



Original Article



## Relationship between changes in blood glucose, glycosylated hemoglobin [HbA1c], cholesterol, and triglyceride and changes in hepatic enzymes

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### Article Info

### Abstract



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The main risk factors for non-alcoholic fatty liver disease (NAFLD) are strongly associated with obesity, diabetes, hyperlipidemia, and metabolic syndrome. The best clinical evaluation of the liver is done through studying changes in liver enzymes' activity, especially alanine aminotransferase, aspartate aminotransferase, and alkaline phosphatase. Therefore, this study aimed to investigate the relationship between changes in factors such as blood glucose, cholesterol, glycosylated hemoglobin, and triglyceride and changes in hepatic enzymes in patients who visited Fajr Hospital in Tehran. Samples with SGPT levels > 40 U/L were selected and blood samples from the same individuals were collected in the next testing which was six months later. The changes in four factors of blood glucose, glycosylated hemoglobin, cholesterol, and triglyceride were calculated in these two consecutive visits, and finally, they were compared with changes in the hepatic enzymes and the relationship between them was evaluated by SPSS V. 23. Fifty-seven individuals with a mean age of  $48 \pm 15$  years and SGPT > 40 U/L were included in the present study. Six samples were female (10.52 %) and 51 samples were male (89.48 %). The results showed that there was no significant relationship between blood glucose and glycosylated hemoglobin changes and hepatic enzymes. However, there was a significant relationship between cholesterol and triglyceride changes and hepatic enzymes of SGPT and SGOT ( $p < 0.05$ ). Based on the results of the current study, changes in FBS and HbA1c in two consecutive visits cannot be used to follow up on the treatment of fatty liver. However, changes in cholesterol and triglyceride can be used for monitoring the treatment in people with abnormal levels of hepatic enzymes.

**Keywords:** Fatty liver disease, Hyperlipidemia, Metabolic syndrome, HbA1c

### 1. Introduction

Liver is one of the main organs of the body that detoxification of drugs, disposal waste products due to red blood cells' death and regeneration in the form of bile, produces blood coagulation factors, stores sugar in the form of glycogen, and regulates sugar and fat metabolism are among its most important roles in the body. Moreover, its role should not be neglected in absorption of fat and defending against germs and toxins absorbed through food [1].

The main risk factors associated with non-alcoholic fatty liver disease (NAFLD) are obesity, diabetes, hyperlipidemia, and metabolic syndrome [2, 3]. The laboratory diagnostic technique is based on changes in hepatic enzymes. These enzymes are found in hepatic cells and enter the patients' serum after hepatic cell destruction. Their increase is a sign of hepatic cell destruction. Increase of hepatic enzymes does not have a direct relationship with disease intensity and it is observed in 50 % of patients suffering from fatty liver. This increase reaches up to 80 % in advanced stages of the disease. Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) are the most

important hepatic enzymes increased in this disease [4].

Furthermore, hepatic enzymes of the serum are increased in other disorders. Increase of some of the hepatic enzymes such as ALT, AST, and alkaline phosphatase (ALP) are widely used in evaluation of hepatic cell necrosis [5].

Blood glucose level is linked to changes in hepatic enzymes. It is well known that liver has a prominent role in maintaining normal blood glucose levels during hunger and after meals. ALT, AST, and gamma-glutamyl transferase (GGT) are the common liver enzymes that examine together is used in liver function testing [6]. ALT is specifically an indicator of liver function, but AST and GGT are indicators with less specificity since they exist in other tissues as well [7].

As stated above, conditions such as insulin resistance, hyperglycemia, and hypercholesterolemia are described as causes of NAFLD. Therefore, there must be a relationship between hepatic enzymes and cholesterol, triglyceride, and blood glucose. It has been observed in various studies that there is a relationship between hepatic en-

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zymes and blood levels of glucose, cholesterol, and triglyceride [8-10]. Nevertheless, there has been no study on the relationship between changes in the levels of blood glucose, cholesterol, and triglyceride, and changes in the hepatic enzymes of patients in two consecutive visits. Thus, the aim of this study was to investigate the relationship between changes in three factors of the blood, i.e., blood glucose, cholesterol, and triglyceride, and changes in the hepatic enzymes of the patients who visited Fajr Hospital of Tehran.

