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NON-ALCOHOLIC FATTY LIVER DISEASE WITH METABOLIC SYNDROME

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ABSTRACT

Non alcoholic fatty liver disease is the most common health burden in developed countries.The spectrum of liver damage includes NASH, advanced fibrosis and rarely progresses to cirrhosis. Insulin resistance, oxidative stress, lipid peroxidation,mitochondrial dysfunction play a major role in the development of NAFLD. Our study strongly suggest that the association of non alcoholic fatty liver disease as a possible component in metobolic syndrome. 1000 people participated in this study whose age was 30 and above. Anthropometry measurements, random blood sugar, blood pressure measurements, BMI, and USG were evaluated to screen for metabolic syndrome. A questionnaire was used to obtain information regarding history and quantity of alcohol consumption. Metabolic syndrome was defined in all participants based on national cholesterol education program adult treatment panel lll (NCEP/ATP lll) for clinical diagnosis of metabolic syndrome. Non alcoholic fatty liver disease was detected in 33.1% and 27.4% of men and women respectively. NAFLD is mainly associated with the development of MetS. However, it was not possible to determine whether NAFLD preceded the development of MetS.

Key Words:- Non-alcoholic fatty liver disease, Metabolic syndrome, NCEP/ATP-III, Waist circumference, Hyperglycemia

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INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is a spectrum of disease ranging from simple steatosis to steatohepatitis, with degrees of inflammation and fibrosis, which progresses to cirrhosis and hepatocellular carcinoma.[1] NAFLD is now more common than alcoholic liver disease owing to the rapid rise in the prevalence of obesity, and NAFLD is the most common cause of abnormal liver function tests.[2] Previous studies shown that around 80% of population with elevated liver enzymes have NAFLD. 30% of the general adult population and up to 60-70% of obese patients with diabetes mellitus patients have NAFLD. MetS is a cluster of conditions with increased blood pressure, high blood sugar, excess body fat around the waist, abnormal triglyceride levels-that occur together, increasing the risk of developing heart disease, stroke, and Diabetes. NAFLD and MetS have been linked by relationships between central obesity, steatosis, and insulin resistance.[3]

MATERIALS AND METHODS

Study Population

The lifestyle nature of this town is rural and in this study, the demographic and anthropometric characteristics of the participants were documented in the questionnaire. The questioners were trained how to fill the questionnaire and how to measure systolic and diastolic blood pressure, waist circumference, hip circumference, weight and height. The blood samples were transferred to our lab within an hour under standard conditions. We included ≥30year-old volunteers who had undergone ultrasonography confirming fatty liver. We excluded those who were alcohol users, who were being treated for NAFLD or using medications such as amiodarone, tamoxifen, pregnant women and HbsAg positive patients.

Measurements

The demonstration of areas of hyperechogenicity on sonography is used in the diagnosis of NAFLD in all individuals. Sonograms were obtained using static and real time scanning with commercially obtained units. A transducer with 3.5-MHz was routinely used, with a transducer of 2.25-MHz reserved for areas to penetrate is difficult. The patients are examined in both supine and left posterior oblique positions, with longitudinal, transverse, and oblique scanning planes. The severity of echogenicity were graded as 0,1,2 & 3. Systolic and diastolic blood pressures were measured as duplicate on the left upper arm and the average used for analysis. WC between the lowest rib and the iliac crest at the level of umbilicus was measured in duplicate to the cm using a flexible tape. Plasma glucose for the subjects was measured using the glucose-peroxidase colorimetric enzymatic method with a sensitivity of 5 mg/dL and intra-assay coefficients of variation (CV) of I.7% in the lower limit and 1.4% in the upper limit concentrations. Inter-assay coefficients of variation (CV) for the assay were 1.1% in the lower limit and 0.6% in the upper limit concentrations respectively. Serum cholesterol and triglyceride for all individuals were measured after 12–14 hours of fasting with colorimetric method with a sensitivity of 5 mg/dl. Intra-assay and inter-assay CV for the assay were 1.6% and 1.1% in lower limit and 0.6% and 0.9% for upper limit concentrations. HDL-C were measured after precipitation of the apolipoprotein B containing lipoproteins with phosphotungstic acid.

