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The relationship between nonalcoholic fatty liver disease and obesity in children

Mahyar Mohammadifard: Associate Professor of Radiology, Birjand University of Medical Sciences, Birjand, Iran. mahyar.mohammadifard@yahoo.com
Mahmoud Zardast: (**Corresponding author*) Birjand Atherosclerosis and Coronary Artery Research Center, Assistant Professor of Pathology, Birjand University of Medical Sciences, Birjand, Iran. dr.zardast@yahoo.com
Vahideh Sabeti: MD. Birjand University of Medical Sciences, Birjand, Iran.

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Abstract

Background and Objective: Obesity in childhood increases the risk of fatty liver disease. With respect to the increased prevalence of obesity in Iran and the world, this study aimed to investigate the relationship between fatty liver and obesity in 6 -18 year-old children.

Methods: In this case-control study, 25 overweight children and 24 obese children, who had inclusion criteria, were selected by convenience sampling method. Then 27 children and teenagers with normal weight and the same sex and age were selected as the control group. Weight and height of the participants were measured and recorded, liver enzymes ALT and AST were performed for them. Data was analyzed in SPSS software using chi-square test, one-way ANOVA, Tukey range follow-up, and logistic regression. The significant level was set at $p<0.05$.

Results: The results showed that the relative frequency of occurrence of fatty liver increased significantly along with increasing body mass index ($p<0.001$). There was a significant relationship between sex, body mass index, and the prevalence of fatty liver in the participants. However, no significant relationship was found between fatty liver disease and AST and ALT ($p>0.05$).

Conclusion: There was a strong relationship between NAFLD and the abnormal body mass in children. It will be very useful if obese children to screen for susceptible to NAFLD.

Keywords: Fatty Liver, Obesity, Children

Introduction

Fatty liver is a chronic liver disease that is associated with lipid accumulation in hepatocytes and is usually created as the result of fat accumulation in the liver at the rate of more than 5% of the liver weight. This disorder is variable from steatosis (simple fatty liver, which is a benign disorder) to non-alcoholic steatohepatitis (where fat accumulation is associated with inflammation and injury and fibrosis to liver tissue) and finally to advanced fibrosis and cirrhosis (1).

Nonalcoholic fatty liver disease (NAFLD) is increasing in pediatric age group parallel to the growing prevalence of obesity and overweight all around the world (2). NAFLD has become the most common cause of liver disease worldwide (3).

The prevalence of fatty liver in obese children has been reported in various studies to be from 42.6% to 77.1% (4-6). Shiasi Arani et al (2013) reported the prevalence of fatty liver disease in the obese children and adolescents who referred to Children Hospital at Kashan University of Medical Sciences to be 53.3% (7), and Adibi et al reported the prevalence of fatty liver in obese children to be 54.4% (8).

The main risk factors associated with fatty liver disease are obesity, insulin resistance, hyperlipidemia, hypertension and cardiovascular diseases (9,10).

With the change of living conditions in recent decades, obesity is alarmingly on the rise in most communities and children are no exception to this phenomenon. Childhood obesity is one of the most serious public health challenges of the 21st century Globally, in 2013thenumberofoverweight children under the age of five years old, is estimated to be over 42 million. Close to 31 million of these

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are living in developing countries. In the WHO African Region alone the number of overweight or obese children increased from 4 to 9 million over the same period. The vast majority of overweight or obese children live in developing countries, where the rate of increase has been more than 30% higher than that of developed countries. If current trends continue the number of overweight or obese infants and young children globally will increase to 70 million by 2025.

Without intervention, obese infants and young children will likely continue to be obese during childhood, adolescence and adulthood (11). High fat and obesity attack the children who are in a golden age of personality growth that its effects may never be compensated (12). Like many developing countries, cardiovascular disease and its associated risk factors such as obesity as a public health problem is increasing in Iran (13). The findings of one study revealed a prevalence of 9.6%, 9.2%, and 15.7% for overweight, obesity, and central obesity among Birjand's elementary schools' students, respectively (14.). Studies indicate the total prevalence of obesity in Iranian population is even more than America, England, France, Holland and Italy (12). Obesity can predispose individuals to CVD complications and diabetes (15). They are more likely than non-overweight children to develop diabetes and cardiovascular diseases at a young rage, which in turn are associated with a higher chance of premature death and disability. (11). In obese children growth rate increases with increasing calorie intake, and the bone age is slightly advanced, and there is often a family history of overweight. In addition, the rapid weight gain during the first 6 months of life is a risk factor for overweight in childhood and adulthood, and physical inactivity in the growing years especially due to watching television is strongly associated with overweight (16).

