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Original Article

Elevated liver enzymes and diabetes in the PERSIAN Guilan cohort study

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Abstract

Background: Diabetes mellitus (DM) is highly consequential to global health among chronic diseases. Due to a limited researches that have examined relationships between liver enzymes and DM, this study aimed to investigate the link between elevated liver enzymes and diabetes among Prospective Epidemiological Research Studies in Iran (PERSIAN) Guilan cohort study (PGCS) population.

Methods: This cross-sectional study was conducted on 10519 individuals. The demographic and clinical information of the participants was recorded. The changes in alanine aminotransferases (ALT) and aspartate aminotransferases (AST), alkaline phosphatase (ALP), and γ-glutamyltransferase (GGT) were evaluated. IBM SPSS Version 21 was used to analyze the data, with a significance level < 0.05.

Results: The frequency of diabetes was 24.1% and was more prevalent in women than men (27.4% vs. 20.2%, p< 0.001). After removing all confederates, patients with elevated ALT, AST, GGT, and ALP levels were 1.27, 1.27, 1.52, and 1.46 times more likely to have diabetes, respectively. The likelihood of developing diabetes rose in correlation with the number of elevated liver enzymes, up to almost 1.77-fold among subjects with three or four increased liver enzymes.

Conclusion: Patients diagnosed with diabetes exhibited significantly increased levels of liver enzymes compared to those without diabetes. Also, impairment of three or four liver enzymes demonstrated a positive correlation with an elevated likelihood of DM. This indicates the importance of considering the liver status in the management of the DM population.

Keywords: Diabetes, Liver enzymes, Dyslipidemia, Prevalence.

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Diabetes is globally recognized as a significant non-communicable disease and a major contributor to both morbidity and mortality (1). Diabetes mellitus (DM) has affected more than 415 million people aged 20 to 79 worldwide, and it is predicted to rise to 624 million people by 2040 (2). About 80% of people with diabetes live in developing countries with weak economy (3). Appearance of liver disorders in patients with DM have attracted increased consideration due to its post health implications and the financial burden on society (4). A high level of liver enzymes has been reported as an indicator for diabetes. Diabetes raises the level of these enzymes in the blood. This is mainly due to increased oxidative stress in the tissue regions, possibly partly due to elevated blood sugar levels (5, 6). Multiple research studies have established associations between DM and various liver conditions, including non-alcoholic fatty liver disease (NAFLD) and hepatocellular carcinoma (5, 7), and these diseases are believed to be one of the reasons for death in diabetes patients (8, 9). The liver plays a crucial role in maintaining glucose metabolism and homeostasis within the human body (10).

Alanine aminotransferase (ALT), aspartate aminotransferase (AST) and γ-glutamyl transferase (GGT) has been revealed to be excellent predictors of liver health, are closely linked to an increased risk of hepatic insulin resistance and the development of type 2 diabetes (T2D) (11, 12). ALT is found primarily in the liver and is regarded as a particular marker of liver damage (13), whereas GGT appears on most cell surfaces and is extremely active in the liver, pancreas and kidney (14). GGTs mediate glutathione uptake, is involved in oxidative stress and chronic inflammation, and is also thought to be an essential pathway in the pathogenesis of T2D (13, 15, 16).

Therefore, liver enzymes may be the underlying biological markers that link DM with liver disease. Several studies have previously assessed the association between liver enzymes and DM in Asian, European, and American peoples (7, 13, 17-19). Most previous studies investigated links involving just two or three liver enzymes, and there are a few studies that investigated four liver enzymes to assess their association with diabetes. In addition, the results were contradictory. Epidemiological documents regarding the link between increased liver enzymes and DM among Guilan adults are not yet available. Therefore, we performed this study to evaluate the prevalence of ALT, AST, ALP, and GGT among the individuals with and without diabetes among Prospective Epidemiological Research Studies in Iran (PERSIAN) Guilan cohort study (PGCS) population**,** and assess the association of elevated liver enzymes with DM.

