

Association between elevated aminotransferase levels and the metabolic syndrome in Northern Turkey

Beytullah Yildirim,* Fikret Ozugurlu,[†] Semsettin Sahin,[‡] Huseyin Ozyurt,[‡] Omer Atis,[‡] Ali Akbas,[‡] Yeliz Akturk,[‡] Metin Ozdemir,[§] Idris Sahin,^{||} Yunus Bulut,[§] Ilker Etikan,[¶] M.Murat Firat[‡]

* Department of Gastroenterology. [†] Department of Biochemistry. [‡] Department of Radiology. [§]Department of Microbiology. [¶] Department of Biostatistics, Gaziosmanpasa University School of Medicine, Tokat, Turkey. ^{||} Department of Nephrology, Inonu University School of Medicine, Malatya, Turkey.

ABSTRACT

Introduction. Elevated aminotransferase levels(ATLs) are alert the physicians for liver-affecting disease and may reflect liver injury. We aimed to determine the prevalence of elevated ATLs and the association of elevated ATLs with the metabolic syndrome(MetS) in a northern province of Turkey. **Materials and methods.** Elevated ATLs were evaluated among 1,095 individuals of the Tokat Prevalence Study which have been described in detail elsewhere. 1,095 participants had been selected by a simple random sampling method among 530,000 inhabitants in 70 (12 urban and 58 rural) areas in the province of Tokat which is located in the Black Sea Region of Turkey. **Results.** The prevalence of elevated serum ALT, AST, and ALT and/or AST were found as 11%, 7.2%, and 13.3%, respectively. Increased BMI, fatty liver, and MetS were higher in our general population with elevated ATLs. After exclusion of individuals with hepatitis B or hepatitis C infection, 132 individuals with elevated ATLs (91 male and 41 female) were evaluated. MetS was found in 59 participants and its prevalence was markedly higher in females with elevated ATLs ($p < 0.0001$). When the males with elevated ATLs were evaluated, the ALT levels of the persons who have no risk of MetS ($p = 0.007$) and the persons who have one risk of MetS ($p = 0.001$) were lower than the persons with MetS. **Conclusions.** Elevated ATLs are common and it's an important cause is MetS in Northern Turkey.

Key words. Elevated aminotransferase levels. Metabolic syndrome. Risk factors. Turkey.

INTRODUCTION

Elevated aminotransferase levels (ATLs) are alert the physicians for liver-affecting disease and may reflect liver injury. The alanine aminotransferase (ALT) levels are more specific indicators of liver injury than aspartate aminotransferase (AST) levels.¹ Some factors like chronic hepatitis, fatty liver, cholelithiasis, hyperglycemia, hyperlipidemia, obesity, medications, alcohol consumption, hemochromatosis, Wilson's disease, and alpha1-antitrypsin deficiency may affect ATLs.¹⁻³ Moreover, some previous studies shown that the prevalence of elevated liver

enzymes is higher in individuals with metabolic syndrome (MetS).^{4,5}

The causes of elevated ATLs may change according to ethnicity, geographic region, and develop situation of countries. If these causes (which effect liver enzymes) are known, the most of all factors may be forecast. Thus, the etiologic factor should be determined with low cost and less time.

To date, no study has assessed the relationship of elevated ATLs and the MetS in a population-based study of Turkey. In this study, we aimed to determine:

1. The prevalence of elevated aminotransferase levels.
2. The association of elevated aminotransferase levels with the metabolic syndrome in urban and rural population in a northern province of Turkey.

MATERIALS AND METHODS

The individuals of Tokat Prevalence Study, have been described in detail elsewhere,^{6,7} were evaluated in

Correspondence and reprint reques: Beytullah YILDIRIM, MD.
Assistant Professor
Gaziosmanpasa University, School of Medicine
Department of Gastroenterology
TR-60100 Tokat/TURKEY
Phone: +90-356-2129500
E-mail: beytullahy@yahoo.com

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this study. Briefly, one thousand and ninety five participants had been selected by a simple random sampling method among 530,000 inhabitants in 70 (12 urban and 58 rural) areas in the province of Tokat which is located in the Black Sea Region of Turkey.

