Original Article

The Association of Elevated Serum Alanine Aminotransferase with Metabolic Syndrome in a Military Population in Southern Iran

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Background: Metabolic syndrome (MetS) is rapidly rising at an alarming rate through all parts of the world. Elevated serum aminotransferase was proposed as a marker for early detection of MetS. In this investigation we primarily aimed to evaluate the prevalence of MetS and its components among army and secondly to explore the association between elevated serum aminotransferase and the components of metabolic syndrome.
Methods: A total of 380 army personnel from a military camp in Southern Iran participated in this cross-sectional study. Life style related characteristics, anthropometric features, serum aminotransferase and components of MetS, based on National Cholesterol Education Program—Adult Treatment Panel III, were measured. Statistical significant was set as p value less than 0.05.
Results: The mean age of participants was 35.0± 7.5 year-old and the prevalence of metabolic syndrome was 8.1%. The prevalence of the components of MetS including; central obesity, abnormal fasting blood glucose, hypertension, hypertriglycridemia and low HDL cholesterol level was 8.6%, 10.4%, 18.5%, 31%, and 45.5% respectively. MetS had significant relationship with obesity (P<0.001) and abnormal Waist Circumferance/Hip Circumference ratio (P<0.001). Twenty-six percent of subjects had ALT ≥ 41 U/L and 4.9% of them had ALT ≥ 81. Elevated serum aminotransferase had significant association with presence of MetS (P= 0.007).
Conclusion: Although prevalence of metabolic syndrome among the studied army population was not high, life style modification of army members is recommended. Liver function tests should be included in routine health checkup of military personnel.

Key Words: Metabolic Syndrome, Serum Aminotransferase, Central Obesity

Introduction

Metabolic syndrome is a cluster of signs and symptoms associated with abdominal obesity which its components contribute to higher risk of cardiovascular events, diabetes and nonalcoholic fatty liver disease (NAFLD).[1] The prevalence of this syndrome which is incriminated as the cause of non-communicable disease pandemics,[2] is rapidly rising at an alarming rate through all parts of the world. In this setting recent report from population-based studies indicated that there is a significant increase in the rate of obesity and overweight in developing countries including Iran.[3-4] Meanwhile, it is well-established that early diagnosis of this syndrome can play a crucial role in prevention of its complications[5-6]. Given this, during the past years, a large amount of efforts have been devoted to introducing a simple and accurate marker for early detection of metabolic syndrome[7].To date, there is no consensus on a marker having both features. One of the proposed, though not proven, indices in this case is elevated liver aminotransferases[8-9] which are considered to be a strong predictor of adiposity,[10] although it is not included in the criteria of metabolic syndrome.

Prevalence of metabolic syndrome and its components disparately varies in different populations.[11] Situation analysis regarding its frequency is the first step to provide a better estimation for its potential consequences. Despite the fact that military personnel are generally considered as one of the healthiest population layer of each society with a proper physical fitness, the valid data on the prev-

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alence of metabolic syndrome and its components in this population is scarce and not leading.[12-14] In this investigation we primarily aimed to evaluate the prevalence of metabolic syndrome and its components among army and secondly to explore the association of elevated serum aminotransferase with the components of metabolic syndrome.

Patients and methods

Study design and subjects

We conducted this investigation with a cross-sectional design to investigate the prevalence of metabolic syndrome and its components among a military population of the southern part of Iran. The research proposal was approved by the committee of research ethics in the Artesh University of Medical Sciences with the grant number of 2142. The sample size was calculated based on the previous reports from population-based studies in Iran in which prevalence of metabolic syndrome was ranged from 29.9% to 51.4%.[15,16] We considered a power of 80% with the first type of error equal to 0.05. Three-hundred and eighty active members were selected randomly based on the predefined sample size. Everyone with pathological conditions interfering with our measurements, including heart failure, myocardial infarction, renal failure, liver insufficiency, acute or chronic hepatitis and any type of malignancy, excluded from study. The research goals and its procedures were explained to the remaining healthy and active subjects. Having read and signed the informed consent, they were enrolled in this investigation.