Methods

Participants: This cross-sectional survey was conducted on a total number of 10519 individuals including for 2530 individuals with diabetes and 7,989 without diabetes among PGCS population in Guilan province, Iran, in 2022 (20, 21). The study has been confirmed by the Ethics Committee of the Guilan University of Medical Sciences, Rasht, Iran (IR.GUMS.REC.1401.578), and all the participants provided informed consent prior to their involvement. According to PGCS individuals with the age range of 35 to 70 years and individuals with diabetes was included, while individuals who were unable to attend the clinic for a physical examination, had mental retardation, or expressed unwillingness to participate were excluded.

Data collection: In the general field, demographic characteristics such as age, gender, marital status, education level, employment status, habitat, socioeconomic status (SES), physical activity, body mass index (BMI), smoking, alcohol consumption were recorded. The laboratory findings included fasting blood sugar (FBS), total cholesterol, triglycerides (TG), low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, ALT, AST, GGT, and ALP via a biotecnica auto analyzer (BT 1500, Italy) were analyzed in medical laboratory of the cohort center. The precision and accurateness of all processes were evaluated according to the related guidelines.

The history of having fatty liver disease was self-reported that was recorded through face-to-face interview. Also, the record of hepatotoxic medicines was self-reported and based on the check of medications accompanying the patient. Hepatotoxic medicines included paracetamol, NSAIDs, glucocorticoids, Isoniazid and hydrazine categories. Dyslipidemia was defined as follows: Chol ≥200 U/L, TG ≥150 U/L, LDL ≥100 U/L, and HDL ≤40 U/L for men and ≤50 U/L for women (22). Elevated liver enzymes were definite as follows: ALT ≥ 32 U/L in males / ≥ 22 U/L in females, AST ≥ 37 U/L in males/ ≥ 31 U/L in females, GGT ≥ 49 U/L in males/ ≥ 32 U/L in females, and ALP ≥ 307 U/L in both males and females (23, 24). Diabetes was definite as fasting blood sugar ≥126 mg/dL and/or a history of diabetes diagnosis or consumption of anti-diabetic medications (25).

Statistical analysis: Numbers, percentages, and mean±standard deviation (SD) were used to report variables. We evaluated the differences between people with and without diabetes use as t-test for continuous variables and the $\chi 2$ test (or Cochran–Armitage test for trend) for categorical data. The association of diabetes with elevated liver enzymes was examined using logistic regression analysis. Odds ratios (OR) and 95% confidence intervals (CI) were determined. ORs were adjusted for demographic and clinical variables. Model 1 was unadjusted; Model 2 was adjusted for sex and age; Model 3 was adjusted for variables in Model 2 plus marital status, level of education, employment status, habitat, SES, BMI, physical activity, smoking, use of alcohol; and Model 4 was adjusted for variables in Model 3 plus total cholesterol, triglyceride, LDL cholesterol, HDL cholesterol, fatty liver, and consumption of hepatotoxic drugs. IBM SPSS Version 21 was used to analyze all the data, with a significance level of less than 0.05.

Results

Characteristics of participants: The mean age of the individuals was 51.52±8.90 years. Of the participants, 53.6% were females, 90.6% married, 6.1% had university education, 54.5% were employed, 56.2% residents in rural

area, 32.7% had obese-BMI, 24.6% were smokers, and 13.3% consumed alcohol. Compared to participants without diabetes, participants with diabetes were older, more likely to be females, more widowed, more unemployed, more residents in urban area, less smoker, had low SES, high BMI, low psychical activity, more likely to have dyslipidemia and fatty liver and more were reported users of hepatotoxic drugs (table 1).

Prevalence of elevated liver enzymes: Frequency of increased ALT, AST, GGT and ALP was 19.4, 4.6, 11.6, and 5.1%, respectively. Frequency of increased ALT, AST and GGT was greater in women compared to men (P<0.001, P=0.040, P<0.001, respectively). Frequency of elevated ALT decreased = with age (P for trend<0.001), whereas, the prevalence of elevated ALP increased with age (P for trend<0.001) (table 2).