## 2. Materials and methods

### 2.1. Study population

The study population was comprised of individuals who visited Fajr Hospital of Tehran for full body checkup. Written consent was obtained from all the individuals subject to study. Moreover, age and gender characteristics of the subjects were recorded as well.

### 2.2. Sampling

In the first step of this fundamental study, written consent was obtained from all the individuals subject to study from among 300 patients who visited Fajr Hospital of Tehran in a period between August 22, 2020, and August 23, 2021. Additionally, they were questioned with regard to suffering from any type of disease, using any medication, and fasting for 8 to 10 hours. Then, 10 ml of blood was obtained from all the qualified individuals in two consecutive visits that were six months apart, and after coding the samples, blood serum was immediately separated using a centrifuge at 3,200 rpm for 5 min. The serums were kept at -20 °C until the day of testing.

### 2.3. Inclusion and exclusion criteria of the samples

Samples included in this study had an SGPT > 40 U/L and the rest of the samples that did not have this amount were excluded. Out of 300 patients who visited the hospital, 57 had an SGPT > 40 U/L and thus were included in this study.

In a one-year period from August 22, 2020, to August 23, 2021, the mean level of FBS, HbA1c, cholesterol, triglyceride, SGOT, and SGPT was measured by the enzymatic technique using Pars Azmoun kit.

Intervening factors in the test that were mentioned in the kit's brochure were taken into account and acceptable samples were included in the test. and the experiment was performed by Mindray BS800 autoanalyzer.

### 2.4. Statistical analysis of results

In this fundamental study, Quantitative variables are reported as mean  $\pm$  SEM. Pearson correlation coefficient was used for data analysis.

### 2.5. Samples used in the study

Three hundred individuals who visited the hospital were monitored, from which 57 individuals with an average age of  $48 \pm 15$  years who had an SGPT > 40 U/L in one of their two consecutive visits were included in the study. Among them, six samples were female (10.52 %) and 51 samples were male (89.48 %).

### 2.6. Statistical analysis

For analyzing the relationship between the changes in four factors of blood glucose, glycosylated hemoglobin,

cholesterol, and triglyceride, and changes in hepatic enzymes in two consecutive visits, SPSS software program and Pearson correlation coefficient were used, and their results are as follows.

In order to calculate the relationship between changes in the variables in the two visits, first, these changes were calculated using Equation 1.

$$\text{Equation 1. } \Delta\text{FBS} = \text{FBS2} - \text{FBS1}$$

In this formula, FBS1 is the blood glucose level in the first visit and FBS2 is the blood glucose level in the second visit. The same type of calculation was used for all the other variables.

## 3. Results

### 3.1. Evaluating the level of variables in two consecutive visits

In this study, variables of FBS, HbA1c, cholesterol, triglyceride, AST, ALT, and ALP were evaluated in two consecutive visits that were six months apart. Mean values of these variables for all the individuals subject to study in both visits are demonstrated in Figures 1-3.

### 3.2. Relationship between changes in blood glucose and hepatic enzymes in two consecutive visits

Values calculated by formula No. 1 were used to determine this relationship. The means of calculated changes for variables of blood glucose and hepatic enzymes are included in Table 1. Moreover, statistical analysis of Pearson correlation can be found in Table 2. It is determined that there is no significant relationship between changes in

