



# Sonographic fatty liver in overweight and obese children, a cross sectional study in Isfahan

Ultrasonograficznie rozpoznane stłuszczenie wątroby u dzieci z nadwagą oraz otyłych — badanie przekrojowe przeprowadzone w Isfahanie

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## Abstract

**Introduction:** Children's obesity is a known health problem in the world and is a strong predictor of obesity in adulthood which increases the incidence of related diseases such as metabolic syndrome. According to the MONIKA project by the World Health Organization (WHO), Iran is one of the seven countries with a high rate of child obesity. Fatty liver is an abnormality related to metabolic syndrome, with higher prevalence in obese children according to some previous studies. This study investigates the presence of Sonographic Fatty Liver (SFL) in Iranian obese children in comparison with normal and overweight children.

**Material and methods:** This was a cross-sectional study on 962 randomly selected children between the ages of 6 to 18 years. The subjects were divided into three groups of normal, overweight and obese based on body mass index (BMI). A questionnaire including demographic and anthropometric characteristics was filled for each one. To detect the presence of SFL all the subjects underwent assessments with ultrasonography by radiologist who was not aware of their BMI. The incidence of SFL was determined based on the ultrasonographic diagnosis criteria.

**Results:** The average age of the children in the study was  $12.59 \pm 3.25$  years. The mean of the liver span in the normal, overweight and obese groups were  $111.36 \pm 18.73$ ,  $121.18 \pm 16.63$  and  $118.21 \pm 19.15$  respectively. The prevalence of SFL in obese children was 54.4%, which was significantly higher than overweight (10.5%) and normal ones (1%). According to present results, there was no significant difference in prevalence of SFL between sexes.

**Conclusions:** The high rate of detected SFL in obese children in this study suggests that Iranian obese children are at risk of metabolic syndrome. Moreover, the WHO indicated Iran as one of the countries with high rate of obese children. Based on this information, we can conclude that the prevalence of metabolic syndrome and its related non-communicable diseases will be increasing future in . Therefore, it is necessary to develop some plan to control overweight problem including teaching healthy lifestyle in schools and kindergartens as well as mass media. (*Pol J Endocrinol* 2009; 60 (1): 14–19)

**Key words:** sonography, child, obesity, fatty liver, overweight

## Streszczenie

**Wstęp:** Otyłość u dzieci jest znanym na świecie problemem zdrowotnym oraz silnym czynnikiem prognostycznym wystąpienia otyłości w wieku dorosłym, która zwiększa częstość chorób jej towarzyszących, takich jak zespół metaboliczny. Według projektu Światowej Organizacji Zdrowia (WHO, *World Health Organization*) MONIKA Iran jest jednym z siedmiu krajów o dużym odsetku dzieci otyłych. Stłuszczenie wątroby jest zaburzeniem towarzyszącym zespołowi metabolicznemu, zgodnie z wynikami niektórych wcześniejszych badań, często występującym u otyłych dzieci. W niniejszej pracy badano obecność ultrasonograficznie rozpoznanego stłuszczenia wątroby (SFL) w populacji otyłych dzieci irańskich w porównaniu z grupą dzieci z nadwagą i prawidłową masą ciała.

**Materiał i metody:** Niniejsze badanie przekrojowe przeprowadzono w grupie 962 losowo wybranych dzieci w wieku 6–18 lat. Badani zostali podzieleni według wskaźnika masy ciała (BMI) na trzy grupy: o prawidłowej masie ciała, z nadwagą i na grupę dzieci otyłych. W przypadku każdego uczestnika wypełniano kwestionariusz zawierający charakterystykę demograficzną i antropometryczną. U wszystkich uczestników dla wykrycia SFL wykonywano badanie ultrasonograficzne przeprowadzane przez radiologa, który nie znał BMI badanych. Częstość SFL ustalano na podstawie ultrasonograficznych kryteriów diagnostycznych.

