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Original Article

Comparison of Triglyceride-Glucose Index between Patients with Gallstone and Healthy Individuals

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Abstract

Background: Triglyceride-glucose index is a product of triglycerides and fasting plasma glucose (FPG) and is a new index of insulin resistance found to correlate with direct measurements. This study aimed to evaluate the relationship between gallstones and triglyceride-glucose index (TGI).

Methods: A total of 210 patients were included in this retrospective study. Overall, 105 patients with gallstones were included in the patient group. Patients with diabetes mellitus, chronic diseases, malignant diseases, and patients using cholesterol-lowering drugs were excluded from the study. Healthy individuals (105 cases) were selected for the control group. TGI was calculated separately for each individual using the following formula: (TGI) = ln (fasting TG (mg/dL) x fasting glucose (mg/dL)/2)

Results: Plasma triglyceride levels were significantly higher in patients with gallstones compared to the control group (P=0.001). Plasma HDL, LDL, and total cholesterol did not differ between the groups (P>0.05). Fasting blood glucose was significantly higher in patients with gallstones compared to the control group (P=0.001). The triglyceride glucose index was significantly higher in patients with gallstones compared to the control group (P<0.001). When the relationship between body mass index and TGI was analyzed, TGI was lower in patients with normal BMI compared to overweight or obese patients (P<0.001).

Conclusion: Increased triglyceride/glucose index in patients with gallstones is an indicator of insulin resistance. It is instrumental in demonstrating the presence of insulin resistance in patients with gallstones and may be a useful guide in earlier detection, prevention, and treatment of insulin resistance.

Keywords: Gallstones; Triglyceride-glucose index; Body mass index; Insulin resistance

Introduction

Gallstone disease associated with central obesity is common in countries all over the world. Gallstone disease is expected to increase due to the increasing prevalence of obesity (1, 2). Age, ethnicity, genetics, gender, parity, physical inactivity, medications, and diet also play a role in gallstone formation (3). The most common type of stone is cholesterol stones associated with cholesterol supersaturation due to cholesterol metabolism products (4, 5). The relationship between body mass index (BMI) and gallstones has been evaluated in many studies. Studies are showing that increased BMI is associated with gallstone formation. The association between BMI and gallstones is stronger in women compared to men. It has been shown that the estrogen hormone may

be associated with an increase in hepatic cholesterol synthesis and secretion in women (5-7). An increase in plasma insulin levels is a pathophysiological factor that increases the risk of gallstones in obesity. High plasma insulin levels cause cholesterol hypersecretion by increasing 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase activity (8, 9). In addition, insulin resistance and type 2 diabetes mellitus are associated with the formation of cholesterol gallstones (10).

Triglyceride-glucose index (TGI) is a product of triglycerides and fasting plasma glucose (FPG) and is a new index of insulin resistance found to correlate with direct measurements (11, 12). It is more effective than HOMA-IR in determining metabolic syndrome (13). The association of gallstones with insulin resistance in non-obese subjects has not been fully elucidated. There is no study in the literature evaluating the relationship between triglyceride glucose index and body mass index in patients with gallstone disease.

This study aimed to evaluate the relationship between gallstones and triglyceride-glucose index. It is also aimed to evaluate whether there is a relationship between body mass index and triglyceride glucose index in patients with gallstones.

Materials and Methods

Working Design

This retrospective study was conducted between 01.01.2020 and 20.06.2022 at Mersin City Training and Research Hospital, Mersin, Türkiye. A total of 210 patients were included in the study. Patients included in the study were randomized by stratified sampling method. The sample size was determined as 210 patients with a 95% confidence interval, effect size: 0.5, N1/N2=1. Patients with gallstones (n=105) were included in the patient group. Patients with diabetes mellitus, chronic diseases, rheumatic and inflammatory diseases, malignant diseases, and patients using cholesterol-lowering drugs were excluded from the study. In addition, those who consumed omega-3 supplements and supplements with blood sugar and cholesterol-lowering effects, such as cinnamon, were excluded from the study.

The presence of gallstones was demonstrated by whole abdomen ultrasound. The diagnosis of diabetes mellitus was excluded with a 75-gram OGTT according to the American Diabetes Association criteria (14). Patients in the control group (n=105) were selected from patients who did not have any disease, who were shown to have no stones in the gallbladder by whole abdomen ultrasound, and who were admitted to the internal medicine outpatient clinic for routine control and screening.

