Original Article

Prevalence of fatty liver and its related factors in children

Mahnaz Sadeghian[1], Mehdi Vafadar[2], Ala Torabi[3], Sara Torabi[4], Mehrshad Fazel[5]

[1]Associated Professor of Pediatric Gastroenterologist, [2]Assistant Professor of Pediatric Endocrinology, Department of Pediatric, Ali Asghar Children's Hospital, School of Medicine, Iran University of Medical Sciences, Tehran, [3]Assistant Professor of Radiology, Department of Radiology, Shariati Hospital, Tehran University of Medical Science, Tehran, [4]Faculty of Medicine, Tehran University of Medical Sciences, Tehran, [5]Ali Asghar Clinical Research Development Center, School of Medicine, Iran University of Medical Sciences, Tehran, Iran

Abstract

Background: Fatty liver disease is a severe liver condition that affects youngsters. Liver disease in children increases the incidence of liver fibrosis in their adulthood. Due to the importance of this disease and related factors in children, such as diabetes and obesity, our study was conducted to investigate the prevalence of fatty liver in children. **Materials and Methods:** This is a descriptive cross-sectional study done in Ali Asghar Hospital from June 2020 to December 2020. Demographic characteristics and prevalence of fatty liver were assessed. Blood samples were obtained after ten hours of fasting to assess AST, ALT, ALP, and blood glucose levels. Ultrasound was also used to check the health of the liver. Walking to school and exercising were also assessed. Data were analyzed using statistical software. **Results:** This research included 2526 children, and 37 of them had fatty liver. Fatty liver was more common in children with a BMI greater than 30, as well as metabolic and hypoparathyroid illness ($P = 0.02$). A significant association was observed between exercise and walking with fatty liver disease ($P < 0.05$). The majority of the individuals had grade 1 fatty liver (75.5%). Grade 1 fatty liver was seen in 90% of those who did not participate in athletics and 95% of those who did not walk to school. In addition, 94% of patients who exercised for less than ten minutes had grade 1fatty liver. **Conclusion:** Initially, exercise and weight loss had an essential effect on fatty liver disease. In fact, lifestyle changes and prevention of obesity may reduce liver damage.

Keywords: Children, fatty liver, inflammation, liver, prevalence, screening

Introduction

The most significant and prevalent chronic liver disease in the world is non-alcoholic fatty liver disease (NAFLD).[1,2] Many factors are involved in fatty liver disease. A high-fat diet and insulin resistance also promote the buildup of significant quantities of free fatty acids in the liver, which leads to a loss of control and regulation of normal lipid metabolism in the liver.[3,4] Other critical causes of hepatocyte injury in fatty liver include insulin resistance, oxidative stress, reduced ATP, and mitochondrial dysfunction.[5] Obesity severity, diabetes, and hyperlipidemia (particularly high triglycerides) are all predisposing factors for fatty liver, according to studies.[6,7] Because the quantity of estrogen declines with age, the rising incidence of this disease in women indicates that being feminine with age is a risk for this disease, which can express the function of estrogen. In mice, estrogen has been shown to protect against fatty liver disease.[8] The natural lipid metabolism balance is disrupted in fatty liver disease. The intake or synthesis of *de novo* fatty acids rises in comparison to fatty acid oxidation, which drives an increase in

Address for correspondence: Dr. Ala Torabi, Assistant Professor of Radiology, Department of Radiology, Shariati Hospital, Tehran University of Medical Science, Tehran, Iran.
E-mail: vafadar.m@iums.ac.ir

Received: 16-03-2022 **Revised:** 29-05-2022
Accepted: 01-07-2022 **Published:** 14-10-2022

Access this article online

Quick Response Code:

Website: www.jfmpc.com

DOI: 10.4103/jfmpc.jfmpc_626_22

How to cite this article: Sadeghian M, Vafadar M, Torabi A, Torabi S, Fazel M. Prevalence of fatty liver and its related factors in children. J Family Med Prim Care 2022;11:5604-8.

triglyceride synthesis over free fatty acid oxidation. Fatty liver is caused by the accumulation of triglycerides in liver cells.[3] The sickness is usually gradual and painless. The prognosis is favorable if histology specimens show no inflammation or death of liver cells. However, a small percentage of individuals with hepatocellular carcinoma and tissue damage followed by fibrosis may develop severe and chronic liver disease, cirrhosis, and possibly hepatocellular carcinoma due to the condition.[7] Obesity, impaired glucose homeostasis, and cardiovascular problems are all linked to a high-fat diet, according to sufficient evidence. Increased free fatty acids and reduced beta-oxidation of fatty acids inside the cell are the key metabolic factors of this diet.[9]