Metabolic Syndrome criteria

Two different criteria were used in this study, NCEP/ATP-III and CCDMIA. MetS was defined as the presence of three or more of the presented parameters in below table.[4&5]NCEP/ATP-III, National Cholesterol Education Program Adult Treatment Panel III; CCDMIA, Criteria for Clinical Diagnosis of metabolic syndrome in Iranian Adults; WC, Waist Circumference; TG, Triglyceride, SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure; FBS, Fasting Blood Sugar.

RESULTS

We enrolled 359 (33.3%) men and 647 (68.7%) women. Among the individuals ≥30 years there were 202 (80.8%) men and 598 (90.2%) women with a male to female ratio of 1:2.45. below table shows the frequency, percentage and mean ± SD age of all participants, those ≥30 years, and those ≥30 years that had NAFLD with different grades. The men to women ratio in all participants, those ≥30 years, and those ≥30 years who had NAFLD were 1:2.19, 1:2.45, and 1:2.03, respectively. Mild NAFLD was more prevalent in both men and women. However, moderate and severe NAFLD was more prevalent in women compared with men ($p>0.05$). Among those ≥18 years, men were about 4 years older than women ($p<0.001$). NAFLD was detected in 33.1% and 27.4% of men and women, respectively.

The prevalence of MetS and its related NAFLD grades according to NCEP/ATPIII and CCDMIA are presented. As demonstrated, the number of men with MetS based on NCEP/ATPIII was higher than CCDMIA. In the opposite trend, the number of women with MetS based on CCDMIA was higher than NCEP/ATPII. Among men, according to the NCEP/ATPIII and CCDMIA criteria, 65.9% and 30.1% had MetS, respectively. These percentages in women were 64.6% and 73.7%, based on NCEP/ATPIII and CCDMIA criteria, respectively. Also, most of the patients with MetS had mild NAFLD in both sexes based on both criteria

NCEP/ATP-III, National Cholesterol Education Program Adult Treatment Panel III; CCDMIA, Criteria for Clinical

Diagnosis of MetS in Adults

The frequency and its percentage, 95% CI, and odds ratio for each component of MetS in patients with NAFLD is presented. It shows that there were no significant differences between the two genders in none of the components ($p>0.05$). Although, OR for hyperglycemia and abdominal obesity were approximately high in CCDMIA criteria (0.9613 and 1.2082, respectively), the respected differences were not statistically significant.

Table 1: Two Criteria for clinical diagnosis of metabolic syndrome which was used in this study

	Criteria	
Variables	**NCEP/ATP-III**	**CCDMIA**
Abdominal obesity	WC>102 cm in men and>88 cm in women	WC≥95 in both sexes
Hypertriglyceridemia	TG≥150 mg/dL	TG ≥150 mg/dL
Low HDL-C level	<40 mg/dL in men and<50 mg/dL in women	<40 mg/dL in men and<50 mg/dL in women
Hypertension	SBP/DBP≥130/85 mmHg	SBP/DBP≥130/85 mmHg
Hyperglycemia	FBS≥110 mg/dL	FBS≥100 mg/dL

Table 2: Frequency, percentage and mean ± SD of the age of the participants based on different categories

Variables	Grade a	Men	Women		
		Frequency (%)	Age (years)	Frequency (%)	Age (years)
≥ 30 years old		202 (29)	44.1±16.4*	598 (71)	40.2±30.7
NAFLD	All	66 (32.9)	46.5±13.4	163 (27.4)	46.5±12.0
	I	42 (63.2)	45.5±13.6	100 (61.3)	44.6±11.2
	II	20 (30.9)	47.9±12.2	52 (31.8)	49.2±12.3
	III	4 (5.9)	50.4±15.9	11 (6.9)	50.2±13.9

