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Original Article

Prevalence of Non-alcoholic Fatty Liver Disease in Kurdistan Province, Iran, 2013-2014: A Population Based Study

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ABSTRACT

Background:
Generally, 15% to 40% of the world populations are suffering from non-alcoholicfatty liver disease (NAFLD). The aim of this study was to conduct an epidemiological evaluation of NAFLD and its related factors in the west of Iran.

Materials and Methods:
This cross-sectional study was conducted for 12 months, from July 2013 to July 2014, in Sanandaj city, Kurdistan province. In this study, multistage cluster sampling method was used. The general characteristics of the subjects including their age, sex, body mass index, history of diabetes, hypertension, and heart disease were recorded. All the subjects underwent abdominal ultrasonography. Besides, patients with fatty liver underwent blood tests (lipid profile,liver function test, fasting blood sugar,hepatitis B virus antigen, and hepatitis C virus antibody). Statistical analysis was performed using descriptive statistics and logistic regression test.

Results:
A total of 410 patients were included in the study; of whom 145 (35%) had NAFLD. The prevalence of fatty liver in men (43%) was twice more than that in women (22%). The severity of fatty liver disease increased with increasing blood sugar (OR = 3.214, 95% CI: 1.357, 7.612), triglycerides, and total cholesterol (OR = 2.897, 95% CI: 1.245, 6.736).

Conclusion:
Findings of this study show that, the prevalence of NAFLD in the west of Iranis similar to the highest rates reported from other countries and the prevalence was much higher than other Asian countries. It is recommended to implement fast and effective interventions to control fatty liver disease.

Keywords: Prevalence, Non-alcoholicfatty liver disease, Population based planning, Iran

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INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) includes a wide range of liver diseases, which first start with simple fatty liver (hepatic steatosis), damage of liver cells and fibrosis. This stage is also called Non-alcoholic steatohepatitis (NASH). In the later stages, NAFLD can progress to cirrhosis and hepatocellular carcinoma as well. In fact, this disease represents a range of clinical and pathological conditions, which are characterized by considerable deposits of fat in liver cells of people who have no history of alcohol abuse (1-4).

Fatty liver is the most common cause of chronic liver disease in developed countries (3,5-7) and it is expected that by 2020 NASH will be the most common cause of liver transplant in the United States (8,9). Generally, 15% to 40% of the world population is affected by NAFLD (9). Recent studies in China have shown that the prevalence of the disease among the general population in the East and South of the country is 17% and 15%, respectively. In another study, the prevalence of the disease in the adult population in Taiwan was estimated to be 12% (4). The prevalence of NAFLD in the United States is estimated to be 33% to 34%, while the spread of the disease in European countries varies between 25% and 30%. For example, in a study, the prevalence of NAFLD in Italy was reported as 25%. Several studies have shown that the prevalence of the disease in Asia varies from 5% to 40% (10).

The pathophysiology of NAFLD is not fully known yet, however steatogenesis happens in NAFLD because of the increased supply of free fatty acids in the liver and the resulting increase in lipogenesis. Visceral white adipose tissue (vWAT) plays a role not only in fat storage, but also in release of fatty acids. In addition, this tissue acts as an endocrine organ and releases a cytokine called Adipocine; at present, this cytokine is known as the influencing factor contributing to the occurrence of NAFLD and NASH (8,11,12).

To the best of our knowledge There has been no study on the prevalence of NAFLD in Kurdistan province, Iran. The aims of this study were to determine the prevalence of NAFLD and its related factors in the population aged 20 to 70 years in Sanandaj city, west of Iran during the years 2013 and 2014.

MATERIALS AND METHODS

This cross-sectional study was conducted over 12 months, from July 2013 to July 2014, in the city of Sanandaj. In this study, multistage cluster sampling method was used based on 17 health care centers in the city. According to the probable prevalence of 30% for NAFLD in the society and 3% error, sample size was estimated to be 336 people, and considering the design effect, the sample size increased to 430 people.

An adult population of 20-70 year old, who gave written informed consent, participated in the study. The exclusion criteria were patients with chronic liver diseases, a history of alcohol abuse as well as pregnant women.