**Wyniki:** Średni wiek dzieci uczestniczących w badaniu wynosił  $12,59 \pm 3,25$  roku. Średnie wymiary pionowe wątroby wynosiły:  $111,36 \pm 18,73$ ,  $121,18 \pm 16,63$  i  $118,21 \pm 19,15$  mm odpowiednio w grupach dzieci z prawidłową masą ciała, z nadwagą i otyłych. Częstość występowania SFL u dzieci otyłych wyniosła 54,4%, co było wartością istotnie wyższą w porównaniu z grupą dzieci z nadwagą (10,5%) i prawidłową masą ciała (1%). Według wyników tego badania nie było znamiennych różnic w częstości występowania SFL między płciami.

**Wnioski:** Duży odsetek SFL wykrywanego u dzieci otyłych w tym badaniu sugeruje, że irańskie otyłe dzieci obciążone są ryzykiem wystąpienia zespołu metabolicznego. Co więcej, WHO określa Iran jako jeden z krajów o dużym odsetku dzieci otyłych. Opierając się na



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tych informacjach, można wysunąć wniosek, że częstość występowania zespołu metabolicznego i związanych z nim chorób niezakaźnych będzie się zwiększać w przyszłości. Dlatego konieczne jest opracowanie określonego planu dla kontroli problemu nadwagi, uwzględniającego nauczanie zdrowego stylu życia w szkołach, przedszkolach i środkach masowego przekazu. (*Endokrynol Pol* 2009; 60 (1): 14–19)

**Słowa kluczowe:** ultrasonografia, dziecko, otyłość, stłuszczenie wątroby, nadwaga

## Introduction

Metabolic syndrome, first defined in 1988, is characterized by insulin resistance, hypertension, dyslipidaemia, type 2 diabetes and other metabolic disorders related to cardiovascular disease in adults [1]. According to the criteria of the Third National Health and Nutrition Examination Survey (NHANES III), about 25% of American adults and 21.9% of Iranian adults have metabolic syndrome [2, 3]. Children may also have metabolic syndrome and studies have shown that overweight children are at a higher risk of metabolic syndrome [4–6]. A strong predictor of metabolic syndrome is fatty liver disease, which is the build-up of fat in the liver cells so that more than 5% of the liver weight becomes fat [7]. Most patients with fatty liver have other disorders related to the metabolic syndrome, including obesity, diabetes mellitus, and some forms of hyperlipidaemia and hypertension [8]. Given the global increase in the prevalence of overweight and obesity in children, some studies highlight the possibility of other changes similar to fatty liver in these children [9].

Fatty liver is one of the chronic disorders associated with lipid accumulation in hepatic steatosis. This disease describes a range of conditions involving the liver. The mildest type is simple fatty liver (steatosis), but a potentially serious type is non-alcoholic steatohepatitis (NASH), which is associated with liver-damaging inflammation and, sometimes, the formation of fibrosis. A more serious type is progressive fibrosis and cirrhosis. Simple fatty liver is often a silent disease and only shows itself occasionally in increasing liver enzymes. The only visible signs of the disease occur in cirrhosis or hepatic failure complications [10].

Today childhood obesity is a global problem [11]. It is a strong predictor of obesity in adulthood and increases the risk factors for cardiovascular diseases such as hypertension, diabetes and dyslipidaemia [12]). About 80% of obese adolescents will grow to obese adults, and overweight adolescents are at greater risk of serious diseases. The prevalence of overweight and obesity is increasing worldwide at an alarming rate in both developing and developed countries [13–14]. Body mass index (BMI) with its divisions based on percentiles is normally used to measure obesity in children [15, 16].

According to the MONICA project (monitoring of cardiovascular diseases) carried out in 1998 by the World

Health Organization (WHO), Iran is one of seven countries with a high prevalence of obesity among children [17]. Since the 1990s there has been a rapid increase in BMI and overweight and obesity have become prevalent in Iran owing to rapid changes in eating habits on the one hand and lack of physical exercise on the other [18, 19]. As a result, between 1993 and 1999 overweight and obesity among Iranian children doubled [20]. This study aimed to investigate the prevalence of sonographic fatty liver among overweight adolescent Iranians in comparison with those of normal weight.