DISCUSSION

This study assessed the prevalence of MetS and its associated components in different grades of NAFLD. We found no difference between both men and women in NAFLD prevalence nor in MetS based on both criteria. The diagnosis of NAFLD requires an invasive and non-invasive tests. Mild to moderately increased levels of aspartate aminotransferase and alanine aminotransferase were the most common findings[8]. However some studies suggest that the use of liver enzymes as a marker of NAFLD underestimate its prevalence[9]. Ultrasound has a sensitivity of 84% and 76% and a specificity of 90% and 84% in detecting steatosis and increased fibrosis, respectively[8], and therefore we used this noninvasive easy technique in our study.

The prevalence of NAFLD was determined to be 27.4% in this study, which is different from the one report from Taiwan[10]. Other reports show rates of 10-30% from Taiwan, Japan, India[11], and USA, Europe, and Indonesia[12]. Also, the prevalence of MetS in patients with NAFLD ranged from 61-65%, based on CCDMIA and NCEP/ATPIII, respectively which was 1.8 to 3.1 times more than previous reports. This is moderately higher than that reported by Uchil et al. among Indian adult patients with NAFLD (47%)[8]. The higher prevalence of NAFLD in men compared with women in our study (33.1% vs. 27.4%) was similar to a previous report from Taiwan[8]. Despite the difference in criteria for the two components of MetS and gender, the prevalence of mild NAFLD (grade I) in patients with MetS was approximately high (about 50%). In the present study, hyperglycemia (OR: 1.21, 95% CI: 0.90-1.62) and abdominal obesity (OR: 0.96, 95% CI: 0.72-1.28), based on CCDMIA were the most NAFLD related components of MetS. NAFLD and MetS have been tangentially linked in the association with central obesity and insulin resistance[3]. This fact was highlighted in a large multicenter study, which showed that metabolic syndrome and insulin resistance were associated with NAFLD by multivariate analysis. In the adult population of the Tehran Lipid and Glucose Study (TLGS), MetS was found in 42% of women and 24% of men with a total age-standardized prevalence of 33.7%. Also, it has been reported that obesity is now recognized as a major health problem and is the prominent underlying factor in MetS[16]. The findings from our study support the relationship between obesity and hyperglycemia with MetS. Marchesani et al. showed that 80% of patients with NAFLD were obese[12] that is obviously higher than our estimation (47.2% in NCEP/ATPIII and 52.8% in CCDMIA).

The prevalence of MetS differed widely in different studies according to the population sample studied and the diagnostic criteria used. In our study population, the prevalence of MetS (65.25% and 51.90%) was different based on the diagnostic criteria used (NCEP/ATP-III or CCDMIA). The prevalence of MetS tended to be higher in men when the NCEP/ATP-III criteria were used, and tended to be higher in women when the CCDMIA were used. For these two definitions, the greatest difference is of the diagnosis of hyperglycemia and abdominal obesity.

Our study suffered from three important limitations: First, in our participants, volunteers women were more refereed than men due to occupational busy of men; Second, NAFLD diagnosis and grading was made only based on sonography. The most important reasons for this limitation were performing sonography in asymptomatic volunteer population and also its inexpensiveness and non-invasiveness; Third, our participants did not have any control group.

In conclusion, although our study demonstrated that NAFLD was associated with MetS, from this analysis it was not possible to determine whether NAFLD predating the development of MetS. Moreover, difference in detected MetS prevalence between NCEP/ATP-III and CCDMIA demonstrated that criteria in MetS are still a controversial subject and definition of better and more effective criteria for diagnosis of MetS in different population is seriously needed. Further well-designed case-control studies with follow-up and using of concurrent different criteria are needed to elucidate the causative relationship between these two conditions.

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