Interviewers visited the subjects in each cluster at their living place. After giving explanations and obtaining informed consent, a standardized questionnaire was administered to determine the age, sex, occupation, history of diseases (hypertension, diabetes, cardiovascular disease, dyslipidemia, liver disease), subestance abuse (smoking, alcohol use), drug history, history of pregnancy in women, and economic level of the family. Socio-economic status of each person was determined based on the family assets and using principal component analysis. Each of the participants was given an asset score and thus the socioeconomic status was determined. Bases on the socio-economic status, the participants were divided into three groups of rich, middle income, and poor.

Body mass index (BMI) was calculated as body weight in kilogram divided by square of height in meter. Blood pressure was measured in the right arm twice with a time interval of five minutes in a sitting position.

After recording all the items in the questionnaire, the subjects Referred to the health center for an abdominal sonography to examine their liver, spleen, and gallbladder.

Ultrasonographic examination of liver was carried out by an experienced radiologist, who did not have any information about the medical history of the subjects and the data collected in their questionnaires. The device utilized for this purpose was an Aloka ultrasound machine, SSD1700 model, made in Japan, and Convex 3.5 MHZ probes were used. In addition, diagnosis and classification of fatty liver were based on the following criteria:

Fatty liver grade 1: mild steatosis: is defined as the small increase in echogenicity of liver with normal vessels and full observation of diaphragm.

Fatty liver grade 2: moderate steatosis: is defined as the moderate increase in echogenicity of liver with partial blurring of the liver vessel wall and discontinued observation of diaphragm.

Fatty liver grade 3: severe steatosis: is defined as severe increase and diffused echogenicity of the liver with non-visible blood vessels and not observing the diaphragm (13).

In the next step, all individuals who were diagnosed with fatty liver, referred to the specified laboratory, after 14-h fasting, and the following tests were performed for all of them: fasting blood sugar (FBS),

triglycerid (TG), high density lipoprotein (HDL), low density lipoprotein (LDL), total cholesterol, aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (Alk.P) hepatitis C virus antibody (HCVAb), hepatitis B virus antigen (HBSAg).

AST, ALT, Alk.P, FBS, TG, HDL, LDL, and Total cholesterol were performed by a Prestige automated analyzer, 24i model, made in Japan, and using the kits manufactured by the Pars Azmon Company. HCVAb and HBSAg tests were performed using ELISA Reader Stat fax machine and using the kits manufactured by Pishtaz Teb Company.

Throughout all the stages of this study, researchers observed all ethical principles and the study protocol was in line with all the treaties of Declaration of Helsinki 1975.

Statistical Analysis

The data were entered into STATA 11.0 software and the quantitative descriptive objectives were achieved through the calculation of means, standard deviations, modes, and medians. In univariate analysis, the objectives of quantitative analysis were obtained through the use of t-test. In order to conduct the qualitative univariate analysis, chi-square and Fisher exact tests were used and for multivariate analysis of the categorical variables, logistic regression was used. Taking into account the sampling method, Stata survey analysis was used so that the results would be generalized to the studied population. $P < 0.05$ was considered as significant.

RESULT

In this study, out of the 430 people who were selected for the study, 410 patients underwent abdominal ultrasound and the rest were excluded from the study because they were either reluctant to participate in the study or they met the exclusion criteria (response rate = 95%). The mean age of participants was 37.75 years. According to surveys carried out during the study, 10% of the participants had Irritable Bowel Syndrome (IBS) and 30% were affected with Gastro-Esophageal Reflux. Before carrying out different measurements and performing ultrasound and laboratory tests on the subjects, several questions were asked about participants' age, sex, occupation, history of hypertension, diabetes, history of heart disease, reflux, irritable bowel syndrome, and smoking, the results are shown in table 1.

Table 2 shows the results of different measured variables, including sex, age, socio-economic level, blood pressure, diabetes, smoking, and body mass index in terms of the risk of fatty liver disease. Based on the results of ultrasound test, a total of 145 subjects from both sexes were affected by fatty liver disease. The prevalence rate differed in terms of sex. The difference in prevalence of fatty liver between different socio-economic groups was not significant. In addition, the results showed that the prevalence of NAFLD in smokers (56.5%) is almost twice as much as that in non-smokers (27%) and the difference was statistically significant (OR = 3.395, CI = 1.735, 6.641).