With regard to the increased prevalence of obesity in Iranian children and teenagers, this study was conducted to investigate the relationship between fatty liver and obesity in 6 -18 year old children in Birjand City.

Methods

In this case-control study, among the 6-18 year old children and adolescents present in the Master Plan of Metabolic Syndrome from *Atherosclerosis and coronary artery research center* at Birjand University of Medical Sciences, 3 groups selected. that protocol was approved by the Medical Ethics Committee of Birjand University of Medical Sciences (IR.BUMS.1394.271). Inclusion criteria included informed consent of the individual and their parents, lack of mental retardation, lack of chronic drug use, lack of chronic disease and genetic symptoms and syndromes or abnormal symptoms, absence of signs of liver disorder, lack of symptoms of endocrine diseases, diabetes and metabolic diseases. Children with secondary obesity due to drugs or endocrine or genetic disorders were also excluded from the study subjects were referred to the authors' pediatric clinic by their general practitioner or primary care pediatric consultant.

Using the following formula:

$$n = \frac{\{z_{1-\frac{\alpha}{2}}\sqrt{2\bar{p}\bar{q}} + z_{1-\beta}\sqrt{p_1q_1 + p_2q_2}\}^2}{(p_1 - p_2)^2}$$

and the results of the study by Adibi et al (8), P1=0.54 and p2=0.1, the sample size of 21 individuals in each group was obtained, and in this study 27 individuals were included in normal weight group, 25 individuals in obese group and 24 individuals in overweight group.

First, questionnaires of demographic information such as age and gender were completed. With minimum clothes on, the weights of all individuals were measured using a German Seca digital scale. Standing and without shoes, their heights were measured two times by using meter, and the average of the two measures was recorded. Body mass index (BMI) was obtained by dividing weight (kg) by the square of height (m), and BMIs with the percentile less than 85 were regarded as normal, 85-94 as overweight, and 95 or higher as obese.

Then, the individuals were introduced to the Laboratory the blood sample was poured into a vacuum 5ml tube containing gel separator and clot activator, which had been made in Becton Dickinson Co. (USA). AST and ALT tests were performed by using COBAS INTEGRA clot detection set with the German ROCH kit.

For all the individuals, sonographies were performed by one radiologist. To determine the presence of fatty liver, the increased parenchymal echogenicity in the liver was specified to the extent of echogenicity of fat and visibility of portal veins and hepatic arteries. Then, in deep inspiration, the portal vein diameter was measured, and on the basis of sonographies the diagnoses were confirmed.

The data were analyzed through SPSS v.18 using chi-square, one-way variance analysis, Tukey's post hoc test and logistic regression at a significant level of 0.05.

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Table1. Relative frequency of occurrence of fatty liver in the studied groups

Fatty Liver	No	Yes	P value
Groups	number (percent)	number (percent)	
Normal weight	(81.5) 22	(18.5) 5	<0.001
Overweight	(44) 11	(56) 14	
Obese	(16.7) 4	(83.3) 20	

Table2. Comparison of the liver enzymes AST and ALT in individuals from the three groups

Variable	Normal weight	overweight	Obese	P value
	Mean ± standard deviation	mean ± standard deviation	mean ± standard deviation	
AST	25.30±15.11	22.20±4.98	24.96±9.21	0.54
ALT	16.74±13.49	17.60±6.98	24.96±11.65	0.02

Table 3. Risk factors of the occurrence of fatty liver disease in the studied individuals

Variable		OR (CI 95%)	Level of significance
gender	Female	1	
	Male	5.67 (1.29-24.95)	0.02
Body Mass Index	Normal	1	
	Overweight	8.36 (1.43-48.75)	0.02
	obesity	15.62 (2.11-115.51)	0.007
	Abnormal	1.20 (0.11-12.73)	0.88
Age		1.13 (0.80-1.13)	0.99
AST		1.01 (0.89-1.13)	0.99
ALT		1.02 (0.91-1.14)	0.76

Results

Of 76 subjects under study, 27 individuals (35.5%) had normal weight, 25 cases (32.9%) were overweight and 24 individuals (31.6%) were obese. 11 subjects of those who had normal weight (40.7%), 9 persons of those with overweight (36%), and 13 ones of the obese participants (54.2%) were male (p=0.41). The average ages of the individuals with normal weight, overweight and obesity were 12.85±2.7, 12.6±1.7 and 12.75±1.6 respectively (p=0.91).