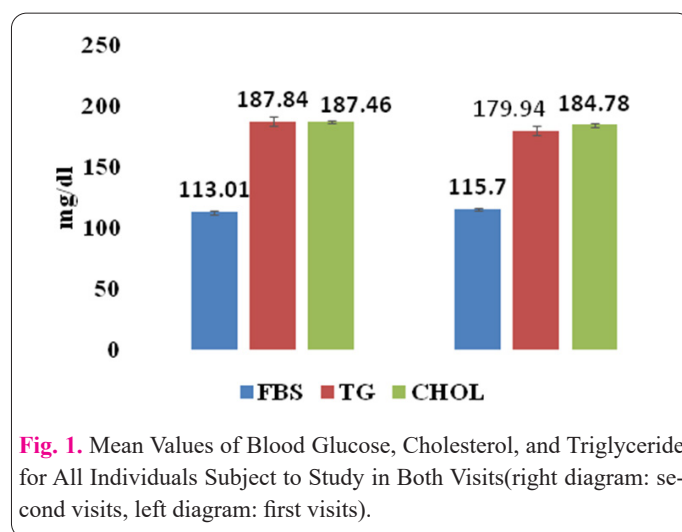


Fig. 1. Mean Values of Blood Glucose, Cholesterol, and Triglyceride for All Individuals Subject to Study in Both Visits (right diagram: second visits, left diagram: first visits).

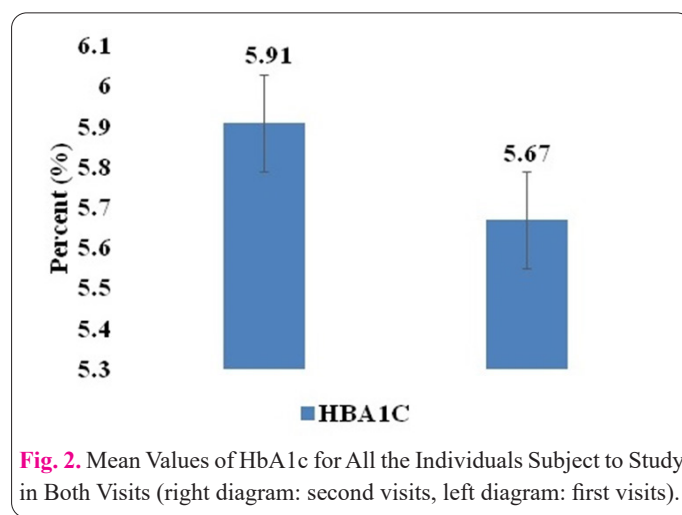
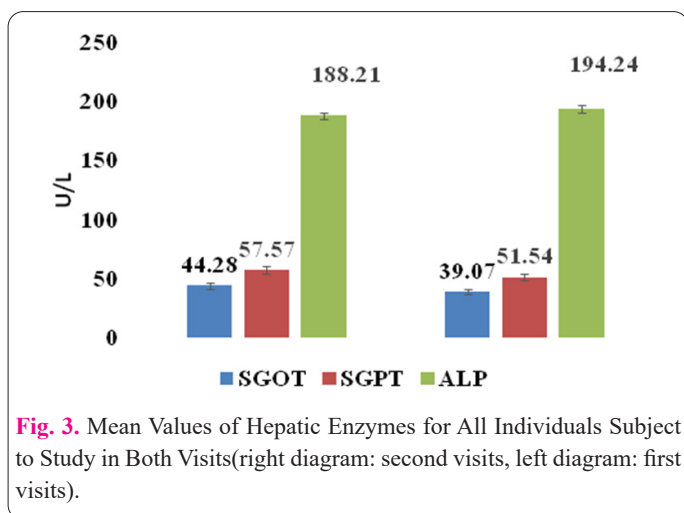


Fig. 2. Mean Values of HbA1c for All the Individuals Subject to Study in Both Visits (right diagram: second visits, left diagram: first visits).



blood glucose and hepatic enzymes in the two consecutive visits ( $p > 0.05$ ).

### 3.3. Relationship between changes in triglyceride and hepatic enzymes in two consecutive visits

Values calculated by formula No. 1 were used to determine this relationship. The mean of calculated changes for the triglyceride variable was  $-7.89 \pm 94.197$ . Moreover, statistical analysis of Pearson correlation can be found in Table 3. It is determined that there is a significant relationship between changes in triglyceride and hepatic enzymes of SGPT and SGOT in the two consecutive visits ( $p < 0.05$ ). In addition, there was not a significant relationship between changes in triglyceride and the ALP enzyme in the two consecutive visits ( $p > 0.05$ ).

Pearson correlation coefficient was positive for changes in triglyceride and hepatic enzymes of SGPT and SGOT (Table 3) meaning that by reduction in triglyceride, SGPT and SGOT enzymes are significantly reduced as well.

