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## Research Article

# Non-Alcoholic Fatty Liver Disease Frequency among Healthy Blood Donors in the West of Iran

### Abstract

**Objectives:** To investigate the prevalence of NAFLD as well as the determination of associated metabolic abnormalities in Iranian blood donors. The aim of this study was to review cases of non-alcoholic fatty liver disease and to determine the prevalence of non-alcoholic fatty liver disease as a cause of elevated alanine aminotransferase in healthy blood donors and also assess risk factors of NAFLD such as BMI and correlation with metabolic syndrome in these subjects.

**Background:** Non-alcoholic fatty liver disease has been increasingly recognized as the most common pathological conditions affecting the liver. Non-alcoholic fatty liver disease is now recognized as the hepatic component of the metabolic syndrome, which includes hyperlipidemia, glucose intolerance, obesity, and systemic hypertension.

**Methods:** This cross-sectional study was conducted among a sample of 479 blood donor aged between 17-66 years in Hamedan, Iran. The donor answered a questionnaire that included age, gender, and medical history, and were submitted to a complete physical exam and abdominal ultrasound. Biochemical exams included: ALT, AST, ALP, fasting glucose, cholesterol and triglycerides. Criteria for NAFLD included: the presence of steatosis in ultrasound and/or elevated ALT/AST with negative intake of alcohol, negative use of drug, negative investigation for hepatitis A, B, C, auto-immune hepatitis, Wilson disease and hemochromatosis.

**Results:** From August, 2012 to January, 2013, the study included 479 subjects between 17 and 66 years of age and a mean age of  $33.3 \pm 10.5$  years. The prevalence of NAFLD was 35.7% (mild 21.3%, moderate 13.4%, severe 1%). From lower to higher BMI category; alanine aminotransferase (ALT), total cholesterol, LDL cholesterol and triglycerides statistically increased significantly. In all BMI categories, ALT increased significantly by increasing the number of the components of the metabolic syndrome. Odds ratio for elevated liver enzymes and sonographic fatty liver increased significantly with higher BMI categories before and after adjustment for age.

**Conclusion:** There was a strong relationship between NAFLD and the abnormal metabolic variables in blood donors. It would be very useful if people are exposed to some determination such as waist circumference, blood pressure, FBS and serum lipid profile in order to screen those susceptible to NAFLD.

## Introduction

Nonalcoholic fatty liver disease (NAFLD) is a clinico-pathological condition of wide spectrum, which includes steatosis and steatohepatitis that has a potential to advance to cirrhosis and hepatocellular carcinoma [1]. NAFLD is probably the most common underlying cause of cryptogenic cirrhosis [2,3]. NAFLD is the most common liver disorder in the world, affecting 2.8% to 24% of the general population [4] and is the most common cause of persistently elevated serum ALT in the asymptomatic Iranian blood donors in Tehran [5]. In adults visceral obesity has been considered the main risk factor for the development of NAFLD [6,7]. Different studies have shown that NAFLD is associated with older age, diabetes mellitus, obesity and dyslipidemia (especially increased triglyceride) [8,9]. In most instances, an incidental finding of abnormal serum aminotransferase leads to the diagnosis of fatty liver or NAFLD in adults [10]. This study determined the prevalence of NAFLD as a cause of elevated alanine aminotransferase in healthy blood donors in hamedan and also risk factors of NAFLD, such as raised BMI and the metabolic syndrome in these subjects.

## Materials and Methods

### Population selection

In a cross-sectional study during six-month period from August, 2012 to January, 2013, we collected data from in the Blood Donation Center of Hamedan, 479 healthy blood donors (age between 17-66 years), were recruited in this study with no history of alcohol consumption and also any kind of liver diseases such as hepatitis and liver metabolic disease. According to the regulations of the Blood Transfusion Organization of Iran, the following individuals are not allowed to donate blood: those who have had major chronic disease, those with any mild to severe acute disease and intravenous drug users.

**Exclusion criteria:** Previous historic or serologic markers for liver diseases (hepatitis A, B, C), auto-immune disease, metabolic diseases such as Wilsons Disease and hemochromatosis and intake of alcohol above 140 g/wk.

## Clinical evaluation

Demographic information, as well as baseline characteristics like age, drug and disease history was collected for each individual by trained interviewers.