## Material and methods

This was a cross-sectional study carried out in 2006–2007 in Khorshid Hospital, Isfahan. The subjects were chosen from healthy children aged from 6 to 18 years from Isfahan schools, who had been randomly selected for the Isfahan Healthy Heart Program (IHHP), a national project in the Isfahan Cardiovascular Research Centre. The children were divided into three groups on the basis of their BMI: 408 subjects (42.9%) in the normal group (BMI equal to or lower than the 86<sup>th</sup> percentile), 314 (33%) in the overweight group (BMI between the 85<sup>th</sup> and the 94<sup>th</sup> percentile) and 230 (24.2%) in the obese group (BMI equal to or higher than the 95<sup>th</sup> percentile). The groups were matched according to gender and socioeconomic status.

The selected students entered the study of their own will and with their parents' permission. If a student was unwilling to participate, he/she was replaced by another student fulfilling the same criteria. All the children were examined by a specialist. Data concerning age, gender, educational level and history of previous diabetes, liver disease and endocrine disorders were collected by means of a questionnaire. Those treated with chronic medication, those with a history of diabetes or metabolic diseases and those suffering from mental disabilities, chronic medical diseases, genetic syndromes or symptoms, symptoms of liver disorders or endocrine diseases were excluded from the study.

The body weight and height of the subjects were calculated by a Seca scale, and the BMI was calculated by dividing the weight in kilograms by the square of the height in metres. Then, on the basis of the BMI percentile for the age of the subjects, they were divided

**Table I. Fatty liver-related indicators in three groups of adolescents: normal, overweight and obese (mean  $\pm$  SD)****Tabela I. Wskaźniki związane ze stłuszczeniem wątroby w trzech grupach dzieci: z prawidłową masą ciała, z nadwagą i otyłych (średnia  $\pm$  SD)**

	Normal (408)	Over weight (314)	Obese (230)	P value
Age (year)	12.18 $\pm$ 3.44	13.23 $\pm$ 3.09	12.45 $\pm$ 2.98	< 0.001
Fatty liver (%)	4 (1)	33 (10.5)	124 (54.4)	< 0.001
Liver span [mm]	111.36 $\pm$ 18.73	121.18 $\pm$ 16.63	118.21 $\pm$ 19.15	< 0.001
Splenic span [mm]	91.13 $\pm$ 15.33	97.04 $\pm$ 12.82	99.10 $\pm$ 13.95	< 0.001
CBD diameter [mm]	2.89 $\pm$ 1.05	2.68 $\pm$ 1.18	2.56 $\pm$ 1.1	0.011
Portal vein diameter [mm]	6.14 $\pm$ 2.95	6.06 $\pm$ 3.52	6.05 $\pm$ 3.37	0.911

P values are reported between the first and third columns

into three groups: normal, overweight and obese [21]. All the subjects underwent ultrasound examination by two radiologists synchronously who knew the purpose of the study but did not know the subjects' BMI or the related grouping. An ultrasound multi-frequency curvilinear 3.5–5 MHz probe by Siemens Company (Sonoline G50 series, model number 7474922) was used for the liver ultrasound to check for sonographic fatty liver (SFL) and other sonographic criteria.

To perform the ultrasound examination the liver's superior and inferior contours were found by calculating the span along the midclavicular line, the distance being measured by a standard ruler. The liver parenchyma was then viewed from subcostal windows in the RUQ and alongside the axial lines in the coronal area. The presence of SFL was defined as increased echogenicity of the liver parenchyma to the extent that it was reported by ultrasound and disturbed the visibility of the portal vein and liver artery [23]. Then, in deep inspiration, the diameter of the portal vein and common bile duct (CBD) were measured [23]. The data collected were recorded using Epi Info™ software, and the Statistical Package for the Social Sciences (SPSS) version 15 (SPSS Inc., Chicago, IL, USA) was used to analyze data. The  $\chi^2$  test was used to compare SFL in the three groups of normal, overweight and obese children. Analysis of variance (ANOVA) was used to compare the ages of the three groups. Including age as a covariate, analysis of covariance (ANCOVA) was used to compare the groups for liver span, splenic size and portal vein and common bile duct diameters. Results with P values less than 0.05 were considered statically significant.

