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Comparison of fatty liver disease development in overweight, obese and normal weight children

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Abstract

Introduction: Prevalence of obesity can predispose children to development of fatty liver disease which, given the asymptomatic nature of this disease, may turn into cirrhosis at the end of adolescence if it is not treated.

Objectives: This study aimed to compare overweight and obese children with normal weight ones in terms of prevalence of fatty liver disease.

Patients and Methods: This cross-sectional study was conducted from 2019 to 2020. A total of 952 children in the 6-18 years age group admitted to the Children medical and training center (Tabriz University of Medical Sciences) were enrolled using multistage cluster random sampling. The participants included 408 normal weight, 314 overweight, and 230 obese children. Chi-square and ANOVA tests were performed to compare the demographic information, anthropometric indices, and liver ultrasound results of the members in the three groups. *P* value less than 0.05 was considered significant.

Results: The prevalence rate of fatty liver disease in all participants was 16.91%, whereas that in the overweight and obese children was 29.59%. The results suggested that the prevalence of fatty liver was increasing in normal weight, overweight, and obese children.

Conclusion: Overweight and obesity in children led to the development of fatty liver. Preventive measures must be taken because one third of the studied obese and overweight children developed fatty liver disease.

Keywords: Overweight, Obesity, Child, Fatty liver

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Introduction

Metabolic syndrome was first defined in 1988 with symptoms such as insulin resistance, hypertension, dyslipidemia, type 2 diabetes and other metabolic disorders associated with cardiovascular diseases (CVDs) in adults (1). According to the Third National Health and Nutrition Examination Survey (NHANES III), about 25% of American adults and 22% of Iranian adults suffer from metabolic syndrome (2).

Not only adults but children can suffer from metabolic syndrome. According to studies, overweight children are at a higher risk of developing this syndrome. Metabolic syndrome is a predictor of fatty liver, which often occurs when fat accumulation in the liver exceeds 5% of liver weight (3). Most fatty liver patients suffer from other metabolic syndrome-related disorders such as obesity, diabetes mellitus, and some forms of hyperlipidemia and hypertension (4). Given the increasing prevalence of overweight and obesity in children, some studies suggest that changes similar to those caused by fatty liver may occur in these children (5).

Fatty liver is a chronic liver disorder associated with accumulation of lipids in hepatocytes. The various forms of this disorder range from simple fatty liver (a form of steatosis), to non-alcoholic steatohepatitis (NASH, a form of fatty liver in which lipid changes are accompanied by liver tissue inflammation, damage, and fibrosis), and eventually by advanced fibrosis and cirrhosis (6, 7). Simple fatty liver is a benign disorder that can progress to fibrosis and end-stage liver disease. This silent disease sometimes manifests itself as elevated liver enzymes. Symptoms only emerge when its complications occur as cirrhosis and liver failure (8, 9). The disorder is usually associated with obesity, insulin resistance, and many other components of metabolic syndrome (10).

Nowadays, childhood obesity is considered a global problem. It increases the risk of obesity in adulthood and leads to the development of CVD risk factors such as hypertension, diabetes, and dyslipidemia. According to studies, 80% of obese adolescents become obese adults. Obesity has many effects on an adolescent's health status. Childhood and adolescent obesity rates are not only high in developed countries, but are increasing in developing countries. In children, obesity is often determined by their body mass index (BMI)-for-age percentile (11, 12).

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Implication for health policy/practice/research/ medical education

A total of 952 children in the 6-18 years' age group admitted to the Children medical and training center (Tabriz University of Medical Sciences) were enrolled using multistage cluster random sampling. The participants included 408 normal weight, 314 overweight, and 230 obese children. Results show Overweight and obesity in children led to the development of fatty liver. Preventive measures must be taken because one third of the studied obese and overweight children developed fatty liver disease.

Monitoring of Trends and Determinants in Cardiovascular Disease (MONICA) Project (1998) listed Iran among the 7 countries with high prevalence of childhood obesity. Since the 1990s, the diet of Iranians has changed rapidly, and their physical activity has decreased (13). These issues have led to a rapid increase in BMI values and a high prevalence of overweight and obesity in children. In addition, the prevalence of overweight and obesity among Iranian children and adolescents doubled between 2019 and 2020.

Objectives

Accordingly, considering the growing prevalence of obesity in Iranian children and adolescents, this study aimed to compare overweight and obese children with normal weight children in terms of prevalence of fatty liver disease.