Definition

Based on the National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATPIII) (2005) criteria,[18] subjects were considered to have metabolic syndrome if they fulfilled three or more of the following five risk factors: 1.Waist circumference ≥ 102 cm in men 2.Triglyceride≥150 mg/dl 3.HDL≤40 mg/dl 4. Systolic blood pressure ≥130 mm Hg or on antihypertensive medications or diastolic blood pressure≥85 mm Hg 5. Fasting blood glucose level of ≥ 100 mg/dl

Measurements

Each eligible participant was evaluated in the military service clinic in Shiraz, Southern Iran. From every one, demographic and life style information including; age, marital status, level of education, duration of the occupation as the member of military service, the length of physical activity per week, history and frequency of smoking and alcohol drinking, were obtained. The participants were asked to sit still for 5 minutes before their arterial blood pressure were taken twice from the right arm by a calibrated digital instrument. Then anthropometric features including; weight, height, body mass index (BMI), waist circumference (WC), hip

Table 1: Demographic features of subjects

Characteristics			Number (%)
Age (Years)	<30		108 (29.6)
	30-39		153 (42.4)
	≥40		104 (28.0)
Education	Primary level		48 (13.1)
	Secondary level		158 (43.2)
	Undergraduate University level		144 (39.4)
	Postgraduate education		15 (4.1)
Marital Status	Single		35 (9.6)
	Married		330 (90.4)
Physical Activity (> 30 min three times per week)	No		30 (7.1)
	Yes		335 (92.9)
Smoking	Passive smoker		93 (25.5)
	Withdrawn		22 (6.0)
	Active smoker	Cigarette	57 (15.6)
		Hubble Bubble	15 (4.1)
		Opium	2 (0.5)
Race	Fars		221 (60.5)
	Lorish		56 (15.3)
	Turkish		60 (16.4)
	Other		28 (7.7)

Table 2: Relationship of metabolic syndrome between different demographic and life style related information

Demographic and life style related information		No Number (%)	Yes Number (%)	P value
Age	<30	102 (96.2)	4 (3.8)	
	30-39	134 (90.5)	14 (9.5)	0.124
	≥40	88 (88.9)	11 (11.1)	
BMI (kg/ m$^{2)}$	<25	123 (99.2)	1 (0.8)	
	25-30	166 (92.2)	14 (7.8)	<0.001
	>30	38 (73.1)	14 (26.9)	
Physical Activity (> 30 min three times per week)	Yes	297 (92.2)	25 (7.80	0.108
	No	19 (82.6)	4 (17.4)	
Smoking	No	271 (92.5)	22 (7.5)	0.363
	Yes	57 (89.1)	7 (10.9)	
Race	Fars	198 (91.2)	19 (8.8)	
	Lorish	47 (90.4)	5 (9.6)	
	Turkish	57 (95.0)	3 (5.0)	0.779
	Other	26 (92.9)	2 (7.1)	
Marital Status	Single	294 (91.3)	28 (8.7)	0.337
	Married	34 (97.1)	1 (2.9)	
WC/HC ratio*	<0.9	185 (97.9)	4 (2.1)	
	0.9-1.0	137 (85.6)	23 (14.4)	<0.001
	>1.0	6 (75.0)	2 (25.0)	

*WC: waist circumference; HC: hip circumference

circumference (HC), and WC/HC ratio were measured by standard methods. WC was determined by measuring waist diameter of the level of midpoint between iliac crest and lower border of tenth rib. The average of three measurements was considered as WC. Central obesity was considered as WC > 102 cm for our male participants. BMI was calculated by weight in kilogram divided by square of height in meter (kg/m^2). On the same day 5cc of venous fasting blood was drawn from antecubital area of the subjects. The subjects were asked to refrain from having oily meals the night before sampling. Blood samples ,while keeping at C°, were brought directly to the laboratory to be checked for fasting blood glucose, lipid profile consisting of total cholesterol, LDL, HDL, triglyceride and liver function tests including alanine aminotransferase (ALT) and aspartate aminotransferase (AST). The cut-off values for designating abnormalities were set in this study, based on the army lab reference, at ≥240 mg/dl for serum cholesterol, ≥150 mg/dl for triglycerides, ≥100 mg/dl for plasma glucose, and ≥ 41 U/L for ALT.