Values calculated by formula No. 1 were used to determine this relationship. The mean of calculated changes for the cholesterol variable was  $0.61 \pm 57.899$ . Moreover, statistical analysis of Pearson correlation can be found in Table 4. It is determined that there is a significant relationship between changes in cholesterol and hepatic enzymes of SGPT and SGOT in the two consecutive visits ( $p < 0.05$ ). In addition, there was not a significant relationship between changes in cholesterol and the ALP enzyme in the two consecutive visits ( $p > 0.05$ ). Pearson correlation coefficient was positive for changes in cholesterol and hepatic enzymes of SGPT (0.274) and SGOT (0.319) (Table 4), meaning that by reduction in cholesterol, SGPT and SGOT enzymes are significantly reduced as well.

### 3.4. Relationship between changes in glycosylated hemoglobin and hepatic enzymes in two consecutive visits

Values calculated by formula No. 1 were used to determine this relationship. The mean of calculated changes for the glycosylated hemoglobin variable was  $-0.24 \pm 1.018$ . Moreover, statistical analysis of Pearson correlation can be found in Table 5. It is determined that there was no significant relationship between changes in glycosylated hemoglobin and hepatic enzymes in the two consecutive visits ( $p > 0.05$ ).

## 4. Discussion

NAFLD is defined as steatohepatitis without secondary liver fat accumulation, including alcohol consumption, statogenic drugs, [Statins include atorvastatin [Lipitor], fluvastatin [Lescol XL], lovastatin [Altoprev], pitavastatin [Livalo], pravastatin [Pravachol], rosuvastatin [Crestor, Ezallor] and simvastatin [Zocor, FloLipid.] or hereditary disorders. Non-alcoholic fatty liver [NAFL] and non-alcoholic steatohepatitis (NASH) belong to NAFLDs [11].

**Table 1.** Mean and Standard Deviation of Changes Calculated for Blood Glucose and Hepatic Enzymes Variables.

	Mean	Standard deviation	Number
FBS	68.2	175.34	57
SGOT	21.-5	879.15	57
SGPT	06.-6	558.19	57
ALP	6.04	820.33	57

**Table 2.** Statistical Analysis of Pearson Correlation for Determining Relationship Between Changes in Blood Glucose and Hepatic Enzymes in Two Consecutive Visits.

		Correlations			
		FBS	SGOT	SGPT	ALP
FBS	Pearson correlation	1	-0.053	-0.113	-0.200
	Sig. (2-tailed)		0.694	0.401	0.136
	N	57	57	57	57
SGOT	Pearson correlation	-0.053	1	0.686**	0.090
	Sig. (2-tailed)	0.694		0.000	0.505
	N	57	57	57	57
SGPT	Pearson correlation	-0.113	0.686**	1	0.052
	Sig. (2-tailed)	0.401	0.000		0.703
	N	57	57	57	57
ALP	Pearson correlation	-0.200	0.090	0.052	1
	Sig. (2-tailed)	0.136	0.505	0.703	
	N	57	57	57	57

\*\* . Correlation is Significant at 0.01 Level (2-tailed).

**Table 3.** Statistical Analysis of Pearson Correlation for Determining Relationship Between Changes in Triglyceride and Hepatic Enzymes in Two Consecutive Visits.

		Correlations			
		TG	SGOT	SGPT	ALP
TG	Pearson correlation	1	0.324*	-0.318*	-0.037
	Sig. (2-tailed)		0.014	0.016	0.785
	N	57	57	57	57
SGOT	Pearson correlation	0.324*	1	0.686**	0.090
	Sig. (2-tailed)	0.014		0.000	0.505
	N	57	57	57	57
SGPT	Pearson correlation	0.318*	0.686**	1	0.052
	Sig. (2-tailed)	0.016	0.000		0.703
	N	57	57	57	57
ALP	Pearson correlation	-0.037	0.090	0.052	1
	Sig(2-tailed)	0.785	0.505	0.703	
	N	57	57	57	57

\*. Correlation is Significant at 0.05 Level (2-tailed); \*\*. Correlation is Significant at 0.01 Level (2-tailed).