Table 1. Demographic and clinical characteristics of the participants

	Total (n=10519)	Diabetes (n=2530)	Non-Diabetes (n=7989)	P- value
Age (years)				
35-44	3138 (29.8)	441 (17.4)	2697 (33.8)	
45-54	3854 (36.6)	862 (34.1)	2992 (37.5)	<0.001*
55-64	2730 (26.0)	942 (37.2)	1788 (22.4)	
≥ 65	797 (7.6)	285 (11.3)	512 (6.4)	
Mean±SD	51.52±8.90	54.65±8.64	50.52±8.75	<0.001**
Gender				
Male	4886 (46.4)	988 (39.1)	3898 (48.8)	<0.001*
Female	5633 (53.6)	1542 (60.9)	4091 (51.2)	
Marital status				
Single	305 (2.9)	46 (1.8)	259 (3.2)	
Married	9526 (90.6)	2244 (88.7)	7282 (91.2)	<0.001*
Widow	566 (5.4)	218 (8.6)	348 (4.4)	
Divorced	122 (1.2)	22 (0.9)	100 (1.3)	
Education level				
Illiterate	1738 (16.5)	636 (25.1)	1102 (13.8)	
1-5	3312 (31.5)	808 (31.9)	2504 (31.3)	<0.001*
6-12	4831 (45.9)	973 (38.5)	3858 (48.3)	
University	638 (6.1)	113 (4.5)	525 (6.6)	
Mean±SD	6.63±4.52	5.60±4.60	6.95±4.45	<0.001**
Employment status				
Unemployed	4781 (45.5)	1409 (55.7)	3372 (42.2)	<0.001*
Employed	5738 (54.5)	1121 (44.3)	4617 (57.8)	
Habitat				
Urban	4612 (43.8)	1166 (46.1)	3446 (43.1)	0.009*
Rural	5907 (56.2)	1364 (53.9)	4543 (56.9)	

	Total (n=10519)	Diabetes (n=2530)	Non-Diabetes (n=7989)	P- value
SES				
Quartile 1	2630 (25.0)	674 (26.6)	1956 (24.5)	
Quartile 2	2630 (25.0)	695 (27.5)	1935 (24.2)	<0.001*
Quartile 3	2630 (25.0)	618 (24.4)	2012 (25.2)	
Quartile 4	2629 (25.0)	543 (21.5)	2086 (26.1)	
Mean±SD	0±1	-0.09±0.95	0.03±1.01	<0.001**
BMI (kg/m2)				
Underweight	141 (1.3)	22 (0.9)	119 (1.5)	
Normal	2746 (26.1)	545 (21.5)	2200 (27.5)	<0.001*
Overweight	4198 (39.9)	1021 (40.4)	3177 (39.8)	
Obese	3435 (32.7)	942 (37.2)	2493 (31.2)	
Mean±SD	28.14±5.09	28.91±5.37	27.90±4.97	<0.001**
Physical activity (MET)				
Quartile 1	2630 (25.0)	804 (31.8)	1826 (22.9)	
Quartile 2	2630 (25.0)	676 (26.7)	1954 (24.5)	<0.001*
Quartile 3	2630 (25.0)	598 (23.6)	2032 (25.4)	
Quartile 4	2629 (25.0)	452 (17.9)	2177 (27.2)	
Mean±SD	41.26±8.88	39.45±7.95	41.83±9.09	<0.001**
Smoking				
Non-smoker	7935 (75.4)	1982 (78.3)	5953 (74.5)	<0.001*
Smoker	2584 (24.6)	548 (21.7)	2036 (25.5)	
Alcohol consumption				0.813*
No	9124 (86.7)	2198 (86.9)	6926 (86.7)	<0.001*
Yes	1395 (13.3)	332 (13.1)	1063 (13.3)	
Total Cholesterol	192.79±38.98	190.66±41.89	193.47±37.98	0.002**
Triglycerides	160.27±103.28	180.43±118.36	153.88±97.16	<0.001**
LDL-C	112.85±32.05	107.87±34.15	114.42±31.20	<0.001**
HDL-C	48.38±10.97	47.55±10.85	48.64±11.00	<0.001**
Dyslipidemia				
No	2542 (24.2)	507 (20.0)	2035 (25.5)	<0.001*
Yes	7977 (75.8)	2023 (80.0)	5954 (74.5)	
Elevated ALT	2043 (19.4)	583 (23.04)	1460 (18.3)	<0.001*

