (4): 435–440

10. Kawamoto R, Kohara K, Kusunoki T, Tabara Y, Abe M, et al. Alanine aminotransferase/aspartate aminotransferase ratio is the best surrogate marker for insulin resistance in non-obese Japanese adults. Cardiovasc Diabetol. 2012; 11: 117.
11. Hsueh WA, Quinones MJ. Role of endothelial dysfunction in insulin resistance. Am J Cardiol. 2003; 92(4): 10j–17j.
12. Abel ED, OShea KM, Ramasamy R. Insulin resistance: metabolic mechanisms and consequences in the heart. Arterioscler Thromb Vasc Biol. 2012; 32(9): 2068–2076.
13. YeJ. Mechanisms of insulin resistance in obesity. Front Med. 2013;7(1):14 –24.
14. mechanisms. J Lab Prec. Med 2023; 8: (6) 22 – 68.
15. LeeK, YangJH. Which liver enzymes are better indicators of metabolic syndrome in adolescents: the Fifth Korea National Health and Nutrition Examination Survey.Metab Syndr Relat Disord. 2013; 11(4): 229–235.
16. Mahran HN,Saber LM,Alghaithy A A,Elareefy A A.The role of elevated alanineaminotransferase (ALT), FasL and atherogenic dyslipidemia in type II diabetes mellitus. J Taibah Univ Med Sci. 2017; 12 (1): 8–13.
17. Gao F, Pan JM, Hou XH, Fang QC, Lu HJ. et al. Liver enzymes concentrations are closely related to prediabetes: Findings of the Shanghai Diabetes Study II (SHDS II). Biomed Environ Sci. 2012; 25: 30 –37.
18. Jeong JH, Susie Jung S, Kim KN. Considering serum alanine aminotransferase and gamma-glutamyltransferase levels together strengthen the prediction of impaired astingglucose risk:across- sectional and longitudinal study. Sci Rep 2021; 11: 3333.
19. Yamada, J. Tomiyama H, Yambe M, Koji Y, Motobe K, et al. Elevated serum levels of alanine amino transferase and gamma glutamyl transferase are markers of inflammation and oxidative stress independent of the metabolic syndrome. Atherosclerosis 2006; 189, 198– 205.

20. Li Y, Wang J, Han X, Hu H. Wang F. et al. Serum alanine transaminase levels predict type 2 diabetes risk among middle-aged and elderly Chinese population. Ann. Hepatol. 2019;18,298 – 303.
21. SG-Junior R, Dhamija RK, Gurtoo A, Singh R. Correlation of ALT/AST Ratio with insulin resistance in metabolic syndrome. Int. J. Adv. Res. 2017; 5(3), 1677-1684.
22. Feng X, Wen Y, Peng FF, Wang N, Zhan X, et al. Association between amino transferase/alanine amino transferase ratio and cardiovascular disease mortality in patients on peritoneal dialysis: amulti- center retrospective study. BMC Nephrol. 2020; 21(1): 209.
23. McPherson S, Stewart SF, Henderson E, Burt AD, Day CP. Simple non-invasive fibrosis scoring system scan reliably exclude advanced fibrosis in patients with non-alcoholic fatty liver disease.Gut. 2010; 59 (9): 1265–1269.
24. DeFilippis AP, Blaha MJ, Martin SS, Reed RM, Jones SR. et. al. Nonalcoholic fatty liver disease and serum lipoproteins: the Multi-Ethnic Study of Atherosclerosis. Atherosclerosis. 2013;227:429– 436.
25. Chatrath H, Vuppalanchi R, Chalasani N. Dyslipidemia in patients with nonalcoholic fatty liver disease. Semin Liver Dis.2012; 32: 22–29.
26. Ipsen DH, Lykkesfeldt J, Tveden-Nyborg P. Molecular mechanisms of hepatic lipid accumulation in non-alcoholic fatty liver disease. Cell Mol Life Sci 2018; 75: 3313–3327.
27. Speliotes EK, Balakrishnan M, Friedman LS, Corey KE. Treatment of dyslipidemia in common liver diseases**.** Clin Gastroenterol Hepatol. 2018; 16(8): 1189–1196.
28. Ghadir MR, Riahin AA, Havaspour A, Nooranipour M, Habibinejad AA. The relationship between lipid profile and severity of liver damage in cirrhotic patients. Hepat Mon 2010; 10(4):285–288.
29. Mehboob F, Ranjha FA, Masud S. Changes in serum lipid profile among patients suffering from chronic liver disease**.** ANNALS 2007; 13 (3): 209 – 211.
30. Siagris D, Christofidou M, Theocharis GJ, Pagoni N, Papadimitriou C, et al. Serum lipid pattern in chronic hepatitis C: histological and virological correlations. J Viral Hepat. 2006;13(1):56 –61.

31. Selimoglu MA, Aydogdu S, Yagci RV. Lipid parameters in childhood cirrhosis and chronic liver disease. Pediatr Int. 2002; 44(4): 400–403.
32. Gurnani V, Kumar N, Khan SI, Nawaz MU, Ahmed H, et al. Biochemical Risk Factors Associated with Hyperkalemia in Cirrhotic Patients. Cureus 2021; 13 (9): e18356.
33. Jagdish RK, Maras JS, Sarin SK. Albumin in Advanced Liver Diseases: The good and bad of a drug. Vol. Hepatology. 2021;74(5):2848–2862.
34. Aykara B, Ozturk G, Mutlu HH, Arslan E. Relationship Between Vitamin D, Calcium, and Phosphorus Levels. J Acad Res Med. 2020;10 (3): 252–257.
35. Nakchbandi IA. Osteoporosis and fractures in liver disease: Relevance, pathogenesis and therapeutic implications. World J Gastroenterol. 2014; 20 (28): 9427–9438.
36. Zechner C, Zechner C, Adams-Huet B, Gregory B, Moe OW, et al. Hypophosphatemia in acute liver failure of a broad range of etiologiesis associated with phosphaturia without kidney damage or phosphaton in elevation. Transl Res 2021; 238: P1-11.
37. Mohsin ZS. Study of Na+ and K+ concentration in cirrhosis and chronic liver disease. Al Mustansiriyah J Sci. 2012; 23: 55–64.
38. Cai JJ, Wang K, Jiang HQ, Han T. Characteristics, risk factors, and adverse outcomes of hyperkalemia in acute-on-chronic liver failure patients.BiomedResInt.2019;2019: 6025726.
39. Maiwall R, Kumar S, Sharma MK, Wani Z, Ozukum M, et al. Prevalence and prognostic significance of hyperkalemia in hospitalized patients with cirrhosis. JGastroenterolHepatol.2016; 31:988–994.
40. Palmer B, Clegg DJ. Physiology and Pathophysiology of Potassium Homeostasis: Core Curriculum. Am J Kid Dis. 2019; l74 (5): 682 – 695.
41. Milionis HJ, Elisaf MS. Hyperkalaemia in a patient with hepatic cirrhosis. Nephrol Dial Transplant. 1999; 14: 2505–2506.
42. Fernandez-Esparrach G, Sanchez-Fueyo A, Gines P, Uriz J, Quinto L, et al. A prognostic model for predicting survival in cirrhosis with ascites. J Hepatol. 2001; 34(1): 46–52.
43. Bhandari A, Chaudhary A. Hyponatremia in chronic liver disease

among patients presenting to a teriary care hospital. JNMA J Nepal Med Assoc 2021;59