Demographic data, weight, and height information were obtained from patient files. Body mass index (BMI) was calculated by dividing weight (kilogram) by height squared (meter). Based on the WHO classification, patients were further classified as normal weight (BMI<24.99), overweight (BMI between 25 and 29.99), and obese (BMI>30) (15). Concerning previous study, the TGI was calculated separately for each individual with the formula ln (fasting TG (mg/dL) x fasting glucose (mg/dL)/2) (16). All of the patients evaluated in terms of exercise in the International Physical Activity Questionnaire (IPAQ) had exercise levels in the minimally active category (17). All patients had a mediterranean diet history. All patients had a history of carbohydrate-containing food intake in their diets. Biochemical parameters of the patients were obtained from the hospital database. Fasting blood sugar, HbA1c, total cholesterol, triglyceride, high-density lipoprotein, and low-density lipoprotein were assessed using an Abbott Architect 16200 autoanalyzer (Abbott Inc., Princeton, NJ, USA).

Ethics committee approval dated 20.07.2022 and numbered 2022/492 was obtained from Mersin University Ethics Committee before starting the study.

Statistical Analysis

Shapiro-Wilk test was used to test whether the variables conformed to normal distribution. Normally distributed variables were presented as

mean±standard deviation and an Independent Sample *t*-test was used for comparisons between two independent groups. The one-way Analysis of Variance (ANOVA) test was used for comparisons between three independent groups. Confounding factors were not used in the study. Non-normally distributed variables were presented as median (minimum-maximum) values and the Mann-Whitney U test was used for comparisons between two independent groups. Categorical variables were presented as frequency and percentage values and Pearson chi-square test was used for comparisons. Spearman Correlation Analysis was used for the relationships between the variables.

Statistical analyses were performed in IBM SPSS Statistics 22.0 program. The significance level was taken as α=0.05.

Results

The mean age of patients with gallstones was 52 years, while the mean age of the control group was 50 years. There was no difference between the groups in terms of age (*P*=0.869). There were 79 women and 26 men in both groups.

Plasma triglyceride levels were significantly higher in patients with gallstones compared to the control group (*P*=0.001). Plasma HDL, LDL, and total cholesterol did not differ between the groups (*P*>0.05). Fasting blood glucose was significantly higher in patients with gallstones compared to the control group (*P*=0.001). The triglyceride glucose index was significantly higher in patients with gallstones compared to the control group (*P*<0.001). Demographic characteristics and comparative analysis results of patients with gallstones and the control group are given in Table 1.

Tabe 1: Examination of the groups in the scope of the research according to various variables

Variables	***Groups***		***Test t*/Z*****	***P Value***
	Gallstone group (n=105)	Control group (n=105)		
Age (year)*	52(20-65)	50(20-66)	-0.165	0.869
Fasting blood sugar (mg/dL)**	97(71-127)	89(73-106)	-8.319	*<0.001*
HbA1c (%)**	5.5(4,1-8,6)	5.6(4,1-6,1)	-1.095	0.274
Total cholesterol (mg/dL)**	184(100-332)	190(117-311)	-0.919	0.358
Triglyceride (mg/dL)**	170(69-765)	146(44-307)	-3.467	*<0.001*
High-density lipoprotein (mg/dL)**	47(24-105)	50(28-85)	-1.356	0.175
Low-density lipoprotein (mg/dL)**	106(48-195)	106(48-195)	-0.160	0.873
Triglyceride-glucose index (TGI)*	9.04±0.41	8.71±0.44	5.726	*<0.001*

P<0,05, *Independent Sample t-Test, **Mann Whitney U Test

A significant difference was found between the groups in terms of BMI (*P*<0.001). Participants in the control group were more likely to be of normal weight than obese, whereas patients with gallstones were more likely to be obese than normal weight. There was no statistically significant difference between the other groups (*P*>0.05). The results of the statistical analysis are given in Table 2.

Table 2: Examination of the groups within the scope of the research by gender and body mass index groups

Variable			*Groups*		*P value*
			Gallstone group (n=105)	Control group (n=105)	
BMI Groups	Normal weight	n	15	39	<0.001
		%	27.8%	72.2%	
	Overweight	n	34	23	
		%	59.6%	40.4%	
	Obese	n	56	43	
		%	56.6%	43.4%	

P<0,05, Pearson Chi-Square Analysis

The TGI values of the patients in the group with gallstones did not show a statistically significant difference according to the body mass index groups. (*P*>0.05). Statistical results are shown in Table 3.