Patients and Methods

Study design

This cross-sectional study was carried out from 2019 to 2020. A total of 952 children in the 6–18 years age group admitted to the Children Medical and Training Center (Tabriz University of Medical Sciences) were enrolled using multistage cluster random sampling. The participants were assigned to the three groups of normal weight (≤85th BMI percentile; n = 408), overweight (85th -94th BMI percentile; n = 314), and obese (>94th BMI percentile; n = 230) children. Almost the same number of male and female students was assigned to each group. In all three groups, the participants were matched in terms of gender and socioeconomic status.

Informed consent was obtained from the selected students and their parents. Students who were unwilling to participate in the study were replaced by individuals with similar demographic characteristics. The participants were all examined by a pediatric endocrinologist. An initial questionnaire (which included information on age, gender, and grade of the students and the results of clinical examinations for measuring their height, weight, waist circumference, and blood pressure, and of examinations related to diabetes, liver disease, and endocrine diseases) was completed for all the participants. The students who took medications regularly, those with intellectual disability, chronic diseases, and genetic or abnormal symptoms or syndromes, and those who displayed symptoms of liver disorders, endocrine diseases, diabetes and metabolic disorders, were excluded from the research.

BMI is calculated by dividing an individual's weight (kg) by the square of his/her height (m). BMI values were measured using a Seca scale, and the participants were assigned to three groups based on age-specific percentiles. Ultrasounds were performed for all the participants by two radiology residents (who were not members of the research team). These individuals were aware of the type of study and research objectives, but they had no information about the classification of students and their BMI values. The method developed by Goodman et al was followed to perform liver ultrasounds in order to determine the criteria for ultrasound grading and presence of fatty liver in the participants. For this purpose, a SIEMENS SONOLINE G50 ultrasound system with 3.5-5 MHz probe was used. To calculate the liver span along the midclavicular line, the superior and inferior borders of the liver were first outlined and this distance was measured with a standard fixed ruler. Liver parenchyma was then evaluated by two subcostal and right upper quadrant windows in a coronal section along the axillary lines. Increased echogenicity of liver parenchyma to maximum echo time of lipids and level of visibility of portal veins and hepatic veins were considered two criteria for diagnosing individuals with fatty liver. Finally, the portal vein diameter was measured in deep inspiration.

Statistical analysis

The data were analyzed in SPSS version 23. The chi-square test was used to compare the prevalence of fatty liver among the participants in the three groups. The analysis of variance (ANOVA) test was performed to compare the three groups in terms of liver span, spleen size, portal vein diameter, and common bile duct (CBD) diameter. In addition, age was considered the covariance. P values < 0.05 were considered statistically significant.

Results

The participants included 537 female and 415 male children and adolescents (n = 952) in the 6–18 years' age group with a mean age of 12.19 ± 3.41 years. The mean age of normal weight, overweight, and obese children were 12.41 ± 3.29, 12.06 ± 3.52, and 12.25 ± 3.14 years, respectively (P = 0.637). The mean BMI values of normal weight, overweight, and obese children were 16.52 ± 4.29 kg/m^2, 23.85 ± 3.16 kg/m^2, and 30.24 ± 5.09 kg/m^2, respectively (P = 0.011).

The ultrasound results showed that 161 children (16.9%) had fatty liver. In this regard, no significant difference was found between female and male students (P = 0.259). The incidence of fatty liver was found to be increasing in normal weight, overweight, and obese participants, respectively. The mean liver size in normal weight participants was significantly smaller than those

in the students of both overweight and obese groups. However, the mean liver size of overweight participants was insignificantly larger than that in the obese group (P = 0.145). Similar results were obtained for the three groups in spleen size. There was a significant difference between normal weight and obese participants in CBD diameter (P = 0.011). No significant difference was observed between the three groups in mean portal vein diameter (Table 1).

There was no significant difference between the female and male participants in age and development of fatty liver; however, the pattern of differences (between the healthy, overweight, and obese groups) established for the entire sample was almost the same as that developed for female and male groups. The mean liver, spleen, and CBD sizes in male students were significantly larger than those in female students; however, the mean portal vein size of the boys was smaller than that of the girls. An insignificant difference was found between the mean liver size of the boys in obese and overweight groups (P = 0.924). However, the mean liver size in the boys of both the obese and the overweight groups was significantly larger than that in the healthy group (P = 0.001). In the girls, the largest liver size was observed in the overweight group (P = 0.001) compared to the normal (P = 0.004) and obese groups; however, there was no significant difference between the girls in the obese and healthy groups with respect to the mean liver size (P = 0.687). The mean spleen sizes of both female and male students in the obese and overweight groups were significantly larger than that in the healthy group (P = 0.001); however, there was no significant difference between the mean spleen size of those in the obese and overweight groups (boys: P = 0.336; girls: P = 0.749). While no significant difference was found between the male students in the three groups in terms of the mean CBD diameter, this indicator was significantly larger in healthy female students than that in the overweight (P = 0.023) and obese (P = 0.001) groups. In addition, there was no significant difference between the mean portal vein size of female and male students in the three groups.