**Table 4.** Statistical Analysis of Pearson Correlation for Determining Relationship Between Changes in cholesterol and Hepatic Enzymes in Two Consecutive Visits.

		Correlations			
		CHOL	SGOT	SGPT	ALP
CHOL	Pearson correlation	1	0.319*	0.274*	0.053
	Sig. (2-tailed)		0.016	0.039	0.696
	N	57	57	57	57
SGOT	Pearson correlation	0.319*	1	0.686**	0.090
	Sig. (2-tailed)	0.016		0.000	0.505
	N	57	57	57	57
SGPT	Pearson correlation	0.274*	0.686**	1	0.052
	Sig. (2-tailed)	0.039	0.000		0.703
	N	57	57	57	57
ALP	Pearson correlation	0.053	0.090	0.052	1
	Sig. (2-tailed)	0.696	0.505	0.703	
	N	57	57	57	57

\*. Correlation is Significant at 0.05 Level (2-tailed); \*\*. Correlation is Significant at 0.01 Level (2-tailed).

**Table 5.** Statistical Analysis of Pearson Correlation for Determining Relationship Between Changes in Glycosylated Hemoglobin and Hepatic Enzymes in Two Consecutive Visits.

		Correlations			
		HbA1c	SGOT	SGPT	ALP
HbA1c	Pearson correlation	1	-0.055	-0.132	-0.211
	Sig(2-tailed)		0.683	0.329	0.115
	N	57	57	57	57
SGOT	Pearson correlation	-0.055	1	0.686**	0.090
	Sig. (2-tailed)	0.683		0.000	0.505
	N	57	57	57	57
SGPT	Pearson correlation	-0.132	0.686**	1	0.052
	Sig. (2-tailed)	0.329	0.000		0.703
	N	57	57	57	57
ALP	Pearson correlation	-0.211	0.090	0.052	1
	Sig. (2-tailed)	0.115	0.505	0.703	
	N	57	57	57	57

\*\*. Correlation is Significant at 0.01 Level (2-tailed).

Blood lipids are linked to NAFLD. Nakahara et al., [12] reported that LDL hypercholesterolemia (hyper LDL) and HDL hypercholesterolemia (hyper HDL) were respectively found in 37.5 and 19.5 % of the patients suffering from NAFLD that had liver biopsy. Hypertriglyceridemia has more prevalence in patients suffering from NAFLD.

Ma et al., [13] performed multivariate analysis (MVA) on 949 old retirees and reported that HbA1c and triglyceride are independent indicators of NAFLD. Sung et al., [14] followed up on healthy workers who did not have NAFLD for 4.4 years in order to observe the prevalence of NAFLD. In their study, TG was independently related to



NAFLD. Generally, conditions such as hyperglycemia, hypertriglyceridemia, and hypercholesterolemia are described as causes of NAFLD [15].

In the current study, 57 individuals with an average age of  $48 \pm 15$  years and SGPT  $> 40$  U/L were included in the study. Among them, six samples were female (10.52 %) and 51 samples were male (89.48 %). Variables of FBS, HbA1C, cholesterol, triglyceride, AST, ALT, and ALP were evaluated in this study in two consecutive visits that were six months apart. Therefore, contrary to previous studies that had evaluated the relationship between hepatic enzymes and increase and decrease of blood glucose, triglyceride, and cholesterol, this study assessed the relationship between changes in hepatic enzymes and changes in the mentioned variables in two consecutive visits of the patients.

Briefly, the results of the current study showed that there was no significant relationship between changes in blood glucose and hepatic enzymes in the two consecutive visits ( $p > 0.05$ ). Although there was a significant relationship between changes in triglyceride and hepatic enzymes of SGPT and SGOT in two consecutive visits ( $p < 0.05$ ), no significant relationship was found between triglyceride changes and ALP enzyme in two consecutive visits ( $p > 0.05$ ). Moreover, there was a significant relationship between changes in cholesterol and hepatic enzymes of SGPT and SGOT in two consecutive visits ( $p < 0.05$ ). On the other hand, no significant relationship was found between cholesterol changes and ALP enzyme in two consecutive visits ( $p > 0.05$ ). Pearson correlation coefficient was positive for changes in cholesterol and hepatic enzymes of SGPT (0.274) and SGOT (0.319), meaning that by decrease in cholesterol, there is a significant reduction in SGPT and SGOT enzymes as well. Results also showed that there was no considerable relationship between changes in glycosylated hemoglobin and changes in hepatic enzymes in the two consecutive visits ( $p > 0.05$ ).