Statistical analysis

The data were mathematically processed. All the calculations were performed with the Statistical Package for Social Sciences (SPSS) version 15. Pearson Chi-Square test and Fisher's exact test were applied to identify relationship between cardiovascular risk factors and demographic data. Statistical significance was set as p value less than 0.05.

Results

After exclusion of 15 subjects, 365 male participants were enrolled for final analysis. Mean age was 35.0 years with standard deviation of 7.5 years. Table 1 shows further demographic and life style related information. Prevalence of overweight, obesity and central obesity were 50.6%, 14.4% and 8.5% respectively. There was a significant relationship between increment in BMI level (P= 0.009) and WC/HC ratio (P< 0.001) and advancing age in the participants. The prevalence of metabolic syndrome was 8.1% while low HDL cholesterol level was reported to be the most prevalent component of metabolic syndrome among participants (45.5%). The least frequency of the component of metabolic syndrome was shown for the waist circumference (8.6%). Prevalence of the metabolic syndrome and its components are illustrated in Figure 1. The

Table 3: Comparison of the components of metabolic syndrome in respect with alanine aminotransferase (ALT) level

Components of Metabolic Syndrome		ALT< 41 Number (%)	41≤ ALT < 81 Number (%)	ALT≤81 Number (%)	P value
Waist circumference (cm)	<102 cm	228 (69.5)	85 (25.90	15 (4.6)	0.396
	≥102 cm	19 (61.3)	9 (29.0)	3 (9.7)	
Blood pressure	Systolic ≥ 130 or diastolic ≥ 85 mm Hg	207 (70.2)	77 (26.1)	11 (3.7)	0.072
	Systolic <130 or diastolic <85 mm Hg	43 (64.2)	17 (25.4)	7 (10.4)	
Triglycerides	≥ 150 mg/dL	194 (77.0)	50 (19.8)	8 (3.2)	<0.001
	<150 mg/dL	58(51.3)	45 (39.8)	10 (8.8)	
HDL Cholesterol	≥ 40 mg/dL	125 (62.5)	61 (30.7)	13 (6.5)	0.016
	< 40 mg/dL	127 (76.5)	34 (20.5)	5 (3.0)	
Fasting blood glucose	≥ 100 mg/dL	228 (29.9)	84 (25.8)	14 (4.3)	0.234
	<100 mg/dL	24 (63.2)	10 (26.3)	4 (10.5)	
Metabolic syndrome	No	229 (69.8)	86 (26.2)	13 (4.0)	0.007
	Yes	17 (58.6)	7 (24.1)	5 (17.2)	

relationship of metabolic syndrome with different demographic and life style related information is demonstrated in the Table 2. Twenty-six percent of subjects had ALT ≥ 41 U/L and 4.9% of them had ALT ≥ 81. Prevalence of abnormal AST was almost similar to ALT as 25.2% of participants had AST≥ 41 U/L while 4.9% of them had AST ≥ 81. As Table 3 compares the components of metabolic syndrome in respect to the level of ALT, elevated serum aminotransferase had significant association with presence of MetS (P= 0.007)

Discussion

According to the NCEP-ATPIII criteria, the findings of this study indicate a prevalence of 8.1% for metabolic syndrome in the studied population. Although worldwide prevalence of this syndrome varies, it seems that the observed frequency of the components of metabolic syndrome was considerably lower than previous reports released from Iran.[19] The comparison of our findings with available data from military populations, despite limitations in the number and quality, confirms that the rate of metabolic syndrome in military populations is less