Table 2 shows the differences between the genders in age and liver ultrasound indicators separately for the groups with fatty liver and the healthy groups. There was no significant difference between the mean age of girls and boys in the healthy groups and the groups with fatty liver. The pattern of gender differences observed in the healthy students was similar to that in the fatty liver group except for the CBD size as there was no significant difference between the mean CBD sizes of male and female students with fatty liver.

Discussion

The prevalence of fatty liver was much higher in obese children and adolescents than in normal weight participants. In addition, gender differences did not affect the development of fatty liver disease in the participants. The association between obesity and fatty liver disease in adults has been demonstrated since the 1970s; however, the prevalence of the disease in children was assessed several decades later. About 13 years ago, Moran-Lev et al published the first report on severe hepatitis and fibrosis in three 10-year-old obese children (14).

In an epidemiologic study, Schwimmer et al performed autopsies on American children and adolescents in the 2–19 years age group and examined their histological changes to assess the prevalence of fatty liver in this target group. The autopsy results showed that the prevalence of fatty liver in the study sample was 9.6% (15). In a study on 84 obese Chinese children, Chan et al used an ultrasound technique to assess the prevalence of fatty liver. They observed evidence of fatty liver in 77% of the participants. In addition, the overall results of alanine aminotransferases (ALT) blood tests and ultrasounds confirmed the development of fatty liver in 24% of the studied individuals(16). The different prevalence rates reported in various studies on frequency of liver involvement and incidence of liver failure in overweight and obese children have resulted from using different diagnostic methods.

In a multicenter research carried out in Italy, serum ALT levels were higher than normal in 10-25% of the obese children (17). In another study conducted in Italy, steatosis was observed in 42% of the participants, and ultrasound results showed that there was a relationship between steatosis and BMI (18). Due to the use of different research approaches and diagnostic methods, there are substantial differences between the values mentioned in different studies for the prevalence of fatty liver in obese children. Prevalence rates of 9.6% and 77% were reported in studies conducted in the United States (autopsy method) and China (ultrasound method), respectively.

This study only used ultrasound techniques to diagnose

Table 1. Fatty Liver-Related Indicators for Normal Weight, Overweight, and Obese Participants

Variable	Participant groups			*P* Value
	Normal weight (n = 408)	Overweight (n = 314)	Obese (n = 230)	
Fatty liver (%)	4 (1%)	33 (10.5%)	124 (54.4%)	0.001
Liver span (mm)	111.41 ± 3.59	120.59 ± 3.41	122.85 ± 3.14	0.145
Spleen size (mm)	91.45 ± 5.25	97.69 ± 5.19	100.74 ± 5.96	0.114
CBD diameter (mm)	2.79 ± 1.14	2.55 ± 1.19	2.23 ± 1.09	0.011
Portal vein diameter (mm)	6.15 ± 1.41	6.06 ± 1.34	6.03 ± 1.19	0.129

CBD, common bile duct.

Table 2. Fatty liver-related indicators for normal weight, overweight, and obese children and adolescents with or without fatty liver

Variable	Healthy (n = 788)			Fatty liver (n = 161)		
	Boys (n = 334)	Girls (n = 454)	*P* value	Boys (n = 81)	Girls (n = 80)	*P* value
Age	12.96 ± 2.81	12.59 ± 3.41	0.195	13.04 ± 2.03	12.88 ± 2.25	0.654
Liver size (mm)	117.85 ± 11.9	111.45 ± 10.2	0.001	125.96 ± 1.3	116.41 ± 9.11	0.002
Spleen size (mm)	96.87 ± 3.63	92.14 ± 3.96	0.001	102.75 ± 8.52	93.41 ± 8.52	0.001
CBD diameter (mm)	2.63 ± 0.41	2.41 ± 0.22	0.001	2.63 ± 0.24	2.35 ± 0.33	0.351
Portal vein diameter (mm)	5.83 ± 1.25	6.59 ± 1.41	0.009	5.33 ± 1.06	6.14 ± 1.14	0.041

CBD, common bile duct.

patients with fatty liver. Despite the use of the same diagnostic approach (sonography), the prevalence of fatty liver in Iranian obese children (57%) was lower than that in Chinese obese children (77%). This is probably due to the fact that the mean BMI value in the study by Chan et al was larger than that obtained in the present study (30.3 versus 27). On the other hand, in the present study the sample size was larger than that of the research by Chan et al; however, the mean age of the participants in both studies was almost equal (16).