	Total (n=10519)	Diabetes (n=2530)	Non-Diabetes (n=7989)	P- value
Elevated AST	480 (4.6)	141 (5.6)	339 (4.2)	0.005*
Elevated GGT	1222 (11.6)	423 (16.7)	799 (10.0)	<0.001*
Elevated ALP	536 (5.1)	187 (7.4)	349 (4.4)	<0.001*
Fatty Liver Disease				
No	9823 (93.4)	2284 (90.3)	7539 (94.4)	<0.001*
Yes	696 (6.6)	246 (9.7)	450 (5.6)	
Use of hepatotoxic drugs				
No	8784 (83.5)	1721 (68.1)	7063 (88.4)	<0.001*
Yes	1732 (16.5)	807 (31.9)	925 (11.6)	

BMI: Body Mass Index; SES: Socioeconomic status; LDL-C: Low Density Lipoprotein-Cholesterol; HDL-C: High Density Lipoprotein-Cholesterol; ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase; GGT: Gamma-Glutamyl Transferase; ALP: Alkaline Phosphatase; SD: Standard Deviation; *Chi-squard test; **Independent t-test. *P*-value of less than 0.05 was considered statistically significant

Prevalence of diabetes: In this study, the prevalence of diabetes was 24.1% and was more prevalent in females than in males (27.4% vs. 20.2%, *P*<0.001). The frequency of diabetes increased with age, being highest at 35.8% in people aged 65 years and older (*p* for trend<0.001) (table 2).

Elevated liver enzymes and diabetes: The prevalence of diabetes was higher among participants with elevated ALT than those with normal ALT level (28.5% vs. 23.0%, *P*<0.001). The similar consequences were also determined for AST, GGT and ALP (table 3).

In unadjusted model (model 1), an elevation in ALT levels was found to be related to a 34% elevated likelihood of developing diabetes, with an OR of 1.34 and a 95% CI ranging from 1.20 to 1.49. Similar results were also obtained for AST (OR=1.33, 95% CI: 1.09–1.63), GGT (OR=1.81, 95% CI: 1.59–2.05), and ALP (OR=1.75, 95% CI: 1.45–2.10).

After adjustment for variables in models 2 and 3, these associations weakened but remained significant. In fully adjusted model (Model 3), the presence of increased ALT, AST, GGT and ALP elevated the odds of diabetes by 1.27-fold (95% CI: 1.13–1.43), 1.27-fold (95% CI: 1.02–1.57), 1.52-fold (95% CI: 1.32–1.75), and 1.46-fold (95% CI: 1.20–1.78), respectively (table 3).

Table 2. Prevalence of elevated liver enzymes and diabetes among the participants

Variables	Elevated ALT n (%)	Elevated AST n (%)	Elevated GGT n (%)	Elevated ALP n (%)	Diabetes n (%)
Total	2043 (19.4%)	480 (4.6%)	1222 (11.6%)	536 (5.1%)	2530 (24.1%)
Age					
35-44	673 (21.4%)	154 (4.9%)	346 (11.0%)	101 (3.2%)	441 (14.1%)
45-54	779 (20.2%)	168 (4.4%)	431 (11.2%)	170 (4.4%)	862 (22.4%)
55-64	481 (17.6%)	126 (4.6%)	358 (13.1%)	202 (7.4%)	942 (34.5%)
≥ 65	110 (13.8%)	32 (4.0%)	87 (10.9%)	63 (7.9%)	285 (35.8%)
P for trend†	<0.001	0.617	0.111	<0.001	<0.001
Sex					
Male	873 (17.9%)	201 (4.1%)	350 (7.2%)	244 (5.0%)	988 (20.2%)
Female	1170 (20.8%)	279 (5.0%)	872 (15.5%)	292 (5.2%)	1542 (27.4%)
P	<0.001	0.040	<0.001	0.659	<0.001

ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase; GGT: Gamma-Glutamyl Transferase; ALP: Alkaline Phosphatase; *Cochran–Armitage test for trend; *P*-value of less than 0.05 was considered statistically significant

Number of elevated liver enzymes and diabetes: The prevalence of diabetes among the participants with 0, 1, 2, and 3 or 4 elevated liver enzymes was 21.7, 28.9, 30.7 and 37.5%, respectively. In the other words, the prevalence of diabetes rose with increasing number of elevated liver enzymes (p for trend<0.001) (table 3 and figure 1). According to the logistic regression analysis, in unadjusted model, compared with participants without any elevated liver enzymes, the OR of diabetes was 1.47 (95% CI: 1.32–1.65) for participants with one elevated liver enzymes, 1.60 (95% CI: 1.36–1.89) for participants with two elevated liver enzymes, and 2.17 (95% CI: 1.69–2.79) for participants with three or four elevated liver enzymes, with a significant trend in OR with increasing number of elevated liver enzymes. The relations remained significant after adjusting for sex and age (model 2). Similar results (but with lower ORs) were obtained in models 3 and 4 (fully adjusted model) (table 3).

Table 3. Relationship between liver enzymes and diabetes among the participants

	Prevalence of diabetes, n (%)	Model 1 (Unadjusted)		Model 2		Model 3		Model 4	
		OR (95% CI)	P	aOR (95% CI)	P	aOR (95% CI)	P	aOR (95% CI)	P
ALT									
Normal	1947 (23.0%)	1		1		1		1	
Elevated	583 (28.5%)	1.34 (1.20 – 1.49)	<0.001	1.42 (1.27 – 1.59)	<0.001	1.36 (1.21 – 1.52)	<0.001	1.27 (1.13 – 1.43)	<0.001
AST									
Normal	2389 (23.8%)	1		1		1		1	
Elevated	141 (29.4%)	1.33 (1.09 – 1.63)	0.005	1.35 (1.10 – 1.67)	0.004	1.27 (1.03 – 1.57)	0.024	1.27 (1.02 – 1.57)	<0.001
GGT									
Normal	2107 (22.7%)	1		1		1		1	
Elevated	423 (34.6%)	1.81 (1.59 – 2.05)	<0.001	1.68 (1.47 – 1.92)	<0.001	1.58 (1.38 – 1.81)	<0.001	1.52 (1.32 – 1.75)	<0.001
ALP									
Normal	2343 (23.5%)	1		1		1		1	
Elevated	187 (34.9%)	1.75 (1.45 – 2.10)	<0.001	1.50 (1.24 – 1.81)	<0.001	1.45 (1.20 – 1.76)	<0.001	1.46 (1.20 – 1.78)	<0.001
No of elevated liver enzymes									
0	1637 (21.7%)	1		1		1		1	
1	563 (28.9%)	1.47 (1.32 – 1.65)	<0.001	1.45 (1.29 – 1.63)	<0.001	1.39 (1.23 – 1.56)	<0.001	1.30 (1.15 – 1.47)	<0.001
2	228 (30.7%)	1.60 (1.36 – 1.89)	<0.001	1.61 (1.36 – 1.91)	<0.001	1.52 (1.28 – 1.80)	<0.001	1.48 (1.24 – 1.76)	<0.001
≥ 3	102 (37.5%)	2.17 (1.69 – 2.79)	<0.001	2.04 (1.57 – 2.65)	<0.001	1.87 (1.44 – 2.43)	<0.001	1.77 (1.35 – 2.32)	<0.001