All subjects gave informed consent and the study protocol was approved by The Ethics Committee of Gaziosmanpasa University. These individuals were interviewed face to face by an internist and a radiologist. Demographic data were obtained, upper abdomen ultrasonographies were done, weight, height, and waist and hip circumference were measured, and blood samples were drawn for each subject. Waist circumference was measured at the mid-point between the lower border of the rib cage and the iliac crest, whereas hip circumference was similarly obtained at the widest point between the hip and buttock, waist-to-hip ratio was calculated. Fatty liver was diagnosed by ultrasonographic findings of liver-kidney contrast, vascular blurring, and deep attenuation.⁸ Systolic and diastolic blood pressure was measured twice on the right arm with a sphygmomanometer (Erka, Germany) and the mean of both measurements used for the analyses.

BMI (kg/m^2) was calculated as weight divided by the square of height. Subjects with $\text{BMI} \geq 25 \text{ kg/m}^2$ were classified as overweight. Physical activity was categorized as scarce, mild, intensive, and competitive. Ethanol intake was assessed by a validated questionnaire and expressed as weekly (g/wk) consumption. The cut-off value listed by the test manufacturer for ALT and AST were 55 U/L and 37 U/L, respectively.

MetS, define according to the Adult Treatment Panel III of the National Cholesterol Education Program, was the identification of 3 of the following 5 risk factors: abdominal obesity ($>102 \text{ cm}$ in male and $>88 \text{ cm}$ in female), elevated triglycerides ($\geq 150 \text{ mg/dL}$), decreased HDL levels ($< 40 \text{ mg/dL}$ in male and $< 50 \text{ mg/dL}$ in female), elevated blood pressure ($> 130/85$), and elevated fasting plasma glucose levels ($>110 \text{ mg/dL}$).

Statistical Analysis: Data are expressed as the mean \pm SD. Statistical comparison was done by using the Chi-Square and Independent Samples Test or Mann-Whitney U Test according to distributions or numbers of values. Values of p less than 0.05 were evaluated as statistically significant.

RESULTS

The prevalence of elevated serum ALT, AST, and ALT and/or AST were found as 11% (120 indi-

viduals), 7.2% (79 individuals), and 13.3% (146 of 1095 individuals), respectively. The mean age of 146 persons were 41.7 ± 16.1 years (range, 18-86) and the rate of male/female was 97/49 (66.4/33.6 percent). In the participants with elevated ATLs, the mean of elevated serum alanine aminotransferase levels in males and in females were $68.7 \pm 22.0 \text{ U/L}$ and $67.4 \pm 31.2 \text{ U/L}$, respectively and statistically significance was not found between gender ($p = 0.8$). The prevalence of elevated ATLs was higher in males than females ($p < 0.0001$).

There have a history for drug using in 27 persons (18.5%), for smoking in 50 persons (34.2%), for alcohol intake ($\geq 40 \text{ g/wk}$ of ethanol) in 4 persons (2.7%), HBs Ag positivity in 8 persons (5.5%), and Anti-HCV positivity in 6 persons (4.1%). Grade 1, grade 2, and grade 3 steatosis were detected in 25 (17.1%), 14 (9.6%), and 1 (0.7%) individuals of the 146 participants, respectively. The distributions of factors associated with elevated ATLs are shown in table 1. All individuals have a history of at least one risk factor.

After exclusion of individuals with hepatitis B or hepatitis C infection, 132 individuals with elevated

Table 1. Demographic characteristics of individuals with elevated aminotransferase levels (ALT and / or AST).

	n
Sex	
male/female	97/49
Residence	
rural/urban	77/69
Drug using	
no/yes	119/27
Smoker	
no/yes	96/50
Body mass index (kg/m^2)	
normal/elevated	39/107
Diabetes mellitus	
no/yes	124/22
Fatty liver	
no/yes	106/40
Cholelithiasis	
no/yes	136/10
Hypercholesterolemia	
no/yes	115/31
Hypertriglyceridemia	
no/yes	71/75
Alcohol intake	
Abstainers	126
< 40 g/wk of ethanol	16
$\geq 40 \text{ g/wk}$ of ethanol	4
Hepatitis markers	
HBs Ag and/or Anti-HCV positivity	14

Table 2. The p values of comparisons between normal and elevated aminotransferase levels in all participants, male and female.