Many studies have evaluated the relationship between hepatic enzymes and factors such as HbA1c, blood glucose, triglyceride, and cholesterol. Al-Jameil et al., 2014, observed that ALT and GGT have a positive and significant relationship with FBS, PPBS, HbA1c, TC, triglyceride, LDL-C, and a negative correlation with HDL-C [16]. Moreover, Idris et al., reported similar results [17]. Studies have also found a positive relationship between increased hepatic enzymes and glucose levels in fasting from midnight and after meals [18]. Contrarily, Saligram et al., reported an increase in ALT levels with high triglyceride and low HDL-C, but not with controlling the blood glucose level [15]. Liver as a central organ is involved in metabolism of carbohydrates and lipids, and its function is disrupted in diabetes due to insulin resistance. Insulin helps in degradation of liver by its pre-inflammatory effect [19]. Insulin resistance is a proinflammatory state contributing to liver injury. Hyperlipidemia profile is observed due to increase in transfer of lipids to liver, considering the reduction in oxidation. A disruption in the natural process of synthesis and destruction of triglycerides may lead to fibrosis, cirrhosis, and hepatocellular carcinoma [20, 21]. Marchesinia reported a link between ALT activity and blood lipids [22]. In addition, one study found a link between ALT activity and increase in hepatic lipids [23]. In accordance with other studies, regression analysis has shown that HbA1c has a positive relationship with hepatic

enzymes and hepatic steatosis [24, 25]. Therefore, it has been determined that hepatic enzymes have a significant relationship with factors such as FBS, HbA1c, cholesterol, and triglyceride.

In the present study, reduction of blood glucose level after six months did not lead to significant reduction of hepatic enzymes, and this could be related to the fact that increased hepatic enzymes in these individuals had different reasons than blood glucose levels since not all the samples studied in the current work belonged to diabetic patients.

On the other hand, with reduction of triglyceride over the course of six months, AGOT and AGPT enzymes had a considerable reduction as well. The Pearson correlation coefficients for SGOT and STPT were 0.342 and 0.318, respectively. If Pearson correlation coefficient is between 0.3 and 0.7, there is a moderate correlation between the variables. Therefore, there was a moderate correlation between triglyceride reduction and AGOT and AGPT enzymes' reduction after six months. Similar to triglyceride, reduction of cholesterol led to reduction in AGOT and AGPT enzymes after six months. The correlations between cholesterol reduction and SGPT and SGOT reductions were weak (less than 0.3) and moderate, respectively. These results show that dietary treatments that lead to reduced triglyceride in people's blood can greatly help in reducing hepatic enzymes in them.

## 5. Conclusion

Based on the results of the current study, changes in FBS and HbA1c were not significantly different in two consecutive visits. Therefore, changes in these two parameters cannot be used for treatment of fatty liver [changes in hepatic enzymes]. However, changes in cholesterol and triglyceride can be used for monitoring the treatment of people who have abnormal levels of hepatic enzymes. This study shows that future research using global data will enable more precise management and treatment strategies for these patients.

## Conflict of Interests

The author has no conflicts with any step of the article preparation.

## Consent for publications

The author read and approved the final manuscript for publication.

## Ethics approval and consent to participate

This study was performed on patients at Fajr Hospital in Tehran with their consent.

## Informed Consent

This study was performed on patients at Fajr Hospital in Tehran with their consent.

## Availability of data and material

The data that support the findings of this study are available from the corresponding author upon reasonable request.

## Authors' contributions

Mahboobeh Talebi Mehrdar: Research design and supervision; Wei Lu: Advisor; Adel Rahanjam: Perform all laboratory procedures.

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