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Evaluation of Risk Factors of Nonalcoholic Fatty Liver Disease in the Adult Population of Zahedan, Iran

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Abstract

***Background*:** Non-alcoholic fatty liver disease (NAFLD) is the most common form of chronic liver disease. It has been reported that visceral fat releases free fatty acids and arises fat accumulation in the liver. Therefore, this study aimed to evaluate the some biomarkers of NAFLD risk in adult general population.

***Materials and Methods*:** An analytical - descriptive study was carried out on a total of 1529 randomly selected individuals (797 male and 732 female) aged 30–88 years in Zahedan. The characteristics of socio-demographic, medical history, food habits and lifestyle factors were obtained by a validated questionnaire, liver ultrasonography and routine laboratory tests were performed with the use of standard techniques. The assessment of waist circumference (WC) and waist to hip ratio (WHR) was performed as central obesity indices.

***Results*:** The mean levels of WC and WHR were 92±11.7 cm and 0.91±0.06 in men, and 91.2±12.4 cm and 0.88±0.07 in women, respectively. 39.7% and 37% of subjects had hypercholesterolemia and hypertriglyceridemia, respectively. Ultrasonography findings demonstrated diffuse fatty liver in 40.9% subjects. Data also showed low consumption of fruits and vegetables and fish, and high consumption of saturated fatty acids (SFAs) and fast foods in the majority of obesity and NAFLD subjects compared with normal subjects.

***Conclusion*:** The results showed that a large proportion of the study population is at risk of central obesity and NAFLD. The formation of non-alcoholic fatty liver may be associated with obesity and unhealthy dietary patterns which warrants further research.

Introduction

Nonalcoholic fatty liver disease (NAFLD) refers to a wide spectrum of liver diseases ranging from fatty liver (accumulation of fat in the liver), to nonalcoholic steatohepatitis (NASH) and to cirrhosis [1]. NAFLD is now recognized as a major public health issue in the medical community [2]. The mean prevalence of fatty liver (as measured by ultrasonography) in the general population in Western countries, ranges from 20% to 60%, is much more prevalent in obese people (76-89%) and alcohol abusers (46-50%); it is more usual in men than women (3/1 ratio) [3]. The pathogenesis of NAFLD is probably multi-factorial [4], but fatty liver is an obesity-associated liver disease that the high prevalence of it is probably due to changes in dietary habits, including an increased consumption of hyper caloric food and saturated fat and sedentary lifestyle [5-9]. The mechanisms responsible for developing NAFLD in obese persons and the effects on liver function are not fully known [2]. It is reported that visceral fat releases free fatty acids and arises accumulation of fat in the liver. Both intra-abdominal fat and liver fat independently predict certain metabolic risk factors [10]. Human data regarding nutrition's role on liver fat content are limited. Several studies have reported that dietary patterns as one of the most important factors for preventing and treatment of diseases [5, 6, 11, 12] are not only related to fatty liver, but are also causing several chronic diseases including obesity, cardiovascular disease (CVD), some types of cancer, type II diabetes, etc. Thus, it is important to identify food patterns that will serve as adjustable risk factors for the prevention of fatty liver and its complications, and other diet -related diseases [6, 7].

Due to limited data on the NAFLD and its risk factors in this area, the current study was planned to assessment of some risk factors of fatty liver (e.g. central obesity and plasma lipids levels associate with dietary patterns in adult general population of Zahedan, in Southeast of Iran.

