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Predictors of Non-Alcoholic Fatty Liver Disease in Egyptian Obese Adolescents

Moushira Zaki, Wafaa Ezzat, Yasser Elhosary, Omnia Saleh

***Abstract*—**Nonalcoholic fatty liver disease (NAFLD) has increased in conjunction with obesity. The accuracy of risk factors for detecting NAFLD in obese adolescents has not undergone a formal evaluation. The aim of this study was to evaluate predictors of NAFLD among Egyptian female obese adolescents. The study included 162 obese female adolescents. All were subjected to anthropometry, biochemical analysis and abdominal ultrasongraphic assessment. Metabolic syndrome (MS) was diagnosed according to the IDF criteria. Significant association between presence of MS and NAFLD was observed. Obese adolescents with NAFLD had significantly higher levels of ALT, triglycerides, fasting glucose, insulin, blood pressure and HOMA-IR, whereas decreased HDL-C levels as compared with obese cases without NAFLD. Receiver–operating characteristic (ROC) curve analysis shows that ALT is a sensitive predictor for NAFLD, confirming that ALT can be used as a marker of NAFLD.

***Keywords*—**Adolescents, Egyptians, obesity.

I. Introduction

NONALCOHOLIC fatty liver disease (NAFLD) is a metabolic disorder characterized by excessive triglyceride accumulation in hepatocytes. It is estimated that approximately a third of the general population has NAFLD [1]-[3]. A combination of lifestyle, environmental, gender, steroid hormone metabolism, genetic predisposition and metabolic factors play a role in the pathogenesis of NAFLD [4]-[7].

Nonalcoholic fatty liver disease (NAFLD) represents a spectrum of conditions ranging from simple hepatic steatosis to potentially fatal nonalcoholic steato-hepatitis and cirrhosis. The most mild form is simple steatosis in which triglyceride accumulates within hepatocytes. A more advanced form of NAFLD, nonalcoholic steatohepatitis (NASH), includes inflammation and liver cell injury. Several investigators have reported that NASH may present with cirrhosis and end-stage liver disease in some children.

Established risk factors for NAFLD in adolescents include obesity, insulin resistance, and type 2 diabetes [8]-[10]. Metabolic syndrome (MS), which involves the combination of risk factors for CVD such as insulin resistance (IR), abdominal fat, dyslipidemia, glucose intolerance, and hypertension, has often been associated with more severe liver abnormalities [11].

Obesity is a pro-inflammatory state that leads to insulin resistance (IR), which is closely associated with NAFLD development and progression. As the number of obese children has increased worldwide, risks for obesity-related metabolic and endocrine derangements, including hyperinsulinemia, hypertriglyceridemia, and hypercholesterolemia, have led to early development and increased incidence of type 2 diabetes, cardiovascular disease, hypertension and NAFLD [12]-[14]. NAFLD has a multifactorial etiology and a combination of environmental, genetic and metabolic factors play a role in the development of advanced disease. Genetic predisposition, overabundance of calorie-rich food and lack of physical activity contribute to development of obesity. So the pathophysiology of NAFLD is not fully understood. It is likely that certain features of MS are closely linked to future risk for development of other diseases associated with insulin resistance, such as T2DM or nonalcoholic fatty liver disease (NAFLD).

NAFLD occurs frequently in obese youth [15]-[17]. The rising prevalence of obesity in the adolescents and the need to develop simple screening tools to help identify those at risk for the development of diseases such as NAFLD and insulin resistance is important to understand. The aim of this study was to investigate the association between NAFLD and the components of MS in obese female adolescents.

II. Subjects and Methods

A descriptive cross-sectional study was conducted on 162 obese females. Their mean age was 16.8 ±1.7 years and body mass index (BMI) was 35.3 ± 6.5 kg/m2. This study protocol was approved by the ethical committee board of the National Research Centre of Egypt (No.10/223). An informed written consent was obtained from all participants. All individuals were clinically evaluated. The diagnostic of NAFLD was established by ultrasonography followed by the exclusion of the secondary causes of hepatic steatosis: (I) alcohol intake of 30 g/day or more for males and 20g/day or more for females, (II) Wilson disease, intestinal bypass surgery, glutenic entheropathy, (III) ingestion of drugs known to produce hepatic steatosis including methotrexate, tamoxifen, amiodarone, nucleoside analogues, (4) a positive serology for hepatitis B or C virus, (5) a history of another known liver disease. The subjects were interviewed to obtain their history of hypertension, diabetes mellitus, dyslipidemia, myocardial infarction, stroke, as well as alcohol consumption and smoking.Standing height without shoes was measured twice with a standard scale to the nearest 0.1 cm. Height was measured with the patients standing with their backs leaning against the stadiometer of the same scale. Body weight was measured with the lightest clothing to the nearest 0.1 kg. BMI was calculated as weight in kilograms divided by height in