Recently, due to the increase in obesity in the community, the incidence of fatty liver disease has increased. The importance of this disease is due to the destruction of liver cells; if not diagnosed early and treated appropriately, it can lead to irreversible liver cirrhosis.[10,11] Fatty liver affects people of all ages. Improper lifestyle and diet put children at risk of fatty liver.[12] The findings show that development of fatty liver in children is usually caused by poor diet and may continue into adulthood. The development of the disease in childhood is likely to increase the risk of long-term complications.[13]

Fatty liver in children is often asymptomatic in the early stages, and symptoms usually appear when the liver is severely damaged. Therefore, it is important to pay attention to the diagnosis of this disease in children. Children's fatty liver disease is now recognised as a serious liver condition. Various studies have found a prevalence of fatty liver in obese children ranging from 49.3% to 77.3%.[14,15] Because fatty liver disease is projected to become the most frequent cause of chronic liver disease in children in the near future, we wanted to look into the frequency of fatty liver disease and its associated variables in children.

Materials and Methods

Study design

This descriptive, cross-sectional study was conducted within Hazrat Ali Asghar Hospital in Tehran, Iran, from June 2020 to December 2020. During this study, children were included in the study after reviewing the inclusion and exclusion criteria. Inclusion criteria considered were children less than 18 years of age. Exclusion criteria included unwillingness to participate in the study and incomplete data. It should be noted that ethical issues were observed during information collection. This review was approved by the hospital research council with the code of ethics.

Patients and data collection

Children (2526) were sent to the ultrasonography room of Hazrat Ali Asghar Hospital in Tehran. After a fatty liver disease diagnosis, the frequency of age and sex variables requested by a questionnaire was evaluated, and the prevalence of fatty liver disease was determined by age and sex. The disease's prevalence was compared in girls and boys. The prevalence of the condition was compared between children aged 0–10 years and children aged 10 years and older. The frequency of obesity and overweight characteristics in patients was calculated, and the prevalence of the condition was assessed separately for obesity and overweight patients' height, weight, and BMI. The prevalence of the condition was compared in the obese (BMI over 30), overweight (BMI between 25 and 30), normal weight (BMI between 18.5 and 25), and lean (BMI below 18.5) groups. The severity of diabetes was measured, and the frequency of each illness level (1, 2, 3) discovered by ultrasonography was calculated and compared. The use of ultrasonography to diagnose the condition was a requirement for participation in the trial. Participants went to the lab to collect a sample after fasting for ten hours. Blood of 5 cc was obtained under sterile circumstances and tested according to laboratory standards for the index of liver activity (AST, ALT, ALP) and blood glucose.[16,17] The criterion for entering the study was diagnosis of the disease by ultrasound.

Statistics

In the descriptive statistics component of this study's statistical analysis, frequency, percentage, and prevalence for qualitative data were employed. The Chi-squared test was implemented to compare the frequencies in groups. After the collection, the data were analyzed using the Statistical Package for the Social Sciences (SPSS) software version 25. The significance level was considered to be less than 0.05.

Result

In this study, 2526 children were referred to the hospital, of which 37 had fatty liver. Table 1 examines the prevalence of children with fatty liver by gender and by age. In the referring

Table 1: The prevalence of children with fatty liver (girls and boys) by age

	Number of participants	*n*	Prevalence %	*P*
Sex				
Female	1237	13	0.010	0.013
Male	1289	24	0.018	
Total	2526	37	0.015	
Age (years)				
Under 10	1752	18	0.010	0.068
Over 10 years	774	19	0.024	
BMI				
Obesity	325	13	0.04	
Overweight	609	8	0.013	0.023
Moderate body mass index	1412	10	0.007	
Lean body mass	179	6	0.033	
Disease				
Diabetes	37	3	0.081	
Nephrotic syndrome	57	4	0.070	0.037
Acute lymphocytic leukemia	43	4	0.093	
Hodgkin's lymphoma	18	3	0.166	
Metabolic disease	10	2	0.200	
Hypoparathyroidism	5	1	0.200	

BMI: Prevalence of fatty liver disease in obese patients with a BMI of 30 or above, overweight patients with a BMI of 25 to 30, moderate patients with a BMI of 20 to 25

population, 0.015% of people had fatty liver. Also, the rate of fatty liver in boys (0.018) was higher than girls (0.010) ($P = 0.01$). Regarding BMI index, the prevalence of 100 fatty liver was higher in obese children (0.04%) and very thin children (0.03%), and this difference was statistically significant ($P = 0.02$). The highest prevalence of fatty liver was observed in children with metabolic and hypoparathyroid disease ($P = 0.03$).

