

Fatty liver disease in obese children in Kashan, Iran

Original Article

Abbas Taghavi Ardakani (MD)¹
Mohammad Reza Sharif (MD)^{2*}
Davood Kheirkhah (MD)³

1. Department of Pediatrics,
Kashan University of Medical
Sciences, Kashan, IR Iran.

* Correspondence:

Mohammad Reza Sharif (MD),
Shahid Beheshti Hospital, 5th Km.
Ghotbe Ravandi Bulv, Kashan, 87159-
81151, IR Iran.

E-mail: mrsharifmd@yahoo.com
Tel: +98 3155540026
Fax: +98 3155548900

Received: 9 March 2014
Revised: 18 March 2014
Accepted: 4 April 2014

Abstract:

Background: Non-alcoholic fatty liver disease (NAFLD) is increasingly a common disease which is created by the accumulation of fat in the liver. About 20% of adults and 5% of children suffer from this disease. In some studies, half of obese children had fatty liver disease and approximately 90% of the patients with fatty liver were obese. The aim of this study was to evaluate fatty liver disease in obese children referred to the pediatric clinic in Kashan, Iran, in 2012.

Methods: This study was done on 200 children aged 5-15 years with Body Mass Index (BMI) more than 95% and other causes of obesity were ruled out. Liver ultrasonography for evaluation of fatty liver and blood sampling were performed for these children.

Results: Of 200 studied children, 122 (61%) and 78 (39%) were male and female, respectively with mean age of 9.07 years. The average of BMI was 27.9. According to liver sonography, 118 (59%) patients had fatty liver that 91.5% of them were grade I and 8.5% grade II. Liver enzyme levels, serum lipids and uric acid were significantly higher in obese children with fatty liver. Fatty liver had a significant relationship with insulin levels but no with Fasting Blood Sugar (FBS).

Conclusions: In this study, the prevalence of fatty liver and associated disorder in obese children was high (59%). Therefore, the lifestyle changes are necessary to prevent childhood obesity and some measures should be carried out for the treatment of fatty liver in children.

Keywords: Fatty Liver, Obesity, Children, Body Mass Index.

Citation:

Taghavi Ardakani A, Sharif MR, Kheirkhah D. Fatty liver disease in obese children in Kashan, Iran. *Caspian J of Pediatr*, March 2015; 1(1): 17-21.

Introduction

Fatty liver is a chronic liver disease that is associated with hepatic fat accumulation. It can be as simple steatosis or steatosis with inflammation (steatohepatitis) in which there is the probability of progression to cirrhosis. Fatty liver disease is the most common liver disease in many countries, and its prevalence is estimated 2.9% in Iran^[1]. Studies show that simple fatty liver is a benign disorder that can lead to fibrosis and end-stage liver disease. This disease is often silent, but sometimes shows itself with increased liver enzymes. The disorder is often associated with obesity, insulin resistance and metabolic syndrome components^[2]. About 21.9% of Iranian adults have metabolic syndrome. Metabolic syndrome is also seen in children especially in obese children. One of the predicting factors for metabolic syndrome is fatty liver and most patients with fatty liver have other disorders associated with metabolic syndrome such as obesity, diabetes mellitus and hyperlipidemia and hypertension^[2].

By changing the life style in recent decades, obesity has a progressive rate in most societies and children are not exempt from this phenomenon [3]. The prevalence of fatty liver disease has increased in parallel with the obesity increasing and currently has been reported 54.4% in Iran [2]. Therefore, it is expected that the fatty liver disease will be as the most common cause of chronic liver and it is necessary to perform more researches in the future.

The aim of this study was to evaluate fatty liver disease in obese children referred to the pediatric clinic in Kashan, Iran, in 2012.

Methods

In this study, the children aged 5-15 years were referred to pediatric clinics in Kashan in 2012. All children with Body Mass Index (BMI) more than 95% were considered obese and all of them were examined to find evidences of liver involvement and other causes of obesity such as Cushing's syndrome and hypothyroidism. Then, obese children with high caloric intake were studied and the other causes were excluded.

The study was explained for the parents of children and was conducted after their consent. This study was performed on 200 children; all of them were checked by using an ultrasonography after 6 h of fasting. Absence or presence of fatty liver and its grading were determined. Normal echogenicity is defined when the echogenicity of liver was same as kidney. Grade I, II and III were defined when the echogenicity of liver is obscured the walls of portal vein branches, obscures the diaphragmatic outline and fatty infiltration, respectively [4]. Also, a series of laboratory tests including AST, ALT, and ALP, TG, Cholesterol, HDL, LDL, Uric acid, Fasting Blood Sugar (FBS) and serum Insulin level were performed after 12 hours of fasting. Data were analyzed by using the SPSS version 16 and parametric statistical tests (t-test & chi-square) were employed to compare the groups.