Materials and Methods

Using a multistage cluster random sampling method, a total of 1,529 adult population (797 male and 732 female) aged 30-88 years old (48±11.7 years) were recruited for this survey from Zahedan, Sistan and Blouchistan Province, which is located in the southeast of Iran. A validated questionnaire was completed regarding demographic and anthropometric data, medical history and lifestyle factors (e.g. smoking and alcohol

consumption, food habits and dietary supplements use (vitamins A, C, E, D, calcium, folic acid, zinc, ferro) by trained personnel through face-to-face interviews. The people, who had history of alcohol consumption, used above food supplements, and smoking, positive HBV and HCV infection, type 2 diabetes mellitus, cardio vascular disease, chronic renal disease, and women with previous gestational diabetes were excluded from study. Anthropometric data included measurement of waist circumference (WC) and waist to hip ratio (WHR). The nonalcoholic fatty liver disease (NAFLD) diagnosis was determined by ultrasonography. A fasting blood sample was also collected after overnight fasting. Routine laboratory measurements such as total cholesterol, HDL, LDL, triglyceride, ALT, AST, were performed with the use of standard techniques. All participants obtained an evaluation of their food habits and their laboratory results. The medical-ethical committee of the Zahedan University of Medical Sciences approved the study protocol and all subjects gave their oral informed consent to participate to the study. A food habits questionnaire based on the 5 different food items consumed by subjects on a daily or weekly basis was filled for each subject. The validity and reproducibility of questionnaire had been confirmed in a pilot study. The different food items included: 1) Milk and dairy products; 2) Fruits and vegetables; 3) Meats group and substitutes; 4) Fats and sauces; 5) Fast foods.

Central obesity is assayed by measuring of waist circumference (WC) and waist to hip ratio (WHR) with an inelastic tape with ‘‘at risk’’ defined as WC >102 cm and WHR >0.9 in men, and WC >88 cm and WHR> 0.8 in women [1, 13]. Subjects were considered to have hyperlipidemia if the level of serum total cholesterol was more than 200 mg/dl, or high density lipoprotein cholesterol (HDL) level less than 40 mg/dl, or low-density lipoprotein cholesterol (LDL) more than 100 mg/dl, or serum triglyceride more than 150 mg/dl. Serum ALT and aspartate aminotransferase (AST) were measured by routine commercial laboratory methods. Abnormal values were defined as ALT greater than 40 U/L, AST greater than 37 U/L [1, 4, 14]. The SPSS-17 (SPSS, Inc, Chicago, Illinois) was used for statistical analysis. Values presented are mean±SD. Associations between socio-demographic factors and food habits and blood biomarkers were investigated by chi-square, *t*-test and one-way ANOVA analysis. Pearson’s correlation coefficients and linear regression was used for the relationship between variables. Differences with *p*-values, less than 0.05 were considered significant.

Results

Demographic characteristics of subjects have been shown in table 1. Generally, the mean levels of WC and WHR were 92±11.7 cm and 0.91±0.06 in men, and 91.2±12.4 cm and 0.88±0.07 in women, respectively. Additionally, 39.7% and 37% of subjects had hypercholesterolemia and hypertriglyceridemia, respectively. Ultrasonography findings demonstrated diffuse fatty liver in 40.9% subjects (grades I: 27.6%; grade II: 9.9%, and grade III: 3.1% (Table 1).

Table 1. Demographic characteristics of studied population

Parameters		Mean ±SD
Age (yr)		48 ±11.7
Gender	M/F	52.1(47.9)
Waist circumference (cm)	Male	92±11.7
	Female	91.2 ±12.4
Waist to hip ratio	Male	0.91 ±0.06
	Female	0.88 ±0.07
Fatty liver [N (%)]	Normal	907 (59.1)
	Grade I	423(27.6)
	Grade II	152(9.9)
	Grade III	47(3.1)
Hypercholesterolemia [N (%)]	Yes	919(60.3)
	No	605 (39.7)
Hypertriglyceridemia [N (%)]	Yes	960(63)
	No	564(37)

The mean levels of cholesterol, triglyceride (p<0.0001), ALT (p<0.01), WC (p<0.0001) and WHR (p<0.01) were significantly elevated with increasing of the liver fat (Table 2). Based on the WC and WHR, 76.6% and 47.7% of obese subjects had types of fatty liver, respectively. The majority of subjects in the aged of above 40 years were also obese (Table 3). In all of the study subjects, obesity, age, hypercholesterolemia, hypertriglyceridemia, AST and ALT were significantly associated with fatty liver (p<0.00001). As shown in table 4, the obesity and NAFLD subjects had low consumption of fruits and vegetables and fish, and high consumption of saturated fatty acids (SFAs) and fast foods compared with normal subjects.