## Results

The study was conducted on 952 students of 6 to 18 years old, their mean age being 12.59  $\pm$  3.25 years. The subjects were divided into three groups on the basis of their BMI: 408 subjects (42.9%) in the normal group, 314

(33%) in overweight group and 230 (24.2%) in the obese group. The mean value for BMI in the normal group was 16.84  $\pm$  3.04, in the overweight group 22.94  $\pm$  3.35 and in the obese group 27.04  $\pm$  3.93. The mean age in the three groups was 12.18  $\pm$  3.44, 13.23  $\pm$  3.09 and 12.45  $\pm$  2.98 respectively (P < 0.001). The average age for the overweight group was higher than for the normal group (mean difference = 1.04; P < 0.001) and the obese group (mean difference = 0.77; P = 0.016), but the age variable did not show any significant difference between the normal and obese groups. Of the 952 subjects 537 were girls (56.4%) and 415 were boys (43.6%), and there was no significant gender difference between the groups (P = 0.344). The ultrasound showed that 161 of all the subjects (16.9%) had SFL and the gender variable showed no significant difference (P = 0.65).

Table I shows the frequency distribution of SFL and the ultrasound indices of the three groups. The frequency of SFL increased from the normal group to the overweight and obese groups. The normal group had significantly smaller livers than the other two groups, and the largest livers were found in the overweight group, although the difference between the overweight and obese groups was not significant (P = 0.138). The situation was exactly the same for the splenic span. The difference in the CBD diameter was significant only between the normal and obese groups (P = 0.011). However, there was no significant difference between the groups in portal vein diameter (P = 0.911).

Table II presents a comparison of the age and sonographic indices for fatty liver in the three groups on the basis of gender. There was no significant difference between girls and boys regarding age and fatty liver. However, in each group both genders followed the same pattern as that found in the whole sample. The boys had significantly larger livers, spleen spans and CBD diameters than girls, but their portal veins were smaller in size. The difference between the liver size of boys in the obese and overweight groups was not significant

**Table II. Fatty liver-related indicators according to sex in three groups of adolescents: normal, overweight and obese (mean  $\pm$  SD)**  
**Tabela II. Wskaźniki związane ze stłuszczeniem wątroby według płci w trzech grupach dzieci: z prawidłową masą ciała, z nadwagą i otyłych (średnia  $\pm$  SD)**

	Female			P value	Total (535)	Male			P value	Total (415)
	BMI					BMI				
	Obese (121)	Overweight (177)	Normal (237)			Obese (109)	Over-weight (137)	Normal (169)		
Age (year)	12.36 $\pm$ 3.07	13.33 $\pm$ 3.14	12.35 $\pm$ 3.49	0.005	12.67 $\pm$ 3.31	12.56 $\pm$ 2.90	13.09 $\pm$ 3.03	11.94 $\pm$ 3.36	0.007	12.48 $\pm$ 3.17
Fatty liver (%)	60 (50.4)	18 (10.2)	2 (0.8)	< 0.001	80 (15)	64 (58.7)	15 (10.9)	2 (1.2)	< 0.001	81 (19.5)
Liver span [mm] <sup>§</sup>	112.32 $\pm$ 19.18	119.12 $\pm$ 15.5	110.67 $\pm$ 18.60	0.001	113.84 $\pm$ 18.12	124.82 $\pm$ 16.91	123.94 $\pm$ 17.66	112.34 $\pm$ 18.94	< 0.001	119.39 $\pm$ 18.91
Splenic span [mm] <sup>§</sup>	96.21 $\pm$ 14.20	95.05 $\pm$ 11.82	89.74 $\pm$ 15.08	< 0.001	92.96 $\pm$ 14.15	102.31 $\pm$ 12.99	99.62 $\pm$ 13.64	93.07 $\pm$ 15.50	< 0.001	97.65 $\pm$ 14.77
CBD diameter [mm] <sup>*</sup>	2.28 $\pm$ 0.93	2.53 $\pm$ 1.24	2.83 $\pm$ 1.16	< 0.001	2.61 $\pm$ 1.16	2.84 $\pm$ 1.21	2.97 $\pm$ 1.32	2.82 $\pm$ 1.01	0.523	2.87 $\pm$ 1.17
Portal vein diameter <sup>*</sup>	6.20 $\pm$ 3.14	6.50 $\pm$ 3.21	6.47 $\pm$ 2.74	0.545	6.42 $\pm$ 2.99	5.75 $\pm$ 3.61	5.29 $\pm$ 3.57	6.01 $\pm$ 3.02	0.672	5.70 $\pm$ 3.37