Table 3 compares the demographic and laboratory parameters in patients with fatty liver disease in terms of the severity of the disease. In this table, the severity of disease is being defined with grade 1 and grade 2 categories. In total, 69% of the patients (101 people) were affected with fatty liver grade 1, and 30% (43 patients) had fatty liver grade 2. It should also be noted that only one patient had fatty liver grade 3, and to facilitate the statistical analysis, this person was also considered as a grade 2 patient.

Table 4 shows the results of a comparison between patients with fatty liver grade 1 and 2 in terms of the level of cholesterol and triglycerides, LDL, HDL, FBS, ALT and AST. It also presents the mean levels of the above-mentioned variables in the patients studied.

In this study, all patients with fatty liver were examined for hepatitis B and C and the results showed that out of the 135 people who were diagnosed with fatty liver, only one person had positive HBS Ag. The results of examinations for hepatitis C showed that HCV Ab was negative in all patients with fatty liver.

DISCUSSION

In this study, 410 people living in the city of Sanandaj underwent abdominal ultrasound and the results showed that 35% (145 patients) were affected with non-alcoholic fatty liver disease. Other studies have shown various statistics about the prevalence of non-alcoholic fatty liver disease in the Americas, Asia, Europe, and Africa. In view of that, the prevalence of the disease is reported as 18.7% - 34% in the general population of the various countries (10,11,14-17). As it is shown, the prevalence of this disease in the city of Sanandaj is among the highest prevalence rates in

Table 1: Features and attributed weights based on the population ratios in the studied subjects

Variable		Total (٪)
Sex	Male	169 (41.11)
	Female	241 (58.89)
Occupation	Public sector employees	33 (8.86)
	Self employed	108 (26.95)
	Soldier / Student	26 (11.58)
	House wife	207 (47.59)
	Retired	31 (3.14)
	Unemployed	5 (1.88)
Age	Mean	37.75
Blood pressure	Yes	203 (39.91)
	No	207 (60.09)
Diabetes	Yes	27 (4.62)
	No	382 (95.38)
Smoking	Yes	48 (11.31)
	No	361 (88.69)
Body mass index	18 >	2 (0.57)
	25 > ≥ 18	119 (35.46)
	30 > ≥ 25	154 (38.17)
	> 30	113 (25.79)

Table 2: Indicators measured in the studied subjects in terms of the risk of fatty liver disease

Variable		Healthy people Total (٪)	Patients with fatty liver Total (٪)	OR (Confidence interval 95%)
Sex	Female	168 (77.53)	73 (22.47)	-
	Male	97 (56.92)	72 (43.08)	2.61 (1.644 - 4.144)*
Age group	20-30	61 (79.45)	16 (20.55)	-
	30-40	62 (73.03)	23 (26.97)	1.427 (0.685 - 2.974)
	40-50	55 (58.39)	40 (41.61)	2.755 (1.382 - 5.492)*
	50-60	49 (53.87)	41 (46.13)	3.31 (1.648 - 6.648)*
	60-70	37 (60.65)	24 (39.35)	2.508 (1.177 - 5.342)*
Socioeconomic level	Poor	82 (69.97)	42 (30.03)	-
	Average	84 (70.52)	44 (29.48)	0.973 (0.545 - 1.737)
	Rich	91 (66.52)	55 (33.48)	1.172 (0.666 - 2.064)
Blood pressure	Normal	148 (75.58)	59 (24.42)	-
	High	117 (59.24)	86 (40.76)	2.129 (1.342 - 3.376)*
Diabetes	Non-diabetic	252 (70.27)	130 (29.73)	-
	Diabetic	12 (42.38)	15 (57.62)	3.214 (1.357 - 7.612)*
Smoking	Non-smoker	240 (72.32)	121 (27.67)	-
	Smoker	25 (43.49)	24 (56.50)	3.395 (1.735 - 6.641)*
Body mass index	25 >	99 (85.08)	22 (14.92)	-
	30 > BMI ≥ 25	97 (66.42)	57 (33.58)	2.885 (1.523 - 5.466)*
	> 30	56 (53.21)	57 (46.79)	5.015 (2.568 - 9.763)*

* Significant values

Table 3: Parameters measured in the studied subjects in terms of the severity of fatty liver disease