Table 2. Biochemical markers and central obesity status of subjects with fatty liver according to ultrasonography

Parameters		Normal	Grade I	Grade II	Grade III	*p*-Value
Cholesterol (mg/dL)		187.3 ± 36.8	199.4 ±42.8	201±45.2	200.4±36.7	0.0001
LDL (mg/dL)		110.3±34	113.4±41.2	114±41.1	112±37.7	NS
HDL (mg/dL)		50.1 ±5	50.5 ±4.6	50.3±4.2	51.5±4.3	NS
Triglyceride (mg/dL)		133±79.2	175.2±92	180.3±101.1	221.4±106	0.0001
AST (IU/L)		22.7±16.2	22.7±10.2	25.5±12.8	27.8 ±14	NS
ALT (IU/L)		26.5±20.8	30.4±19.9	34.7±20.1	40.4±27.7	0.01
Central	WC (cm)	87.2±10.6	*96±10.2	100.8±10.9	107.5±11.7	0.0001
Obesity	WHR	0.89 ±0.07	*0.92±0.06	0.93±0.07	0.95±0.07	0.01

p-Values between fatty liver and normal subjects: *grade I vs. grade III NS: Non-significant

Table 3. Risk factors related to central obesity in the studied population

Variables		Waist circumference			Waist To Hip		
		Normal [N (%)]	High [N (%)]	*p*-Value	Normal [N (%)]	High [N (%)]	*p*-Value
Fatty liver	Normal	845(66.9)	62(23.4)	<0.0001	264(81.2)	590 (52.3)	0.0001
	Grade I	318(25.1)	105(39.6)		52 (16)	355(31.4)	
	Grade II	86(6.8)	66(24.9)		9 (2.8)	137(12.1)	
	Grade III	15(1.2)	32(12.1)		-	47(4.2)	
Hypercholesterolemia	Yes	483(38.3)	122(46.6)	<0.01	96(29.3)	477(42.6)	0.0001
	No	778(61.7)	140(53.4)		232(70.7)	643(57.4)	
Hyper triglyceridemia	Yes	433(34.3)	130 (49.6)	<0.0001	82(25)	448(40)	0.0001
	No	828(65.7)	132(50.4)		246(75)	672(60)	
Age	30-39 (yrs)	352(27.7)	52(19.6)	<0.01	132(40.2)	258(22.8)	0.0001
	40-49 (yrs)	380(29.9)	79(29.8)		89(27.1)	346(30.6)	
	50-59 (yrs)	299(23.6)	90(34)		53(16.2)	316(27.9)	
	>60 (yrs)	238(18.8)	44(16.6)		54(16.5)	211(18.7)	

Table 4. Characteristics of studied population based on the food patterns

NAFLD													
		Normal						Abnormal					
Food intakes		Non -Obese (N=264)			Obese (N=590)			Non -Obese (N=61)			Obese (N=539)		
		Daily	Weekly	Never	Daily	Weekly	Never	Daily	Weekly	Never	Daily	Weekly	Never
Fruits & vegetables [N (%)]		100(11.7)	115(13.5)	48(5.6)	201(23.5)	259(30.3)	130(15.2)	20(3.3)	39(6.6)	2(0.03)	150(25.3)	69(11.6)	320(54)
Dairy products [N (%)]		125(14.6)	104 (12.2)	35(4.1)	115(13.5)	378(44.3)	96(11.2)	15(2.5)	41(6.9)	5(0.08)	450(6.7)	50(8)	39(6.6)
Fish [N (%)]		70(8.2)	102(11.9)	91(10.6)	150(17.6)	414(48.5)	26(3)	12(2)	12(2)	37(1.1)	150(25.3)	116(19.6)	207(34.9)
Fast foods [N (%)]		20(2.3)	43(5)	199(23.3)	113(13.2)	378(44.3)	99(11.6)	22(3.7)	21(3.5)	18(13.5)	321(54.1)	203(34.2)	15(2.5)
Types of oil used	SFAs	30(3.5)	10(1.1)	-	49(5.7)	109(12.8)	5(0.05)	20(3.3)	8(1.3)	3(0.05)	300(50.6)	12(2)	5(0.05)
	PUFAs	191(22.4)	20(2.3)	-	350(59)	30(3.5)	-	15(2.5)	2(0.03)	-	110(18.5)	11(1.8)	-
	Mix	13(1.5)	-	-	41(4.8)	6(0.07)	-	5(0.08)	-	-	89(15)	2(0.03)	-