	All Participants	Male	Female
No. (normal/elevated*)	949/132	444/91	505/41
Age (year)	NS	NS	NS
Physical activity	NS	NS	NS
Height (cm)	0.038	NS	NS
Weight (kg)	< 0.0001	0.004	0.002
Waist circumference (cm)	< 0.0001	0.001	0.003
Hip circumference (cm)	NS	0.015	NS
Waist-to-hip ratio	< 0.0001	0.009	0.023
Systolic blood pressure (mmHg)	NS	NS	NS
Diastolic blood pressure (mmHg)	0.050	NS	0.045
Body mass index (kg/m ²)	0.012	NS	<0.0001
Blood glucose level (mg/dL)	NS	NS	NS
Total cholesterol level (mg/dL)	< 0.0001	< 0.0001	0.002
LDL cholesterol level (mg/dL)	0.004	0.024	0.005
HDL cholesterol level (mg/dL)	0.040	NS	0.010
Triglyceride level (mg/dL)	< 0.0001	< 0.0001	0.003

NS: Not significant; * Except the individuals with hepatitis

Table 3. The distributions of the criteria for MetS in individuals with elevated aminotransferase levels without hepatitis (132 persons).

	n (%)
No risk	12 (9.1%)
One risk	29 (22.0%)
Two risk	32 (24.2%)
MetS (≥Three risk)	59 (44.7%)

MetS: Metabolic syndrome.

ATLs (91 male and 41 female) were evaluated (Tables 2 and 3). MetS was found in 59 participants (44.7%) (31 of 91 males, 34.1%; 28 of 41 females, 68.3%) of these individuals and its prevalence was markedly higher in females with elevated ATLs ($p < 0.0001$). Moreover, the prevalence of MetS in the individuals with elevated ATLs were higher than with

normal ATLs ($p = 0.015$). ALT and AST levels in males with MetS were higher than without MetS ($p = 0.022$ and $p = 0.025$, respectively) (Table 4).

Alcohol intake ($p = 0.015$), smokers ($p < 0.0001$) and drug using ($p = 0.002$) were higher in individuals with elevated ATLs.

The participants with MetS had more elevated ALT levels compared with the participants without MetS, but this difference was not significant (71.4 ± 28.3 U/L *vs.* 64.6 ± 22.8 U/L, $p = 0.136$).

When the males with elevated ATLs were evaluated, the ALT levels of the persons who have no risk of MetS ($p = 0.007$) and the persons who have one risk of MetS ($p = 0.001$) were lower than the persons with MetS (Figure 1, Table 5). However, there were no statistical significant in females with elevated ATLs for risk factors of MetS.

The ALT levels of the participants with elevated aminotransferase in living rural and urban areas

Table 4. The comparisons of participants with elevated aminotransferase levels according to metabolic syndrome.

	All participants (n=132)			Male (n=91)			Female (n = 41)		
	MetS (+) (n = 59)	MetS (-) (n = 73)	p-value	MetS (+) (n = 31)	MetS (-) (n = 60)	p-value	MetS (+) (n = 28)	MetS (-) (n = 13)	p-value
Age, year	46.1 ± 15.9	38.6 ± 14.7	0.006	43.6 ± 17.0	39.5 ± 15.3	NS	48.8 ± 14.4	34.6 ± 9.1	0.002
ALT	71.4 ± 28.3	64.6 ± 22.8	NS	76.8 ± 29.3	63.4 ± 15.8	0.022	65.5 ± 26.4	70.3 ± 43.0	NS
AST	42.8 ± 15.4	35.6 ± 9.8	0.003	40.1 ± 13.3	34.0 ± 8.8	0.025	45.7 ± 17.3	43.2 ± 11.2	NS

MetS: Metabolic syndrome. **NS:** Non significant.

Table 5. The distributions of risk factors for metabolic syndrome in men with elevated aminotransferase levels.

	Metabolic Risk Factors			
	No risk	One risk	Two risk	≥ Three risk (MetS)*
No.	10	23	27	31
Mean ALT	59.8 ± 12.8	59.6 ± 12.6	68.0 ± 18.3	76.8 ± 29.3

* Metabolic syndrome.