Most people with fatty liver referred to the hospital had grade 1 fatty liver (75.5%) [Table 2]. According to the data analysis [Table 3], twenty-eight were grade 1, four were grade 2, one was grade 3 and four were focal fatty change.

Ninety per cent of people who did not attend sports classes had grade 1 fatty liver ($P = 0.04$). In addition, 95% of people who did not walk to school had grade 1 fatty liver ($P = 0.03$) [Table 3]. Grade 1 fatty liver affected 83% of persons who exercised for ten to thirty minutes, 80% of people who exercised for more than thirty minutes, and 94% of people who exercised for less than ten minutes ($P = 0.04$).

The mean AST in grade 1 fatty liver was 49.4, in grade 2 fatty liver was 104.8, and in grade 3 fatty liver was 110. It may be assumed that as the fatty liver grade rises, so does the mean AST [Table 4]. The level of FBS in grade 1 fatty liver has the greatest value. The quantity of FBS in grades 2 and 3 was 89. The mean ALT in grade 1 fatty liver was 54.7, grade 2 fatty liver was 81.6, and grade 3 fatty liver was 98. It might be assumed that as the fatty liver grade increased, so did the average ALT. The mean ALP in grade 1 fatty liver was 628, grade 2 fatty liver was 857, and grade 3 fatty liver was 690, according to Table 4. Furthermore, it may be deduced that fatty liver had the maximum proportion in grade 2.

Table 2: Frequency of 1st, 2nd and 3rd degree fatty liver disease in patients with liver

	n	Percentage
Grade		
1	28	75.7
2	4	10.8
3	1	2.7
Focal fatty change	4	10.8
Total	37	100.0

Table 3: Frequency of sports classes, walk to school and sport activities in different grades of fatty liver

	Grade				*P*
	1 (*n*)	2 (*n*)	3 (*n*)	Focal fatty change (*n*)	
Sports classes					
Missing	40%	30%	20%	10%	0.041
Yes	86%	0%	0%	14%	
No	90%	5%	0%	5%	
Walk to school*					
Missing	40%	30%	10%	20%	
Yes	60%	20%	0%	20%	0.037
No	95%	0%	0%	5%	
Sport activities					
Missing	40%	30%	10%	20%	0.046
10-30 min	83%	17%	0%	0%	
>30 min	80%	0%	0%	20%	
<10 min	94%	0%	0%	6%	

*Frequency of walking to school in different stages of fatty liver in patients

Table 4: Frequency of AST, ALT and FBS in different grades of fatty liver in patients with liver

	Grade (Mean)			
	1	2	3	Focal fatty change
AST (U/L)	49.4	104.8	110.0	30.9
FBS (mg/dL)	112	89	89	108
ALT (U/L)	54.7	81.6	98.0	34.6
ALP (U/L)	628	857	690	500

Discussion

In obese children, NAFLD is the most frequent chronic liver disease.[18] The present study investigated the prevalence of fatty liver disease in children and factors affecting it. Our findings showed that prevalence of fatty liver was higher in boys. The highest prevalence of fatty liver was observed in children with metabolic and hypoparathyroid disease. Also, the frequency of fatty liver was significantly higher in obese and very thin children. In fact, the prevalence of fatty liver in obese children and adolescents is much greater than in children and adolescents of normal weight. In similar studies, Schwimmer *et al.*[19] and Boyraz *et al.*[20] showed that fatty liver is more common in obese children. In the current study published the first case of severe hepatitis and hepatic fibrosis in obese children 13 years ago, in three youngsters aged 10.[18,19]

In our study, 0.015% of the persons in the referring population had fatty liver. In addition, boys had a greater rate of fatty liver than girls. The average BMI in children with fatty liver was determined to be 6.28 based on the measurements. Sartorio *et al.*[21] found that 332 patients (44%) exhibited ultrasound evidence of fatty liver among 933 children with a BMI of more than 20% in the age category of 3–90 years. The research showed that the children with metabolic and hypoparathyroid illness had the most significant frequency of fatty liver. Grade 1 fatty liver was found in the largest percentage of those who did not participate in sports or did not walk to school. The greatest levels of FBS and ALP were seen in grade 1 fatty liver and grade 2 fatty liver, respectively. Other studies found that persons with fatty liver had higher levels of aminotransferases.[20,22,23] Another concern was the prevalence of fatty liver according to gender. The findings showed that the prevalence of fat fatty liver was substantially greater in boys than in girls in a study done by Schwimmer *et al.*[24] on 127 students. It was computed more in boys than girls in our investigation, as it was in this study. In a study on Chinese children, evidence of fatty liver was found in 77% of them, based on ultrasound data. Liver transferase tests were done on all of these people, much like in our study. Overall, the findings of testing and ultrasounds revealed that 24% of these persons had fatty liver.[15] Different diagnostic approaches