Anthropometric measures: waist circumference (WC) was measured at the end of normal expiration in the middle portion between the last rib and the iliac ridge whereas hip circumference was similarly obtained at the widest point between the hip and the buttock. Participants were weighed while not wearing coats or shoes or carrying any objects. A Filizola balance was used, with a scale resolution of 0.1 kg. Height was measured by a stadiometer with no shoes and hair accessories; the resolution was 0.5 cm. BMI (Body Mass Index) was calculated by dividing weight by height squared and categorized according to the classification of National Heart, Lung and Blood Institute of the USA as follows: normal weight (18.5-24.9 kg/m<sup>2</sup>), overweight (25-29.9 kg/m<sup>2</sup>) and obese (30-34.9 kg/m<sup>2</sup>) [11].

All patients underwent superior abdomen ultrasound scan (AUS). The AUS was performed by only one medical doctor. The scanner used was an Aloka, model DynaView II, with colored Doppler and a 3.5 MHz drill. The discrepancy of echogenicity between the liver and kidney was considered as a criterion. Hepatic steatosis was graded as mild, moderate or severe, according to the Saverumuttu et al. [12], classification.

## Serological assays

Blood samples were collected during the same session by the technical staff after a 12 h fasting. The samples were analyzed in a referential laboratory for Alanine aminotransferase (ALT) and aspartate aminotransferase (AST), Alkaline phosphatase (ALP), fasting blood sugar (FBS), total cholesterol, triglycerides (Tg), low-density cholesterol (LDL-C), high-density cholesterol (HDL-C), and anti-HCV antibody (anti-HCV) with the use of a third generation ELISA test (Ortho HCV 3.0 Enhanced SAvE ELISA, Ortho-Clinical Diagnostics, Amersham, UK and Hepanostika HCV Ultrakit, Beijing United Biomedical Co., Beijing, China), and HBsAg were also evaluated by an Enzygnost HBsAg 5.0 kit (Dade Behring, Germany). Normal upper limit for ALT was considered 40 units per liter (U/L).

## Anthropometric measurements

Anthropometric measurements of individuals wearing light clothing and without shoes were conducted by well-trained examiners.

Height was measured to the nearest 0.1 cm with a portable stadiometer.

Weight was measured in an upright position to the nearest 0.1 kg with a calibrated scale.

Body mass index was calculated by dividing weight (kg) by height squared (m<sup>2</sup>).

Waist circumference measurements were taken at the end of normal expiration to the nearest 0.1 cm, measuring from the narrowest point between the lower borders of the rib cage and the iliac crest, whereas hip circumferences was similarly obtained at the widest point between hip and buttock.

## Blood pressure measurements and biochemical analysis

A mercury sphygmomanometer (Baumanometer; WA Baum CO, Inc, Tokyo, Japan) was used to measure the blood pressure of each subject while in a sitting position after a 5-min rest period.

During the 30 minute preceding the measurement, the subjects were required to refrain from smoking or consuming caffeine.

The appearance of the first sound (phase 1 Korotkoff sound) was used to define systolic blood pressure, and the disappearance of sound (phase 5 Korotkoff sound) was used to define diastolic blood pressure.

Blood samples were collected from the antecubital vein in the morning where they had been fasted for 9-12 hours. The samples were subsequently analyzed at a central, certified laboratory. Plasma concentrations of glucose, total cholesterol, triglyceride, HDL cholesterol, and AST, ALT were measured with an auto analyzer.

## Statistical analyses

The data were analyzed using Statistical Package for Social Science (SPSS) 17.0. Mistake type was estimated to be 5%. Spearman was used for the correlation between variables. The data are expressed as percentage, medium and standard deviation. Weighted logistic regression analyses were used to calculate the odds ratio (OR) and 95% confidence interval (95% CI) for each risk factor. A final logistic regression analysis was performed by a backward model selection for age, sex, BMI, Multivariate logistic regression analysis was used to identify independent risk factors for NAFLD. All analyses were two-tailed and P<0.05 was considered to be statistically significant.

## Results

The study included 479 subjects between 17 and 66 years of age and a mean age of 33.3 ± 10.5 years, 442(92.3%) were male and 37(7.7%) female. There was no significant difference between sex (P>0.3).