Another issue is the prevalence of fatty liver by gender. In the study of Schwimmer et al carried out on 127 students, evidence of development of fatty liver was significantly stronger in boys than in girls(19,20); however, the results of the present research showed no significant difference between the girls and the boys in prevalence of fatty liver. This lack of difference may have been due to the low mean age of the participants in our research compared to that in the research conducted in the United States and because of the lack of sex hormones in younger individuals. The findings of the present study generally indicate that an increase in BMI values substantially increases the prevalence of fatty liver in both boys and girls. Accordingly, in both female and male students, the prevalence of fatty liver disease was significantly higher in the obese group than in the other two groups.

Table 2 presents a comparison between the three groups in terms of fatty liver-related indicators (21). Together with increases in the prevalence of fatty liver in both genders at higher BMI values, the indicators related to development of fatty liver including liver size and spleen size in both genders, and CBD diameter in girls increased. Therefore, it may be possible to study these indicators in order to use them as screening indicators for diagnosing fatty liver in obese children and adolescents. In addition, special attention should be paid to overweight because the highest values of liver indicators were observed in the overweight group, and there was no considerable difference between this group and the obese group either in the entire sample or separately for the male and female participants. Moreover, it is noteworthy that significant differences were observed among the three groups in terms of age, which suggest that the prevalence of obesity may increase with age (22). Besides hormonal changes, changes in lifestyle that include changing a lifestyle with considerable physical activity to a sedentary and inactive one may contribute to the prevalence of obesity in older people (23).

The 17% prevalence of fatty liver in the studied sample suggests that we must be concerned with the possible high rate of development of type 2 diabetes and metabolic syndrome in future adults. The prevalence of fatty liver among the obese and overweight participants in this research was 28.8%. Therefore, by assuming the generalizability of the present results to the whole country, taking into account the population of 2-18 year-old Iranian children and adolescents (20 million people), and considering the prevalence of obesity and overweight in Iranian children and adolescents (21%), it can be said that about 1 200 000 children and adolescents suffer from fatty liver in Iran (24). In fact, nearly 1 200 000 Iranian children and adolescents are at risk of developing metabolic syndrome and type 2 diabetes. Given the relationship between these two diseases and CVDs, the prevalence of CVDs is predicted to increase in future.

Higher BMI values are associated with progression of liver disorder to fibrosis and cirrhosis (25). Therefore, correcting weight and controlling obesity can be considered important health priorities. On the other hand, considering the huge influence of mass media, especially television, on regular habits and lifestyle of children and adolescents, they must produce suitable programs aimed at improving the lifestyle of children and adolescents and encouraging them to maintain a healthy weight (26). These programs can encourage children, adolescents, and parents to adopt appropriate programs for maintaining the healthy weight of children and adolescents by raising the issues of the costs of various weight loss procedures as well as the treatment costs of obesity complications such as metabolic syndrome, type 2 diabetes, and CVDs. This age group and their parents must be recommended to regularly measure weight and waist circumference (obesity indicators). Taking these measurements helps the individual to become aware of danger in time and begin treatment. In general, the training and education provided by schools, kindergartens, the media, and parents for children and adolescents are expected to correct the lifestyle of these individuals and prevent incidence of disorders such as fatty liver and non-communicable diseases (27, 28).

Conclusion

Overweight and obesity in children lead to the development of fatty liver in them. Preventive measures must be taken because one third of the studied obese and overweight children in this research developed fatty liver disease.

Limitations of the study

The lack of measurement of biochemical indicators and the lack of involvement of children under 6 years of age were the limitations of this study. It is recommended that future studies reject these limitations.

Authors' contribution

LS is the single author of the manuscript.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical issues

The research followed the tenets of the Declaration of Helsinki. The Ethics Committee of Tabriz University of Medical Sciences approved this study. The institutional ethical committee at Tabriz University of Medical Sciences approved all study protocols(IR.TBZMED.REC.1400.1228). Besides, ethical issues (including plagiarism, data fabrication and double publication) have been completely observed by the authors.

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