Model 1: Unadjusted model. Model 2: Adjusted for sex and age. Model 3: Adjusted for Model 2 plus marital status, years of education, occupation, place of residency, SES, BMI, physical activity, smoking, alcohol consumption. Model 4: Adjusted for Model 3 plus total cholesterol, triglyceride, LDL cholesterol, HDL cholesterol, fatty liver, and use of hepatotoxic drugs. BMI: Body Mass Index; SES: Socioeconomic status; LDL-C: Low Density Lipoprotein-Cholesterol; HDL-C: High Density Lipoprotein-Cholesterol; ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase; GGT: Gamma-Glutamyl Transferase; ALP: Alkaline Phosphatase; OR: crude odds ratio, aOR: adjusted odds ratio; CI: confidence interval; A *P*-value of less than 0.05 was considered statistically significant.

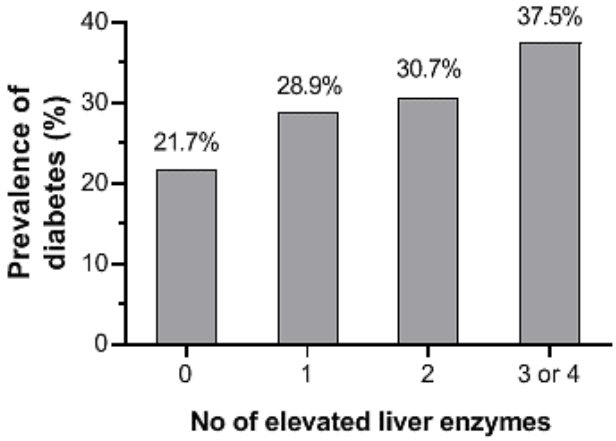

Figure 1. Prevalence of diabetes based on the number of elevated liver enzymes among the participants

Discussion

In this present study, we tried to take a step towards clarifying the path of studies investigating the link between elevated liver enzymes and DM through examining the data related to the Guilan cohort study. Our study suggests that increased ALT, AST, GGT and ALP were significantly more prevalent in participants with diabetes and also were positively related with increased odds of DM. With adjustment for potential confounders, similar results with lower ORs were obtained for all elevated liver enzymes. In present survey, frequency of increased liver enzymes (ALT, AST and GGT) in people with DM has been higher among females than males. Similar studies have been indicated an increase in AST, GGT and ALP enzymes in females relative to the males (7, 17, 26). The body fat distribution and metabolism differences in people can explain sex differences. Differences in reference values, age categories, personal habits, and demographics may also be substantial factors in the observed variability in these studies.

A higher prevalence of increased ALT levels among DM group compared to the individuals without diabetes was reported in previous studies (17, 26, 27). Also, the relevance of elevated serum ALT levels on increasing the probability of DM was reported in previous studies (28-30). Our findings are in complete agreement with these studies. About 23% of patients with diabetes and 18.3 % of individuals without diabetes had elevated ALT levels (<0.001). Findings regarding the link of elevated AST and ALP with increasing chance of DM have been contradictory. In a number of studies, no evidence was obtained in favor of this relationship. This can be caused by the weakness of these articles due to the small number of studied cases (between 48 and 571 patients with diabetes) (13, 30-32). Similar to our result, in a number of other articles, the positive role of AST (26, 33, 34), and ALP (26, 35), on increasing the odds of DM and the higher prevalence among individuals with diabetes have been mentioned (17, 36). Several mechanisms have been suggested as the basis for the association between liver Serum ALT and AST levels and DM. Liver aminotransferases and especially ALT have been reported to have strong correlation with liver fat accumulation (37, 38). Also, ALT and GGT levels were introduced as alternative criteria for the diagnosis of NAFLD (39). Elevated concentrations of free fatty acids in the liver can contribute to several metabolic disturbances, including dyslipidemia, fasting hyperglycemia, excessive insulin secretion from the pancreas, and reduced efficiency of insulin signaling, which result in hyperinsulinemia and an increased risk of developing diabetes (40-42). The other possible assumption is that the elevated liver enzymes can be a sign of underlying chronic inflammation that ultimately leads to impaired insulin signaling (42, 43).