were to blame for the disparity in prevalence reported in other studies in estimating the frequency of liver involvement and the incidence of liver problems in overweight and obese children.[25] Based on the frequency obtained in relation to obesity prevalence among the children and adolescents 2-18 years population in Iran, 21% of them are overweight. In Iran, it was predicted that 1,200,000 children and adolescents suffer from fatty liver disease.[26] As a result, weight loss and obesity management might be health concerns.

In Iran, studies by Sasani *et al*.[27] identified the factors affecting fatty liver and prevention of infection. Our findings of this study showed that there was a sex difference in fatty liver disease, with males being more affected than girls. Increased fatty liver disease in boys and obese individuals might be related to lifestyle factors.[28,29] Findings of Utz-Melere *et al*.[29] showed that lifestyle changes could be effective in reducing fatty liver disease in children by improving weight and physical activity index.

Shapiro *et al*.[30] reported that there were various risk factors for fatty liver disease in children, in addition to low activity in children, such as perinatal factors that affected both the mother and the baby, as well as exposure to toxins. The environment could be effective in children with fatty liver. They also noted the need for progress in non-invasive assessment to improve screening and diagnosis of fatty liver in children. Reports indicate that children with fatty liver disease were more likely to develop serious diseases such as diabetes and depression, and increasing awareness, especially of parents and physicians, can reduce and prevent liver problems.

One of the limitations of the present study was the lack of cooperation of some parents of the children in relation to responsiveness, which was resolved by explaining the research and its safety. One of the strengths of our research was the study population, which certainly showed more accurate results.

In general, our cross-sectional study showed that the prevalence of liver disease in the pediatric population is very acute and it is important to pay attention to it in the field of prevention and treatment. Certainly, the management of fatty liver disease can be effective in children's health. Given that the media transmits many habits and lifestyles to this generation, the media should provide programs to enhance lifestyles and encourage children and adolescents to maintain a healthy weight.

Conclusion

The prevalence of fatty liver was shown to rise with increasing body mass and affected by gender differences as well. Its occurrence is linked to metabolic illnesses as well. The prevalence of fatty liver is closely connected to exercise and walking. High BMI, is linked to the development of liver dysfunction to fibrosis and cirrhosis. As a result, changing children's lifestyles and preventing obesity might be important health goals. Given that the media transmits many habits and lifestyles to this generation, the media should provide programs to enhance lifestyles and encourage children and adolescents to maintain a healthy weight.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Ratziu V, Bellentani S, Cortez-Pinto H, Day C, Marchesini G. A position statement on NAFLD/NASH based on the EASL 2009 special conference. J Hepatol 2010;53:372-84.
2. Day CP. Non-alcoholic fatty liver disease: A massive problem. Clin Med 2011;11:176-8.
3. Jou J, Choi SS, Diehl AM, editors. Mechanisms of disease progression in nonalcoholic fatty liver disease. Semin Liver Dis 2008;28:370-9.
4. Day CP, James OF. Steatohepatitis: A Tale of Two "Hits"? Elsevier; 1998. p. 842-5.
5. Neuschwander-Tetri BA, Caldwell SH. Nonalcoholic steatohepatitis: Summary of an AASLD single topic conference. Hepatology 2003;37:1202-19.
6. Browning JD, Szczepaniak LS, Dobbins R, Nuremberg P, Horton JD, Cohen JC, *et al*. Prevalence of hepatic steatosis in an urban population in the United States: Impact of ethnicity. Hepatology 2004;40:1387-95.
7. Angulo P. Nonalcoholic fatty liver disease. N Engl J Med 2002;346:1221-31.
8. Hamaguchi M, Kojima T, Takeda N, Nakagawa T, Taniguchi H, Fujii K, *et al*. The metabolic syndrome as a predictor of nonalcoholic fatty liver disease. Ann Intern Med 2005;143:722-8.
9. Rojas J, Arraiz N, Aguirre M, Velasco M, Bermúdez V. AMPK as target for intervention in childhood and adolescent obesity. J Obes 2011;2011. doi: 10.1155/2011/252817.
10. Younossi ZM, Stepanova M, Younossi Y, Golabi P, Mishra A, Rafiq N, *et al*. Epidemiology of chronic liver diseases in the USA in the past three decades. Gut 2020;69:564-8.
11. Fernandes DM, Pantangi V, Azam M, Salomao M, Iuga AC, Lefkowitch JH, *et al*. Pediatric nonalcoholic fatty liver disease in New York city: An autopsy study. J Pediatr 2018;200:174-80.
12. Goldner D, Lavine JE. Nonalcoholic fatty liver disease in children: Unique considerations and challenges. Gastroenterology 2020;158:1967-83.e1.
13. Sahota AK, Shapiro WL, Newton KP, Kim ST, Chung J, Schwimmer JB. Incidence of nonalcoholic fatty liver disease in children: 2009-2018. Pediatrics 2020;146. doi: 10.1542/peds.2020-0771.
14. Papandreou D, Karabouta Z, Pantoleon A, Rousso I. Investigation of anthropometric, biochemical and dietary parameters of obese children with and without non-alcoholic fatty liver disease. Appetite 2012;59:939-44.
15. Chan D, Li A, Chu W, Chan M, Wong E, Liu E, *et al*. Hepatic steatosis in obese Chinese children. Int J Obes 2004;28:1257-63.
16. Savadkouhi F, Hosseini TS, Shahabi NS. The frequency of fatty liver in sonography of patients without liver diseases