Results

In this research, 200 obese children aged 5-15 years were studied and they were referred to pediatric clinic. The average age was 9.07 ± 1.88 years and the mean of BMI was 27.9 ± 3.9 . One hundred 22 cases (61%) of them were male and 78 (39%) were female. All subjects underwent ultrasonography for diagnosis of

fatty liver. Of these, 118 (59%) had fatty liver disease that 108 (91.5%) and 10 (8.5%) were grade I and grade II, respectively. None of the patients had grade III of fatty liver. According to Table 1, the average age of children without fatty liver was 6.4 years, the average ages of children with grade I and grade II of fatty liver were 10.7 and 13.5 years old, respectively. There was significant relationship between age and the fatty liver ($P=0.0001$).

Table 1 show that 122 cases (61%) were male and 78 of them (39%) were female. Of 122 male subjects, 43 patients (35.3%) had not fatty liver, 72 of them (59%) had fatty liver grade I and 7 pediatrics (5.7%) had grade II. Of 78 studied female, 39 cases (50%) were without fatty liver, 36 patients (46.2%) were with fatty liver grade I and 3 cases had (3.8%) grade II. Fatty liver disease was more common in boys than in girls ($P=0.03$). As shown in Table 1, the mean of BMI in children without fatty liver was 25.8 and in children with fatty liver grade I and II was 29.3 and 30.1 respectively. ($P=0.0001$).

According to table 2, the mean serum level of AST in children without fatty liver, with fatty liver grade I and grade II was 32.7, 50.2, and 85.5 respectively. ($P=0.001$). The mean serum level of ALT in children without fatty liver, with fatty liver grade I and grade II was 29.3, 107.4, and 135.2 respectively. ($P=0.0001$). But there was no significant relationship between the fatty liver and the serum Alkaline phosphatase ($P=0.23$). The mean serum level of TG in cases without fatty liver, with fatty liver grade I and grade II was 94.9, 125.4 and 148.2 respectively and there was a significant relationship between serum TG and fatty liver ($P=0.0002$). In addition, serum cholesterol level in children without fatty liver, fatty liver grade I and grade II was 145, 164.4 and 178.8 ($P=0.0001$). Serum HDL in cases without fatty liver, with fatty liver grade I and grade II was 48.4, 45 and 40.4 respectively ($P=0.0009$). Serum LDL in three groups was 95.3, 110.2 and 120.4 respectively ($P=0.0001$). The serum uric acid in children without fatty liver was 4.9 and in children with fatty liver grade I and grade II were 5.3 and 6.1 respectively. ($P=0.0023$). Serum FBS in children without fatty liver, with fatty liver grade I and grade II was 97.4, 94.5 and 95.5 respectively ($P=0.48$). But serum insulin level in children without fatty liver was 8.4 and in children with fatty liver Grade I was 14.6 and grade II was 17.2 ($P=0.0001$).

Table 1- Grading of fatty liver in obese children according to of age, sex and BMI

Fatty Liver	N	Mean Age (SD)*	Sex		BMI (SD)*
			Female	Male	
No Fatty Liver	82	6.4 (1.6)	39 (50%)	43 (35.3%)	25.8 (3.4)
Grade I	108	10.7 (2.1)	36 (46.2)	72 (59%)	29.3 (4.2)
Grade II	10	13.5 (1.8)	3 (3.8%)	7 (5.7%)	30.1 (4.3)
	Total: 200	P= 0.001	Total: 78	Total: 122	P= 0.0001

* P≤0.05

Table 2- Mean Table 2- Fatty liver disease in obese children according to biochemical parameters