Moushira Zaki, Wafaa Ezzat, Yasser Elhosary, and Omnia Saleh are with the National Research Centre, Medical Research Division, Egypt (e-mail:moushiraz@yahoo.com).

meters squared (kg/m2). WC and hip circumference (HC) were measured in cm using a plastic, non-stretchable tailor's tape. WC was measured with light clothing at a level midway between the lower rib margin and the iliac crest standing and breathing normally. HC was measured at the level at the widest circumference over the buttocks (at the greater trochanter). The waist hip ratio (WHR) was calculated as WC divided by HC.

Blood samples were collected from all the participants after an overnight fast. Serum levels of alanine transarninas (ALT), aspartate aminotransferase (AST), triglycerides (TG), cholesterol (TC), high density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) and fasting plasma glucose level were measured through standard laboratory methods.

Plasma insulin concentration was analyzed by chemiluminescent immunoassay (Immulite2000, Siemens, Germany) [18]. Insulin resistance was then determined by the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) calculated as the product of the fasting plasma insulin level (μU/mL) and the fasting plasma glucose level (mmol/L), divided by 22.5[19].

A convex-array probe (3.5 MHz) was used to demonstrate liver fatty infiltration. This was defined as increased echogenicity of the liver parenchyma without obvious mass effect and slightly impaired or poor visualization of the intrahepatic vessels and diaphragm. The patients were evaluated by the same radiologist in four groups according to the presence and severity of liver steatosis determined by ultrasonography. The changes of the echogenicity due to the fatty infiltration of liver parenchyma were evaluated according to the adjacent renal parenchyma.

Values published by IDF to identify MS for this specific age group are Triglycerides (TG) ≥150 mg/dL, or specific treatment for this abnormality; HDL cholesterol (HDLc) <40 mg/dL for both sexes, or specific treatment for this abnormality; arterial hypertension with SBP ≥ 130 mmHg or DBP ≥ 85 mmHg or specific treatment for arterial hypertension; and fasting glycemia ≥100 mg/dL or a previous diagnosis of type 2 diabetes [20].

All statistical analyses were performed using SPSS 16.0. Data is expressed as the mean ± standard deviation. Differences between groups were tested using an independent two-sample t-test or Maan-Whitney U-test for continuous variables, and the Pearson chi-square test was used to test for differences in the distribution of categorical variables.

The receiver operating characteristic curve (ROC) of HOMA-IR was used for the identification of NAFLD and detects the sensitivity, specificity and area under the ROC curve.

Logistic regression was used to evaluate the association between potential predictors and NAFLD. Insulin, glucose, ALT, TG and HDL-C were divided by 10 before use in the logistic regression model. All provided. P-values represent the results of two-sided tests. P-values < 0.05 were considered statistically significant.

III. Results

Table I shows significant association between MS and NAFLD. Off 162 obese females 59.87% had MS and 83.7% of those with NAFLD also had the diagnosis of MS, showing a significant association between MS and NAFLD (p = 0.01).

Table II shows a comparative analysis between the groups with and without a diagnosis of NAFLD. The mean HDL-c was significantly lower in patients with NAFLD, whereas SBP, DBP, glucose, insulin, triglycerides, ALT and HOMA-IR were significantly higher in subjects diagnosed with NAFLD. Table III shows the risk factors for NAFLD after being adjusted for age. NAFLD was more likely to occur in subjects with increase of insulin (OR =1.99), glucose (OR =1.89), ALT (OR= 3.4), TG (OR= 2.57) and decrease of HDL-C (OR= 3.46). Fig. 1 shows the receiver–operating characteristic (ROC) curve analysis of ALT in the prediction of NAFLD, the area under curve was .98 confirming its diagnostic value for NAFLD, confirming that the ALT is an accurate biochemical marker of NAFL.