Between sex P-value: \* < 0.01 <sup>§</sup> < 0.001

**Table III. Sonographic indicators in normal and fatty liver groups according to sex (mean  $\pm$  SD)**

**Tabela III. Wskaźniki ultrasonograficzne w grupach ze stłuszczeniem wątroby i bez stłuszczenia według płci (średnia  $\pm$  SD)**

	Fatty liver (n = 161)			P value	Normal (n = 788)		
	Girl (n = 80)	Boy (n = 81)	P value		Girl (n = 454)	Boy (n = 334)	P value
Age (year)	12.85 $\pm$ 3.08	13.06 $\pm$ 2.90	0.654	12.65 $\pm$ 3.35	12.34 $\pm$ 3.22	0.195	
Liver span [mm] <sup>§</sup>	116.16 $\pm$ 20.21	125.66 $\pm$ 17.31	0.002	113.43 $\pm$ 17.77	117.89 $\pm$ 19.00	0.001	
Splenic span [mm] <sup>§</sup>	95.39 $\pm$ 12.86	102.42 $\pm$ 11.80	< 0.001	92.52 $\pm$ 14.26	96.50 $\pm$ 15.20	< 0.001	
CBD diameter [mm] <sup>*</sup>	2.34 $\pm$ 1.21	2.61 $\pm$ 1.05	0.350	2.64 $\pm$ 1.15	2.94 $\pm$ 1.19	< 0.001	
Portal vein diameter <sup>*</sup>	6.45 $\pm$ 3.26	5.33 $\pm$ 3.70	0.044	6.42 $\pm$ 2.95	5.80 $\pm$ 3.29	0.004	

Between sex P-value: \* < 0.01 <sup>§</sup> < 0.001

(0.924), but in both the liver was significantly larger than in the normal group ( $P < 0.001$ ). The largest liver size in girls was found in the overweight group ( $P < 0.001$  in comparison with the normal group and  $P = 0.004$  compared with the obese group), but there was no difference in liver size between the obese and normal groups ( $P = 0.687$ ). The size of the spleen was significantly smaller for both genders in the normal group compared to the two other groups ( $P < 0.001$ ), but there was no significant difference between the obese and overweight groups ( $P = 0.329$  for boys and  $P = 0.757$  for girls). There was no difference in CBD diameter between the boys in the three groups, but this index was significantly higher in normal than in overweight ( $P = 0.023$ ) and obese girls ( $P < 0.001$ ). There was no significant

difference in portal vein diameter between the three groups.

Table III sets out the differences in age and measured sonographic indices for girls and boys separately. The age variable showed no significant difference between girls and boys in the healthy and fatty liver groups. Liver span, splenic span and portal vein diameter were significantly higher in SFL cases than in normal subjects of either sex, but CBD diameter showed no gender-related difference between the two groups.

## Discussion

The results of the study clearly show that the prevalence of fatty liver in obese children is higher than in those

of normal weight. In addition, the results show that the incidence of fatty liver is not related to gender in this age group.

Fatty liver disease was recognized in the 1970s as the prevalence of obesity increased among adults, but it took several decades to determine its prevalence among children. In 1983 for the first time Moran et al. reported three 10-year-old obese children with severe hepatitis and liver fibrosis [24].

In an epidemiological study in 2002, Schwimmer et al. [25] determined the prevalence of paediatric fatty liver as diagnosed by histology in a population-based sample of children who had an autopsy performed by a county medical examiner. The prevalence on autopsy of fatty liver in children aged 2 to 19 was 9.6%. On the assumption that the rate was the same in other states, they concluded that probably 6.5 million children and adolescents in the United States were at risk of fatty liver [25].

In one study on 84 obese Chinese children ultrasound showed that fatty liver was present in 77% of the subjects. The subjects underwent further examinations to determine liver transferases. The results of the examinations showed the presence of fatty liver in a total of 24% of the subjects [26]. The differences between the reported prevalence of fatty liver and liver disorders in overweight and obese children are the result of using different diagnosing methods [27]. In an Italian multi-centre study on liver damage in paediatric obesity, obese children were screened for abnormal serum aminotransferases, which indicated a prevalence of 10–25% [28]. In another study in Italy sonographic liver steatosis was present in 42% of the subjects [29]. A review of the studies shows that the variation in the prevalence of fatty liver in obese children is related to the diagnosing methodology. The number ranges from 9.6%, on the basis of autopsy in the United States, to 77%, on the basis of sonographic indices in China.