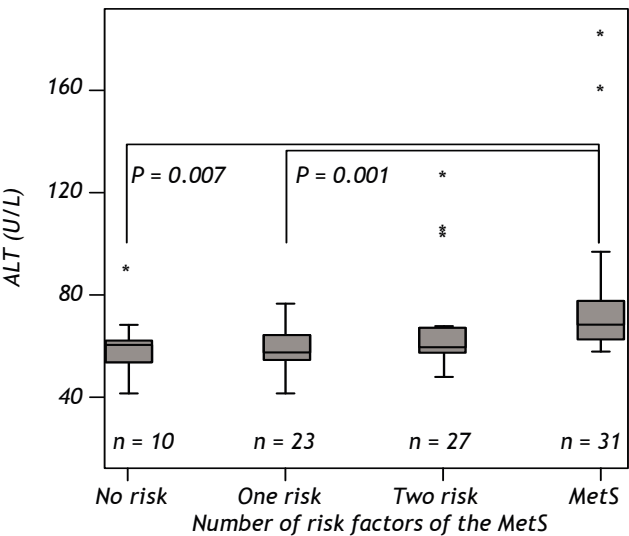


Figure 1. ALT levels according to risk factors for metabolic syndrome in men with elevated aminotransferase levels.

are 67.2 ± 26.7 and 68.1 ± 24.4 , respectively ($p = 0.837$). Similarly, we didn't find statistically significant differences in males and females according to residence ($p = 0.775$ and $p = 0.576$, respectively).

DISCUSSION

The prevalence of elevated serum ATLs (ALT and / or AST) was found 13.3% in our asymptomatic general population. Moreover, about 11% of our participants (120 persons) had elevated ALT levels. Ioannou et al found that the prevalence of elevated ALT, AST, or either ALT or AST were 8.9%, 4.9%, and 9.8%, respectively.⁹ Jamali et al in general population of Iran¹⁰ and Liu et al in Taiwan¹¹ declared that the elevated ALT levels were 7.9% and 7.2%, respectively. Papatheodoridis et al found that elevated liver enzymes are present in approximately 15% of Greek blood donors.¹² Our study showed that the prevalence of elevated ATLs was relatively higher in our population. Although the prevalence of alcohol consumption is very low, this result may relate to the increased ratio of smoking, hepatitis, obesity, and MetS.

It was demonstrated that elevated aminotransferase levels have a relationship with features of the MetS.¹³⁻¹⁵ The most common causes associated with elevated ATLs were elevated BMI, fatty liver, and MetS in our general population. Interestingly, the participants with the MetS had more elevated ALT levels than those without the MetS. However, this difference was not significant. The prevalence of MetS in individuals with elevated ATLs was higher in females than males. Moreover, elevated ATLs have been associated with at least one etiologic factor such as MetS, fatty liver, drug using, hepatitis, etc. in all participants. However, we found that ALT levels have a relationship with risk of MetS only in males with elevated ATLs.

The waist circumference is an important marker of central obesity.¹⁶ When we were evaluate hip-waist circumference, waist-to-hip ratio and BMI between the participants with normal and elevated ATLs, there were a statistical significant for waist-to-hip ratio as waist circumference. This finding shows the importance of waist-to-hip ratio. De Lédinghen, et al. found that liver fibrosis is statistically associated with tobacco use, elevated BMI and diabetes in 272 asymptomatic patients with unexplained chronically elevated ALT levels.¹⁷ Elevated ATLs were more common among males than females.^{12,17,18} Similarly, our study confirmed that the ratio of elevated ATLs was higher in males and in smokers.

Fatty liver was found in 64% of 149 asymptomatic participants with elevated serum aminotransferases.¹⁹ Daniel et al demonstrated that a lot of participants with chronic elevated transaminase have liver steatosis.²⁰ Liver biopsy is often recommended in patients with elevated serum aminotransferases in order to determine the causes. It was a deficiency of our study that we did not perform liver biopsy.

CONCLUSION

Elevated aminotransferase levels are common and MetS is an important cause of elevated ATLs in Northern Turkey. The ALT levels increase with the

number of risk of the MetS in males. Moreover, the results of our study indicate that the most common causes associated with elevated ATLs may be prevented with lifestyle modification such as dietary habits, physical activity in our population.

ABBREVIATIONS

- **ATLs:** Elevated aminotransferase levels.
- **MetS:** Metabolic syndrome.
- **ALT:** Alanine aminotransferase.
- **AST:** Aspartate aminotransferase.

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