With increases in BMI, the relative frequency of occurrence of fatty liver increased significantly in the individuals so that 18.5 % of those with normal weight, 56% of those with overweight and 83.3% of those with obesity had fatty liver (p<0.001) (Table 1). The relative frequency of fatty liver disease was significantly higher in males (68.8%) than in females (38.6%) (p=0.01).

The results showed that the average liver enzyme AST was not significantly different in the individuals of the three groups (p=0.54), but the average enzyme ALT was significantly different in at least two of the three groups (p=0.02). The result of Tukey's post hoc test showed that the average enzyme ALT was significantly higher in those with obesity than in those with normal weight (p <0.5) (Table 2).

The result of logistic regression test showed that the risk of fatty liver is averagely 5.67 times greater in males than in females (p=0.02), and it is on average 8.36 times higher in those with overweigh than in those with normal weight (p=0.02) and is 15.62 times higher in those with obesity than in those with normal weight (p=0.007). However, no significant relationship was obtained between the risk of fatty liver disease and blood sugar, triglycerides, HDL, age, and the liver enzymes AST and ALT (p>0.05) (Table 3).

Discussion

The findings of this study showed that with the increases in BMI, the relative frequency of occurrence of fatty liver increased significantly so that 18.5% of the individuals with normal weight, 56% of the individuals with overweight, and 83.3% of the individuals with obese subjects had fatty liver (p< 0.001)

In the study by Shiasi Arani and colleagues, the prevalence of fatty liver disease was reported in obese children and adolescents in the age group of 4-18 years to be 53.3% (7), and in the study by Adibi and colleagues it was reported to be 54.4% in obese children (8). The results of a study by Poorshams and colleagues on blood donors in Tehran showed that 98% of the patients with fatty liver were overweight and 56.5% were obese (17). In a study by Chan and colleague on 84 Chinese obese children, the evidence of fatty liver based on the results of the ultrasound was showed to be 77% (6).

In the present study, the prevalence of fatty liv-

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er disease in obese individuals was higher than that of the performed studies, and probably the differences reported in various studies on the frequency of liver disorder in children with overweight and obesity are due to different diagnostic methods (18).

The results of the present study showed that there is a significant relationship between sex and body mass index and the prevalence of fatty liver in the studied subjects, but no significant relationship was found between age and liver enzymes AST and ALT and the occurrence of fatty liver disease ($p>0.05$).

The results of various studies have shown that there is a significant relationship between body mass index and fatty liver (5-7), which is consistent with the results of this study.

In a study by Dehghan and colleagues on patients from 20-55 years of age, people with a body mass index over 25 had a 30 times higher chance of developing fatty liver than those with a BMI less than 25. Moreover, 95.6% of the patients with fatty liver had a BMI over 25, while this amount was 41.3% for the group without fatty liver ($p <0.001$) (19).

According to the results of this study and the results of other studies, high BMI is considered to be one of the independent predicting factors of the occurrence of fatty liver disease (20).

In obese individuals, fat tissue becomes insensitive to insulin action. As a result, higher decomposition of triglycerides and overabundance of circulating free fatty acids lead to the development of insulin resistance (21). Insulin resistance itself plays a role in the emergence and development of fatty liver disease. So that with altering the lipid metabolism, it increases lipolysis in peripheral tissues, increases hepatic triglycerides, and increases the harvest of free fatty acids in the liver, all of which can contribute to accumulation of triglyceride in liver cells (22).

In this study, the risk of fatty liver was significantly higher in males than in females, which is consistent with the results of the studies by Schwimmer and colleagues (23) and Tominaga et al (24), but in studies by Fu and colleagues (25) and Adibi et al (8) the occurrence of fatty liver in males and females did not differ significantly.

Conclusion

There was a strong relationship between NAFLD and the abnormal body mass in children. It will be very useful if obese children to screen for susceptible to NAFLD. Due to the increased incidence of obesity and increased prevalence of fatty liver in Iran and across the world, it is necessary that some programs be implemented to modify the people's lifestyles and food, and that some studies be designed to reduce children's weights and treat fatty liver disease. Limitation of this study is the cross sectional nature of the data, and Small sample size. It is recommended to evaluate also other risk factors.

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