The present study is one of the first to evaluate the prevalence of fatty liver in obese children in Iran. In this study only sonographic methods were used to diagnose the fatty liver. As shown by the results, the prevalence is 57%, which is lower than the result of the study in China (77%), also obtained by sonography. It should be mentioned that the mean BMI in that study was larger than in ours (30.3 vs. 27), which may explain the difference. Moreover, our sample size was larger, but the mean age was the same in both studies.

Another considerable variable in the study is gender. In 2005 in a study by Schwimmer et al. on 127 students participating in the CATCH project the presence of fatty liver in boys was significantly higher than in girls [30]. In the present study, however, there was no significant difference related to gender in the prevalence

of fatty liver. This difference may be related to the mean age, which was lower in our study. As the sexual hormones are not present at lower ages this may have led to the difference in the results.

The results of this study show that an increase in BMI significantly increases the prevalence of fatty liver in both boys and girls, and in both genders the prevalence of fatty liver was significantly higher in the obese group than in the overweight and normal groups.

As shown in Table 3, where the gender variable is taken into account, all three groups, namely those of normal, overweight and obese children, are compared in relation to fatty liver indices. The increase in fatty liver prevalence in both genders, along with the increase in BMI, has a direct relationship with the increase in fatty liver indices, including liver and spleen sizes in both genders and CBD in girls.

The important point is the significant difference between the three groups in terms of the age variable, which can predict an increase in the prevalence of obesity as the children grow up. As they mature, not only do their hormones change but their lifestyle also changes and may involve leisure activities that tend away from active behaviour, such as participation in sport, to a sedentary life style centred on TV and computer games. A factor worth consideration, therefore, is lifestyle education for adolescents and encouragement in active leisure activities.

The study results showed the presence of fatty liver in 17% of the children, which can be a predictor for a high rate of type 2 diabetes and metabolic syndrome in adulthood. According to the result, the overall prevalence of fatty liver in the overweight and obese groups was 28.8%. Assuming that this result can be generalized to the whole country, and in view of the fact there are 20 million children and adolescents between the ages of 2 and 18 years, of whom 21% are overweight or obese, about 1.2 million Iranian children and adolescents may have fatty liver [31, 32]. In other words, about 1.2 million Iranian children are at risk of metabolic syndrome and type 2 diabetes and the relation between these complications and cardiovascular diseases suggests that the prevalence of the latter will increase in future.

These results and that of the WHO project, which defined Iranian society as one of seven countries with a high rate of childhood obesity, suggest that it is essential to make intervention programmes to prevent obesity a priority in Iran. Since a high BMI is associated with fatty liver disease, which can progress to fibrosis/cirrhosis [24], weight loss and obesity control should be health priorities. BMI can be a useful and non-invasive index for screening fatty liver disorders and providing community-based interventions for control and

protection. Kindergartens and schools are convenient places to establish contact with children and adolescents, where preventive intervention for lifestyle changes, including eating habits and physical exercise, can be planned and implemented. These interventions can be included in health programmes or the physical education hours of their current curriculum without any burden of expense on the public. Moreover, the mass media, particularly television, have a considerable influence on children and adolescents, and most of their lifestyle features and habits are promoted by the media. The production of television programmes aimed at encouraging children and adolescents to correct their lifestyle and maintain a normal weight therefore forms therefore a valuable contribution. The potential expense involved in weight loss and the treatment of complications of obesity, such as metabolic syndrome, type 2 diabetes and cardiovascular disease, can be brought to the attention of children and adolescents and their parents as an encouragement to weight control. Emphasis should be placed on frequent measurement of waist circumference and body weight as obesity indices, together with monitoring of blood pressure and blood fat. These measurements will help them to be aware of the risk and to start treatment in time. It is expected that education of this kind in schools and kindergartens and through the mass media will lead to lifestyle improvement and prevent disorders such as fatty liver and non-communicable diseases.

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