Discussion

The prevalence of NAFLD in a screening with ultrasonography in obese people (central obesity measured by WHR more than 0.9 for men and more than o.8 for women) was shown in 47.7% and based on the waist circumference more than 102 cm for men and more than 88 cm for women was shown in 76.6%, respectively. However, most of these people have simple fatty liver and not the more serious types of NAFLD. Similar results have been demonstrated from some studies in general population [15-18]. It has been reported that NAFLD can also occur in non- obese people [15, 19]. Similarly in recent study, we found 33.1% and 47.7% prevalence of NAFLD in non-obese subjects by WHR and WC measurement, respectively. There is evidence that shows increasing prevalence of fatty liver in general population in Asian countries like Japan and China is associated with over-nutrition, obesity, IDDM, dyslipidemia, etc. [4, 16, 20-24]. Our findings also showed that the mean levels of cholesterol, triglyceride, ALT, waist circumference (WC) and waist to hip (WHR) significantly elevated with increasing of liver fat. Also, a significant positive correlation was demonstrated between central obesity (r=0.47, p<0.0001), age (r=0.27, p<0.0001) cholesterol (r=0.18, p<0.0001), triglyceride (r=0.23, p<0.0001), AST (r=0.21, p<0.0001) and ALT (r=0.14, p<0.0001) with fatty liver. Nonalcoholic fatty liver disease is often associated with slightly elevated levels of liver enzymes (ALT and AST) in the blood [25]. In this research, mean levels of ALT and AST were in normal range, but weight gain and increased in the liver fat led to a further increase in the level of the liver enzymes. It has been reported that unhealthy dietary patterns are strongly associated with high prevalence of fatty liver and contemporary epidemics of obesity [6, 17, 18, 21]. There are limited data regarding the food habits of patients with fatty liver disease. Based on available data, infrequent intake of fruits and vegetables, and fish and also high consumption of saturated fatty acids (SFAs) and fast foods were demonstrated in the majority of obesity and NAFLD subjects compared with normal subjects. The intake of fruit and vegetables, dairy products and fish, polyunsaturated fatty acids (PUFAs) tended to be lower and animal oils were more in the ages >60 years old (data no shown**).**

High-fat diets leading to excessive energy intakes are strongly linked to the increasing obesity [26] and to producing fatty liver in both animal and human [18]. Modification of dietary patterns may be effective in decreasing risk of chronic diseases [7, 26], in particular, a diet high in whole grains, fish, fruits and vegetables, and legumes and low intake of refined cereals, red and processed meats, sugar-containing beverages, sweets, and desserts, high-fat dairy products and fast foods [7, 12, 27]. The results showed that a large proportion of the study population are at risk of NAFLD. The formation of non-alcoholic fatty liver may be associated with obesity and unhealthy dietary patterns which warrants further research. Thus, efforts supporting of lifestyle modifications that lead to weight reduction, and better nutrition (e.g., concomitant decrease in total dietary fat in particular saturated fats to its minimum, increase the fiber and fish intake) are needed to improve the diet and health of the population. Minimizing fast food intake will also help maintain a healthy diet.

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Authors' Contributions
Dr. Farzaneh Montazerifar: Drafted the manuscript, performed the statistical analysis, Dr. Mansour Karajibani: Drafted the manuscript and Dr. Alireza Ansari-Moghaddam: Designed the study, collected and analysed data.

Conflict of Interest
The authors declare no conflict of interest.

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