TABLE I
Association between the Presence of NAFLD and MS in the Study Subjects

Variable(s)	OR	95%CI
Insulin(mg dl-1/10)	1.99	1.34- 2.14
Glucose(mg dl-1/10)	1.89	1.36- 2.15
ALT (U l-1/10)	3.4	1.45-2.88
TG (mg dl-1/10)	2.57	1.24- 2.34
HDL-C(mg dl-1/10)	3.46	1.34- 2.64

TABLE II
Comparison between the Mean of Biochemical and Anthropometric Variables between the Individuals with and without NAFLD

	Absence of NAFLD	Presence of NAFLD	P
	Mean ± SD	Mean ± SD	
BMI (kg/m2)	35.7 ± 12.5	37.4 ± 11. 2	.64
Waist (cm)	71.5± 12.4	105.5 ± 14.8	.59
WHR	0.79± .6	0.85 ± .7	.78
SBP(mmHg)	101.3 ± 9.3	110.5 ± 13.5	.001
DBP (mmHg)	67.5 ± 16.6	70.0 ± 14.5	.001
ALT(IU/L)	12.6 ± 7. 2	22.0 ± 11.8	.001
AST (IU/L)	23.5 ± 9.02	22.5 ± 10.8	.74
Glucose (mg/dL)	91.3± 7.5	98.6 ± 8.7	.001
Insulin (μU/mL)	4.1 ± 6.3	18.6 ± 9.1	.001
Cholesterol(mg/dL)	160.9 ± 33.6	171.8 ± 34.9	.84
Triglycerides(mg/dL)	69.3 ± 20.2	114.9 ± 35.8	.001
HDL-C (mg/dL)	49.7 ± 19.9	40.5 ±18.7	.001
LDL(mg/dL)	95.21 ± 23.7	103.3 ± 25.8	.45
HOMA-IR	0.87 ± 3. 2	4.6±2.5	.001

TABLE III
Univariable Analysis of Predictors for NAFLD in Obese Children

	Presence of MS		Absence of MS		
	n	%	n	%	p
Presence of NAFLD	77	83.7	15	16.3	
Absence of NAFLD	20	28.6	50	71.4	0.01

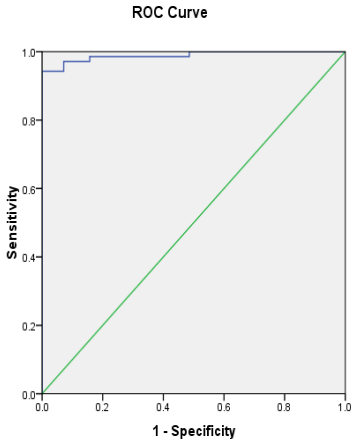

Fig. 1 The Receiver–operating characteristic curve analysis of ALT in the prediction of NAFLD

IV. Discussion

In the present study, MS was diagnosed in 83.7% of individuals affected by NAFLD. This association confirms other findings found a higher prevalence of MS in individuals with NAFLD [21], [22]. Marchesini et al. [23], who studied the components of MS in 304 individuals with NAFLD, found that over 90% of patients with some degree of liver disease have at least one component of this syndrome, with approximately one third of individuals having all components. Moreover, the diagnostic criteria of MS which associated with NAFLD were blood pressure, glucose, insulin, triglycerids and HOMA-IR. Similar trend has been noted when evaluating the clinical and histological features of NAFLD in obese patients, in which more than 50% of the cases had diagnostic criteria for MS [23].

Generally, hypertriglyceridemia and low HDL-c are the lipid fraction disorders most often associated with the presence of steatosis [24], [25]. However, in the study by Dixon et al. [26], which evaluated possible predictors of NAFLD, no correlation was observed between any lipid fraction with more advanced stages of the disease. In the present study, a significant association between IR, as indicated by the HOMA-IR, and the presence of NAFLD was observed. Probably due to the accumulation of abdominal fat, metabolic abnormalities such as these are very prevalent in these individuals, which is in agreement with studies that suggest that NAFLD is a component of MS, associated with visceral adiposity and IR [27], [28]

Many studies have proposed that the risk factors for NAFLD included a high fat diet, a sedentary lifestyle, insulin resistance, metabolic syndrome and its components (obesity, hypertension, dyslipidemia and T2DM) [29], [30].

The logistic regression analysis revealed that Insulin, glucose TG, ALT and HDL-C can increase the risk of NAFLD. ROC curve confirm that ALT had strong diagnostic value for NAFLD among obese female adolescents. Previous studies had reported that obesity and other metabolic factors were associated risk factor with NAFLD. [31], [32]. IR, both in the liver and adipose tissue, has been strongly associated with NAFLD [33], [34], as IR has been shown to increase with disease severity [35].

In conclusion ALT, TG, HDL-C, glucose and insulin are independent predictors of NAFLD in Egyptian obese female adolescents. The determination and monitoring of these components are of crucial importance for the screening of NAFLD among obese adolescents.

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