Test		AST (U/L)	ALT (U/L)	ALP (U/L)	TG (mg/dl)	Cholesterol (mg/dl)	HDL (mg/dl)	LDL (mg/dl)	Uric acid (mg/dl)	FBS (mg/dl)	Insulin (mu/l)
Fatty Liver Mean (SD)	No	32.7 (18.7)	29.3 (16.3)	264.1 (61.2)	94.9 (44.2)	145 (21.8)	48.4 (8.2)	95.3 (20.6)	4.9 (1)	97.4 (12.9)	8.4 (3.1)
	Grade I	50.2 (24.6)	107.4 (24.7)	271.8 (38.3)	125.4 (61.4)	164.4 (27.2)	45 (7.6)	110.2 (26.4)	5.3 (1.2)	94.5 (18.9)	14.6 (5.2)
	Grade II	58.5 (30.8)	135.2 (29.1)	282.9 (42.1)	148.2 (71.5)	178.8 (28.6)	40.4 (7.4)	120.4 (29.8)	6.1 (1.6)	95.5 (14.1)	17.2 (7.9)
P		0.001	0.0001	0.23	0.0002	0.0001	0.0009	0.0001	0.0023	0.48	0.0001

Discussion

In this study, 200 obese children referred to the pediatric clinic were examined and among them 82 (41%) cases were without and 118 (59%) ones were with fatty liver that 108 (54%) had grade I and 10 (5%) grade II.

Adibi et al.'s conducted a cross-sectional study of 952 children with the age of 6 to 18 years in Isfahan according to BMI they were divided into three groups: normal weight, overweight and obese. The prevalence of fatty liver in obese children was 54.4%, which was significantly higher than overweight (10.5%) or normal children (1%)^[2]. Ezzat WM et al.'s in Egypt studied on 155 obese children's aged 4-18 years based on ultrasonography evidence and they found that Fatty liver was detected in 47 (65.3%) children^[5]. In a study in 1997 in Italy by Franzese A et al.'s on 72 obese children (40 boys and 32 girls) aged 4-16 years, 38 (52.8%) had fatty liver based on ultrasonography evidence that 9, 16 and 13 of them were severe, moderate and mild fatty liver, respectively^[6]. The average age of subjects in our study was 9.07 years. The average age in children without fatty liver disease, fatty liver grade I and grade II was 6.4, 10.7 and 13.5 years respectively (P=0.0001). The mean of BMI in present study was 27.9. It was 25.8 in children without fatty liver disease, in fatty liver grade I and grade II was 29.3 and 30.1 respectively (P=0.0001). In a study performed by Tominaga K et al.'s in Japan on 846 students aged 6-15 years showed that the BMI were 18.9 (in cases without fatty liver), 32.3 (in mild to moderate fatty liver) and 26.5 (in serious cases),

respectively (P<0.001)^[7]. Some of these differences may be related to study groups. In this study, obese children (BMI>95%) aged 5-15 years but Tominaga studied aged 6-15 years that had a lower BMI. In a study conducted by Schwimmer JB et al.'s in USA on 347 children, Non-alcoholic fatty liver disease was diagnosed in 55% of children^[8]. In our study, serum AST and ALT levels were higher in patients with fatty liver and were highest in grade II. (P=0.001) but there was no significant difference between Alkaline phosphatase and fatty liver and its grading (P=0.23). In a study conducted by Chan DF et al.'s on Chinese obese children, the prevalence of fatty liver based on ultrasonography was 84 but based on liver enzymes was 24%^[9]. Another study in 1998 in Korea on 1594 obese adolescents aged 10-19 years showed high levels of serum aminotransferases . (3.6% in boys and 2.8% in girls)^[10]. Yoo J et al.'s showed 909 obese children in the age group of 9-12 years based on serum ALT as the criteria for fatty liver. The increase of serum ALT (more than 40 u/L) in males was 33.4% and for girls was 19.6 %.^[11] The present study showed a significant relationship between the fatty liver and serum TG (P=0.002), cholesterol (P=0.001) HDL (P=0.0009) and level of LDL (P=0.0001). Chan DF et al.'s reported high serum TG cholesterol level, low serum HDL level and high serum LDL level in 16 cases (19%), 22 (26%), 47 (56%) and 15 (18%), respectively^[9]. Tominaga K et al.'s studied on 846 middle school students (6 to 15 years) and found that the mean serum TG level in those without fatty liver was 56.2, in subjects who had mild to moderate fatty liver was 80.6

and in cases who had serious fatty liver was 90.5. (P=0.001). Furthermore, they found that the mean serum HDL level in those without fatty liver, with fatty liver grade I and grade II were 36.1, 30.5 and 29.1, respectively. (P=0.001)^[7]. This difference could be due to differences in the groups of study. Because in this study the samples were obese children 5-15 years, but in Tominaga K et al.'s study the subjects were the students aged 6 to 15 years with a various BMI.