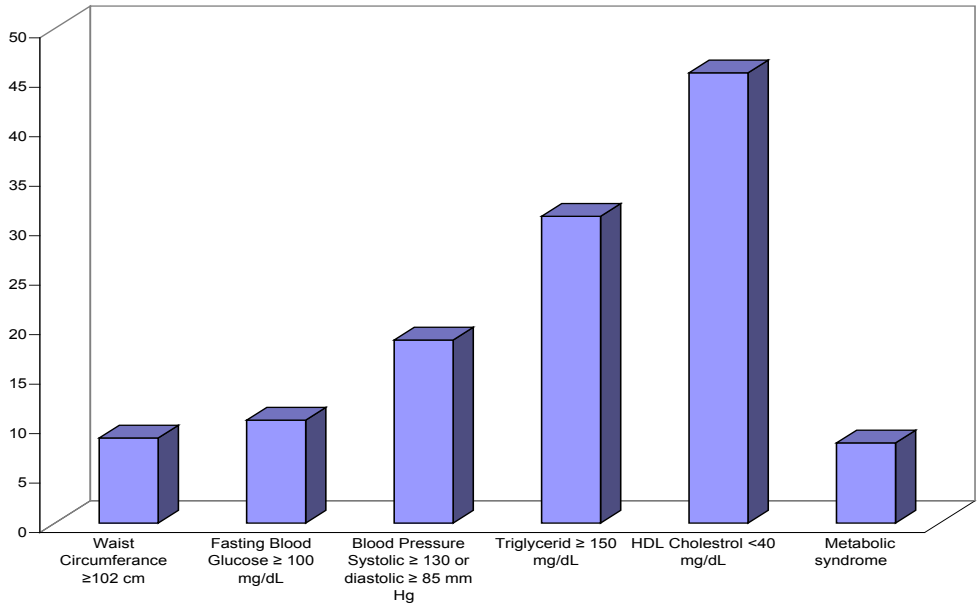

Figure 1. prevalence of metabolic syndrome and its components

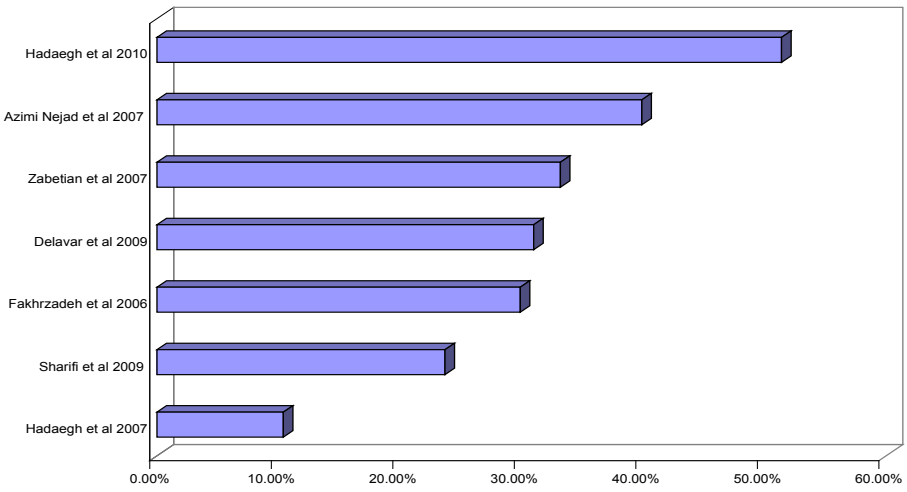

Figure 2. prevalence of metabolic syndrome based on NCEP-ATP III criteria

than the general population from the same country. For example, Bauduceau et al reported a prevalence of 9% for metabolic syndrome among 2045 subjects from military force of France,[13] whereas a population-based study of 62 000 French subjects revealed a prevalence of 12.8% for men.[18]