Table 3: Investigation of Triglyceride-glucose Index by Body Mass Index Groups in Patients with Gallstones

	Variables	*N*	*Mean*	*SD*	*F*	*P value*
BMI Groups	Normal weight	15	9.03	0.58	11.681	0.155
	Overweight	34	8.94	0.38		
	Obese	56	9.11	0.36		

P<0.05, One-Way Analysis of Variance (ANOVA)
BMI, body mass index
SD, standard deviation

There was a positive linear relationship between TGI values and body mass index values of the participants in the group with gallstones (*P*<0.001). As the body mass index values of the participants in the group with gallstones increase, the TGI values also increase. In other words, as the TGI values of the participants in the group with gallstones increased the body mass index values also increase.

Discussion

The prevalence of gallstone disease continues to increase in all countries around the world. Although it is associated with obesity, it can also be seen in non-obese individuals. Hyperinsulinemia has been shown to lead to increased hepatic cholesterol uptake and decreased biliary bile acid secretion. Insulin resistance and type 2 diabetes mellitus are independent risk factors for cholesterol gallstones (10). Previous studies have shown that insulin levels are higher in patients with gallstones (2, 18). Metabolic syndrome and insulin resistance are important factors leading to gallstone formation (19, 20). Another study has shown that glucose intolerance is associated with an increased risk of gallstone formation (21). Blood glucose is associated with insulin, impaired glucose tolerance, biomarkers of insulin resistance such as HOMA or diabetes, and screening-detected gallstone disease (22-24). In our study, fasting blood sugar was significantly higher in patients with gallstones than in the control group (*P*=0.001). These results are similar to the literature (21, 22).

BMI is associated with biliary disease (25-27). BMI and waist circumference were associated with gallstone disease in a meta-analysis (28). In other studies, alternative body fat tissue measurements such as the waist-hip circumference ratio with computed tomography have been associated with gallstone disease (10, 29-31). In our study, BMI was statistically significantly higher in patients with gallstones compared to the healthy control group (P<0.001). These results are similar to the literature (25-28).

In a previous large-scale study, the authors showed that higher total cholesterol, triglycerides, and low-density lipoprotein, and lower high-density lipoprotein levels increase the risk of cholesterol gallstones (18, 32, 33). In our study, plasma triglyceride levels were significantly higher in patients with gallstones compared to the control group (P=0.001). Plasma HDL, LDL, and total cholesterol did not differ between the groups (P>0.05). These results are consistent with the literature (18-20, 32, 33).

The triglyceride-glucose index is a product of triglycerides and fasting plasma glucose (FPG) and is a new index of insulin resistance found to correlate with direct measurements (11, 12, 34). It is more effective than HOMA-IR in determining metabolic syndrome (12, 13, 34). Its association with many diseases has been investigated. Considering the relationship between TGI and insulin resistance, TGI is expected to be higher in obese individuals than in non-obese individuals. Another study suggested that the TGI index in non-diabetic individuals could be used as a diagnostic criterion to identify metabolically obese but normal-weight individuals (35). Another study in the literature showed that the TGI correlated with body mass index in diabetic individuals (36). In our study, when the relationship between body mass index and TGI in patients with gallstones was examined, no statistically significant relationship was found between patients with normal body mass index and obese patients. In our study, there was no patient with a diagnosis of diabetes mellitus in patients with gallstones. When the relationship between BMI and TGI in patients with gallstones was examined, there was a positive linear relationship between TGI values and body mass index values of the participants in the group with gallstones (P<0.001). As the body mass index values of the participants in the group with gallstones increase, the TGI values also increase.

TGI was significantly higher in patients with gallstones compared to the control group (P<0.001). Patients in the gallstone group were non-diabetic individuals. The findings indicate that patients with gallstones without diabetes have insulin resistance. Our study is the first in the literature to investigate the association of gallstones with triglyceride/glucose index. Further studies are needed to clarify the results.

Our study has several limitations. First, the study is retrospective. Secondly, the pathological type of gallstones is not known precisely because the patients were not operated.

Conclusion

TGI, another indicator of insulin resistance, was found to be higher in patients with gallstone disease, even without diabetes mellitus. The increase in TGI values as BMI increases suggests that insulin resistance existed before the body mass index increased significantly in those with gallstones. It may be a useful parameter for the early detection, prevention, and treatment of insulin resistance in patients with gallstones. Since there is not enough research in the literature yet, new, prospective studies may clarify the situation.

Journalism Ethics considerations

Ethical issues (including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, and redundancy) were observed by the authors.

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Conflict of Interest

The authors declare that there is no conflict of interests.

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