Following these results and aligned with the results of our investigation, studies were conducted that pointed to the existence of a positive relationship between liver biomarkers with DM despite the adjustment of factors such as blood lipid levels (34, 44, 45) and fatty liver disease (26, 46). In these studies, the possibility of an alternative path to explain this connection was proposed. Furthermore, there is limited evidence to describe the relationship pathway of ALP with diabetes. The inverse link between ALP and adiponectin (a hormone secreted by adipose tissue) can partially explain this relationship. Decreased serum adiponectin level is known as an independent risk factor for DM (47, 48). Similar to the findings obtained in our review, a significant number of studies have pointed to the strong and independent association of GGT with DM (13, 17, 30). In a randomized Mendelian study, Conen et al., pointed to a causal association between GGT and insulin resistance (49). There is also clear evidence of GGT's role in maintaining

intracellular glutathione levels, which thus, plays an important role in establishing intracellular antioxidant defense (50, 51). The increase in oxidative stress affects the development and progression of diabetes, and in a chronic state it eventually leads to insulin resistance (52, 53). The findings of our present study demonstrate that as the number of impaired liver enzymes increases, there is a corresponding rise in both the prevalence and likelihood of developing diabetes, so that in participants with 3 or 4 impaired LFTs, the prevalence of diabetes was 37.5% (compared to 21.7% participants with normal LFTs) and the odds of diabetes in fully adjusted model was 1.77 times that of the normal population.

There is a need for a comprehensive and prospective study to accurately determine the link between liver enzymes and DM. Perhaps the results of the researches conducted so far have not been sufficient to prove the prognostic power of liver enzymes to determine the exact mechanism, but what is evident is the liver's fundamental role in this process. The current importance is the early diagnosis of liver dysfunction by requesting LFTs in patients with DM. The large study community with inclusion of established diabetes risk factors (BMI, lipids, fatty liver disease and history of hepatotoxic drugs) in addition to the demographic and lifestyle information is the strengths of this present study. Another strength of ours, unlike previous studies, was the determination of patients with diabetes not only based on self-report but also by laboratory findings. Moreover, people's degree of physical activity was determined using a physical activity international questionnaire. The most important limitation of our investigation was the cross-sectional nature of this study; therefore, it did not allow us to investigate whether the occurrence of diabetes preceded the increase in liver biomarkers or not.

Also, chronic or transient abnormalities in LFTs were not evaluated in our study. In this study, we did not use any imaging method to identify patients with fatty liver, and this was determined based on the patient's medical records. Future research should consider examining the potential link between the duration of the disease and the impairment of liver enzymes, as well as their association with FBS and HbA1C levels. Our focus in this study has been on expressing the importance of liver biomarkers evaluations in DM patients. Elevated levels of ALT, AST, ALP and GGT were more common in individuals with diabetes and had positive association with increasing the odds of DM even after adjustment for confounders. Also, participants with three or four impaired LFTs, demonstrating a positive correlation with an elevated likelihood of DM. This topic indicates the high importance of considering liver status in management of DM population.

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Ethics approval: This study was approved by the Ethics Committee at the Guilan University of Medical Sciences (IR.GUMS.REC.1401.578). Informed consent was obtained from all individual participants.

Conflict of interests: The authors declare that they have no competing interests in this work.

Authors' contribution: FJ, MTA, KM and FMGH participated in the research design. FJ, TZ, NF and MRJ participated in writing the first draft. SM and MRN participated in the performance of the research and analytic tools. SM and AP participated in data analysis. All authors reviewed and confirmed the final manuscript.

Availability of data and materials: The study protocol and the datasets analyzed are available from the corresponding author upon request.

Informed consent: Informed consent was obtained from all individual participants.

Consent for publication: Not applicable.

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