Variable		People with fatty liver grade 1 (%)	People with fatty liver grade 2 (%)	OR (Confidence interval 95%)
Sex	Female	50 (70.15)	23 (29.95)	-
	Male	51(74.01)	21(25.95)	0.825 (0.373 - 1.821)
Age group (year)	20-30	14 (86.98)	2 (13.02)	-
	30-40	17 (75.37)	6 (24.63)	2.183 (0.0375 - 12.695)
	40-50	24 (58.78)	16 (41.22)	4.684 (0.927 - 23.656)
	50-60	30 (74.05)	11 (25.95)	2.34 (0.450 - 12.162)
	60-70	14 (62.50)	6 (37.50)	4.008 (0.729 - 22.020)
Socioeconomic level	Poor	27 (66.37)	15 (33.63)	-
	Average	34 (80.57)	10 (19.43)	0.475 (0.170 - 1.328)
	Rich	38 (73.09)	17 (26.91)	0.726 (0.275 - 1.913)
Body mass index (kg/m^2)	> 18	0	0	-
	25 > BMI ≥ 18	18 (78.82)	4 (21.18)	-
	30 > BMI ≥ 25	39 (72.00)	18 (18.00)	1.447 (0.377 - 5.554)
	> 30	39 (73.77)	18 (26.23)	1.323 (0.344 - 5.088)
Blood pressure (mm Hg)	Normal SBP < 130 or DBP < 85	43 (78.22)	16 (21.78)	-
	High SBP ≥ 130 or DBP ≥ 85	58 (67.07)	28 (32.93)	1.762 (0.787 - 3.944)
FBS (mg/dL)	Normal < 100	73 (75.90)	26 (24.10)	-
	Pre-diabetic 100 ≤ FBS < 126	11 (61.82)	7 (38.18)	1.944 (0.627 - 6.027)
	Diabetic ≥ 126	10 (57.68)	9 (42.32)	2.31 (0.778 - 6.860)
Triglyceride (mg/dL)	Normal < 150	52 (82.24)	13 (17.76)	-
	High 150 ≥	42 (61.51)	29 (38.44)	2.897 (1.245 - 6.736)*
Cholesterol (mg/dL)	Normal < 200	45 (77.30)	14 (22.70)	-
	High 200 ≥	49 (67.28)	28 (32.72)	1.655 (0.712 - 3.848)
HDL (mg/dL)	Normal > 40 in men and > 50 in women	28 (74.58)	11 (25.42)	-
	Low ≤ 40 in men and ≤ 50 in women	73 (71.32)	33 (29.68)	1.179 (0.474 - 2.930)
LDL (mg/dL)	Normal < 100	75 (74.26)	28 (25.74)	-
	High 100 ≥	19 (63.74)	14 (36.26)	1.64 (0.649 - 4.143)
ALT	Normal < 40	85 (76.58)	26 (23.42)	-
	High 40 ≥	9 (37.50)	15 (62.50)	5.449 (2.137 – 13.891)*
AST	Normal < 40	87 (70.73)	36 (29.27)	-
	High 40 ≥	7 (58.33)	5 (41.67)	1.726 (0.514 - 5.798)

* Significant values
LDL= low density lipoprotein, HDL: high density lipoprotein, FBS: fasting blood sugar, AST: aspartate amino transferase, ALT: alanine amino transferase.

Table 4: Mean laboratory indicators measured in patients with fatty liver

Variable	Mean values in patients with fatty liver grade 1	Mean values in patients with fatty liver grade 2 and grade 3	Mean values in all patients with fatty liver	*P*
Cholesterol (mg/dL)	202.36 ± 5.01	210.11 ± 6.16	204.53 ± 4.02	0.44
Triglyceride (mg/dL)	166.53 ± 15.05	197.30 ± 15.04	175.15 ± 11.74	0.24
LDL (mg/dL)	127.74 ± 4.19	134.60 ± 5.46	129.66 ± 3.40	0.26
HDL (mg/dL)	40.34 ± 1.09	39.09 ± 1.16	39.99 ± 0.85	0.99
FBS (mg/dL)	102.31 ± 3.39	105.20 ± 5.22	103.12 ± 2.85	0.87
ALT	26.15 ± 1.45	33.20 ± 2.87	28.23 ± 1.35	0.055
AST	29.34 ± 2.14	28.85 ± 1.50	29.15 ± 1.54	0.57