The present study showed a significant relationship between fatty liver and serum uric acid level (P=0.0023). In the study was performed by Tang L et al.'s on 1027 obese children aged 6-14 years, 213 cases (20.7%) had hyperuricemia and older boys had higher serum uric acid level^[12]. The serum uric acid levels in 1729 children including 923 boys and 806 girls aged 9-15 years had been studied by Oyama C et al.'s. Increased serum uric acid level (≥ 7 mg/dl) was observed in 8.8% of boys and 0.6% of girls. The mean of serum uric acid level in boys with high POW (Percentage of Over Weight) was 5.9 and in them with low POW was 5.2. This amount in girls with high POW and with low POW was 4.9 and 4.2, respectively^[13]. The results of this research were consistent with those of the above study. In the present study, there was no significant relationship between fatty liver and FBS (P=0.48), but there was a significant relationship between fatty liver and serum insulin level (P=0.001).

In this study, the prevalence of the fatty liver in obese children was 59% and the prevalence of fatty liver was increased with increasing of BMI. Increased serum liver enzyme levels, lipids and uric acid were associated with fatty liver. Given the high prevalence of fatty liver and other associated disorders, ways of implementing lifestyle changes and proper diet are necessary to prevent and treat childhood obesity. Necessary measures should also be performed for the treatment of fatty liver in children.

Acknowledgment

We thank the nursing staffs of pediatric clinic that have worked in this study with us.

Funding: This study was self-funded.

Conflict of interest: There was no conflict of interest.

References

1- Sohrabpour AA, Rezvan H, Amini-Kafiabad S, et al. Prevalence of Nonalcoholic steatohepatitis in

- Iran: A Population based study. Middle East Journal of Digestive Diseases 2010; 2(1): 14-19.
- 2- Adibi A, Kelishadi R, Beihaghi A, et al. Prevalence of Sonographic Fatty Liver in Overweight and Obese Children A Cross Sectional Study in Isfahan. J of Shaheed Sadoughi Uni of Med Sci (JSSU) 2009; 17(4): 270-8.
- 3- Ebbeling CB, Pawlak DB, Ludwig DS. Childhood obesity: public health crisis, common sense cure. Lancet 2002; 360(9331): 473 –82.
- 4- Saadeh S, Younossi ZM, Remer EM, et al. The utility of radiological imaging in nonalcoholic fatty liver disease. Gastroenterology 2002; 123: 745-50.
- 5- Ezzat WM, Ragab S, Ismail NA, et al. Frequency of non-alcoholic fatty liver disease in overweight/obese children and adults: Clinical, sonographic picture and biochemical assessment, Journal of Genetic Engineering and Biotechnology 2012; 10 (2): 221-7
- 6- Franzese A, Vajro P, Argenziano A, et al. Liver involvement in obese children ultrasonography and liver enzyme levels at diagnosis and during follow up in Italian population. Dig Dis sci 1997; 42(7): 1428-32.
- 7- Tominaga K, Fujimoto E, Suzuki K, et al. Prevalence of non-alcoholic fatty liver disease in children and relationship to metabolic syndrome, insulin resistance and waist circumference. Environ Health Prev Med 2009; 14(2): 142-9.
- 8- Schwimmer JB, Newton KP, Awai HI, et al. Pediatric gastroenterology evaluation of overweight and obese children referred from primary care for suspected non-alcoholic fatty liver disease. Aliment Pharmacol Ther 2013; 38 (10): 1267-77.
- 9- Chan DF, Li AM, Chu WC, et al. Hepatic steatosis in obese Chinese children. Int J Obes Relat Metab Disord 2004; 28(10): 1257-63.
- 10- Park HS, Han JH, Choi KM, Kim SM. Relation between elevated serum alanine aminotransferase and metabolic syndrome in Korean adolescents. Am J Clin Nutr 2005; 82 (5): 1046-51.
- 11- Yoo J, Lee S, Kim K, et al. Relationship between insulin resistance and serum alanine aminotransferase as a surrogate of NAFLD (nonalcoholic fatty liver disease) in obese Korean children. Diabetes Res Clin Pract 2008; 81(3): 321–6.
- 12- Tang L, Kubota M, Nagai A, et al. Hyperuricemia in obese children and adolescents: the relationship with metabolic syndrome. Pediatr Rep 2010; 2(1): e12: 38-41.

13-Oyama C, Takahashi T, Oyamada M, et al. Serum Uric Acid as an Obesity-Related Indicator in Early

Adolescence. *Tohoku J Exp Med* 2006; 209 (3): 257-62.