Over the past decades, we have witnessed pronounced changes in lifestyle pattern of Iranian population,[20] such as an increasing sedentary life, with consequent surge in incidence of cardiovascular disorders.[21] Given that, several recently published studies have shown a high prevalence of cardiovascular risk factors in urban parts of Iran. For instance, in 2009, the third national survey for risk factors of non-communicable disorders in Iran, illustrated the prevalence of diabetes, hypertension, obesity, and central obesity 8.7%, 26.6%, 22.3% and 53.6% respectively which is quite remarkable in comparison with figures from developed countries.[18] Likewise some papers, using NCEP-ATPIII criteria, reported the prevalence of metabolic syndrome as high as 51.4% in general population of Iran.[16] Such a considerable discrepancy between our data and previous reports from Iran (Fig. 2) can be described in different ways. The first and simplest can be attributed to the special features of lifestyle among the members of army forces including routine physical activity, lesser frequency of opium ingestion and alcohol drinking. The next possible reason can be age distribution of participants under study, with 28% aged above 40.

Although overall risk of metabolic syndrome was not high, the frequency of abnormal lipid profile was considerable. This may reflect an unhealthy nutrition of army members either at their work place or their homes. This can be an area for future interventions and may indicate a necessity for more educational programs, since a large portion of military members had pre-college education.

Anthropometric features are easily-calculated indices for which there is a bulk of evidence stating their predictive value not only for development of cardiovascular events but also for chronic kidney disease and mortality among elderly.[22-25] BMI is widely checked in routine evaluations while the value of other features like WC/HC ratio seems to be overlooked. Our study, in line with previous reports,[22,26,27] showed that two latter anthropometric features had a significant relationship with presence of metabolic syndrome. Accordingly, it is strongly suggested that such measurements be added to the periodic health status evaluation of army personnel.

In this study we showed that elevated ALT can predict presence of metabolic syndrome. Our findings are in favor of previous findings, which showed a strong relationship between metabolic syndrome and NAFLD.[28,29] In other word, although NAFLD is not traditionally defined as part of the metabolic syndrome, it was proposed that it can be the hepatic component of metabolic syndrome.[30]

Bethel and colleagues in their study, which aimed to see if ALT could be considered together with features of metabolic syndrome and whether this feature differed across global geographic regions, concluded that elevated ALT can be added

to the components of metabolic syndrome except in Asian regions.[31] In contrast, Kelishadi and colleagues in their recently published report showed that ALT and sonographic fatty liver have significant association with the components of metabolic syndrome in Iranian children and adolescents.[32] Our findings support the latter data and we believe that pathophysiology behind connections between NAFLD and metabolic syndrome does not vary geographically.

Although most of studies demonstrated strong association between elevated ALT and presence of metabolic syndrome, they failed to show a similar relationship between elevated ALT and components of metabolic syndrome. Some investigations showed a relationship with central obesity, hypertension while other studies described an association between abnormal fasting blood glucose and lipid profile.[33-35]

Accumulation of hepatocytes with lipid in the form of free fatty acids (FFA) and triglycerides in NAFLD pathogenesis[36] can explain our finding regarding a significant relationship between elevated ALT and two components of metabolic syndrome; high serum triglyceride level and HDL cholesterol < 40 mg/dL. Progression of both metabolic syndrome and NAFLD is generally silent[37] and prevention of their complications warrants further metabolic and ultrasonographic examinations, especially when there is no other reasonable description for elevated ALT in routine check-up.

To best of our knowledge, this is the first published study from Middle eastern countries to show the status of the components of metabolic syndrome in an army population and its relationship with elevated serum aminotransferase in adults. Even though, our study has certain limitations and some future directions can be proposed. Because of the study design, it was not feasible to obtain serial evaluation of liver enzymes level and determination of its relationship with progression of metabolic syndrome, its components and resulting complications. A longitudinal study can reveal such a casual relationship. Furthermore, due to restricted budget, we could not evaluate second-generation enzymatic liver function test, such as gamma-glutamyltransferase, which are more specific in reflecting hepatocyte injuries.

In conclusion, although prevalence of metabolic syndrome among the studied army population was not high, educational programs and interventions should be instituted in regard to dietary life style modification. It is also suggested to include liver function tests in routine health checkup of military personnel and elevated ALT be considered as an alarming sign for development of cardiovascular disorders.

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