LDL: low density lipoprotein, HDL: high density lipoprotein, FBS: fasting blood sugar, AST: aspartate amino transferase ALT: alanine amino transferase

the world. This condition may be due to changes in lifestyle, decreased mobility, increased prevalence of sedentary jobs, and changes in diets, which occur through increased consumption of saturated fatty acid and less fruit and vegetable intake, leading to weight gain and other metabolic problems. Lower prevalence rates of the disease in China and South Korea can be attributed to the higher levels of physical activity and proper eating habits adopted by the populations in those countries. One of the reasons for the low prevalence of the disease in Sudan, which is less than that in western countries, is the lower prevalence of obesity and being overweight in Sudan (10). Of course, this is not true in the case of India, because despite the fact that obesity and being overweight are lower in India compared to western countries, the prevalence of fatty liver disease is similar in both regions; these differences suggest that fatty liver disease is not caused by being overweight and obese alone, but rather it is a heterogeneous and multi-factorial disease (16).

In this study, 33.5% of overweight individuals (OR = 2.885, CI = 1.523, 5.466) and 46% of obese people (OR = 5.015, CI = 2.568, 9.763) were affected by non-alcoholic fatty liver disease; in both cases, the rate was significantly different from that in individuals who were not overweight. These values, respectively, are 37% and 17% in Sudan and 55% and 23% in the United States of America.

In this study, the prevalence of fatty liver disease in males was almost twice as much as that in females and the difference was statistically significant. In the past (before 1990) it was assumed that non-alcoholic fatty liver disease is more common in females, but recent studies have shown that the disease occurs in males and females alike (18,19). The results of a study by Mohan et al. in southern India are consistent with this finding. However, the findings of Gao Fan et al. in China showed that the prevalence of fatty liver in males was significantly higher than females, and it is in line with the findings of our study. The lower incidence of fatty liver among females can be the result of women's increased level of participation and role in the community, which has in turn increased their activities.

In the present study, the highest and lowest prevalence rate of liver disease was observed in the 50 to 60 years age group (46%) and the 20 to 30 years age group (20%), and the difference was statistically significant (OR = 3.31, CI = (6.648, 1.648). The results of a study in Sudan by Almobarak et al. showed that the peak age of the onset of the fatty liver disease was 53 years, which was compatible with our results. In general, different studies have shown that the highest prevalence rate is between the ages of 46 years to above 50 years old (20).

In this study, the prevalence of fatty liver in people with normal blood pressure and those with high blood pressure, respectively, was 24% and 40% and this difference was statistically significant (OR = 2.129, CI = 1.342, 3.376). This is in line with the results of a 10-year study by Chul Sung et al., who examined the association between fatty liver disease and the increased risk of cardiovascular disease (1). Blood pressure is one of the components of metabolic syndrome and several studies have shown the association between metabolic syndrome and non-alcoholic fatty liver disease and have assumed that non-alcoholic fatty liver disease is the liver manifestation of metabolic syndrome (21,22), and this study also confirms it. The prevalence of fatty liver disease in people who had a history of diabetes (57%) was about two times higher than those who had no history of diabetes (29%) and this difference was statistically significant (OR = 3.214, CI = 1.357, 7.612).

In this study, the prevalence of fatty liver grade 2 in people whose triglyceride level was above the normal range (38%) was two times more than those with normal triglyceride levels (17.7%) and this difference was statistically significant (OR = 2.897, CI = 1.245, 6.736). This is also in line with the results of Mohan et al.'s study in southern India (11), which reported that the risk of non-alcoholic fatty liver disease in the presence of dyslipidemia increases twofold. There was also a significant relationship between fatty liver grade and ALT level As the level of ALT increased in patients with Grade 2.

As one of the limitations of this study, we used ultrasound to diagnose fatty liver; as we know, this method shows some false positive and false negative results. Nevertheless, in this study we tried to minimize false-positive cases via applying the exclusion criteria. One of the other limitations of this study was that, due to budget constraints, blood samples were taken only from patients with fatty liver. Hence it was not possible to compare the values obtained with the normal population. Nonetheless, we conducted a comparison between fatty liver grade 1 and grade 2.

Based on the results obtained, the prevalence of NAFLD in the general population of Sanandaj city is among the highest prevalence rates reported around the

world. It is expected that in the near future, fatty liver disease will become one of the main reasons for liver transplant in Iran. Hence, the results of this study can serve as a warning to initiate serious interventions and promote preventive policies to stop the growth of the disease.

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CONFLICT OF INTEREST

The authors declare no conflict of interests related to this work.

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