BMI (Body Mass Index) in these 479 subjects ranged from 19.1 to 38.2 and mean of BMI in all subjects was 28±4.3. Overweight was observed in 201(42%) and obese 148(30.9%) of studied with central obesity. There was a positive correlation between BMI and WC values and the mean value of BMI was significantly higher in abnormal LFT than in normal LFT. The prevalence of elevated ALT as another diagnostic indicator was 25.3%. WC had a statistically significant correlation with ALT (P < 0.05). Fatty liver was diagnosed by ultrasound in 171(35.7%), divided between mild (21.3%), moderate (13.4%) and severe (1%). Non-alcoholic fatty liver disease was significantly more common in the hypertriglyceridemia and hypercholesterolemia (P<0.0001). The prevalence of NAFLD in obese, overweight and normal weight patients was 30.3%, 5.4% and 0.0% respectively (P<0.000) (Table 1).

## Discussion

Obesity is the most common entity associated with NAFLD and a significant risk factor for the development of fatty liver and is also predictive for the presence of fibrosis [13]. Many epidemiological

studies demonstrated a strong correlation between body mass index and the presence of fatty liver diagnosed by ultrasonography. 30 to 100% of patients diagnosed with NAFLD are Obese [14], in obese persons 76% have NAFLD compare with 16% in normal weight persons [15]. BMI is an important predictor for hepatic steatosis. The risk of hepatic steatosis increase exponentially with the addition of each component of the metabolic syndrome. A study on 271 nondiabetic subjects demonstrated that liver fat was 4-fold higher in subjects with than without the metabolic syndrome. Among the components of metabolic syndrome the best correlation of liver fat was with waist circumference both in women and in men [16]. Positive correlation between BMI and WC in patients, as observed in this study, is also a common finding related to cardiovascular disease in other studies [17,18]. The characteristics of disease appear to be similar to those in other studies. Gender has not been considered to be a risk factor for NAFLD [19].

The diagnosis of NAFLD is often established after the identification of abnormal serum aminotransferase. The gold standard for diagnosis is liver biopsy. Although the procedure is effective as a prognostic indicator, liver biopsy is invasive and costly. Sonography has been used in assessing NAFLD but is lacking in the ability to assess fibrosis [20]. The frequency of NAFLD measured by sonography, which is more compared with the ALT determination, is in agreement with that in the study of Franzese in Italy (reported as 53% in sonography vs 25% through ALT determination) on obese patients [21]. The prevalence of an isolated elevated ALT levels (cut-off value of 41/UL for both men and women) after excluding individuals with viral hepatitis, alcohol and drug etiologies was 25.3% whereas 52(10.9%) of NAFLD had normal ALT. In the study which carried out on Tehran blood donation center prevalence elevated ALT reported 5.71% [22]. This prevalence in the Third National Health and Nutrition study of the population of the United States was 2.8% [23]. We found through sonography as a diagnostic method of NAFLD that elevated ALT and metabolic variables such as high total cholesterol, waist circumference, BMI and LDL were significantly associated with the disease. There are some reports from Korea and Mexico showing that the most important factors associated with NAFLD are high total cholesterol, LDL, triglyceride, ALT, insulin, obesity and low HDL [24,25], which confirms the results reported in our project.

In conclusion, NAFLD in asymptomatic Iranian was most frequent among patients with central obesity. These patients came

from an area in Iran where it is relevant to consider the proportion of Asian descendants, and the influence of ethnicity on the prevalence the NAFLD may be an important factor in this population. However, this hypothesis deserves future study.

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**Table 1:** BMI \* NAFLD Cross tabulation.

			NAFLD				Total
			NORMAL	MILD	MODERATE	SEVER	
BMI	NORMAL	Count	130	0	0	0	130
		% of Total	27.1%	.0%	.0%	.0%	27.1%
	OVERWEIGHT	Count	175	17	9	0	201
		% of Total	36.5%	3.5%	1.9%	.0%	42.0%
	OBESE	Count	3	85	55	5	148
		% of Total	.6%	17.7%	11.5%	1.0%	30.9%
Total	Count	308	102	64	5	479	
	% of Total	64.3%	21.3%	13.4%	1.0%	100.0%	



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