background and its correlation with blood cholesterol and triglyceride. Zahedan J Res Med Sci 2003;5:177-83. Available from: https://brieflands.com/articles/zjrms-95168.pdf.

17. Chen Z-W, Chen L-Y, Dai H-L, Chen J-H, Fang L-Z. Relationship between alanine aminotransferase levels and metabolic syndrome in nonalcoholic fatty liver disease. J Zhejiang Univ Sci B 2008;9:616-22.
18. El-Koofy N, El-Karaksy H, El-Akel W, Helmy H, Anwar G, El-Sayed R, *et al.* Ultrasonography as a non-invasive tool for detection of nonalcoholic fatty liver disease in overweight/obese Egyptian children. Eur J Radiol 2012;81:3120-3.
19. Schwimmer JB, Pardee PE, Lavine JE, Blumkin AK, Cook S. Cardiovascular risk factors and the metabolic syndrome in pediatric nonalcoholic fatty liver disease. Circulation 2008;118:277-83.
20. Boyraz M, Hatipolu N, Sar E, Akçay A, Takn N, Ulucan K, *et al.* Non-alcoholic fatty liver disease in obese children and the relationship between metabolic syndrome criteria. Obesity research & clinical practice 2014;8:e356-63.
21. Sartorio A, Del Col A, Agosti F, Mazzilli G, Bellentani S, Tiribelli C, *et al.* Predictors of non-alcoholic fatty liver disease in obese children. Eur J Clin Nutr 2007;61:877-83.
22. Yoo J, Lee S, Kim K, Yoo S, Sung E, Yim J. 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;81:321-6.
23. Kotronen A, Yki-Järvinen H. Fatty liver: A novel component of the metabolic syndrome. Arterioscler Thromb Vasc Biol 2008;28:27-38.
24. Schwimmer JB, McGreal N, Deutsch R, Finegold MJ, Lavine JE. Influence of gender, race, and ethnicity on suspected fatty liver in obese adolescents. Pediatrics 2005;115:e561-5.
25. Kaur S, Kapil U, Singh P. Pattern of chronic diseases amongst adolescent obese children in developing countries. Curr Sci 2005:1052-6.
26. Chi DL, Luu M, Chu F. A scoping review of epidemiologic risk factors for pediatric obesity: Implications for future childhood obesity and dental caries prevention research. J Public Health Dent 2017;77:S8-31.
27. Sasani M, Izadi M. Assessment of the prevalence of non-alcoholic fatty liver disease in regular and non-regular blood and plasma donors. Sci J Iran Blood Transfus Organ 2021;18:233-40.
28. Katsagoni CN, Papatheodoridis GV, Ioannidou P, Deutsch M, Alexopoulou A, Papadopoulos N, *et al.* Improvements in clinical characteristics of patients with non-alcoholic fatty liver disease, after an intervention based on the Mediterranean lifestyle: A randomised controlled clinical trial. Br J Nutr 2018;120:164-75.
29. Utz-Melere M, Targa-Ferreira C, Lessa-Horta B, Epifanio M, Mouzaki M, Mattos AA. Non-alcoholic fatty liver disease in children and adolescents: Lifestyle change-A systematic review and meta-analysis. Ann Hepatol 2018;17:345-54.
30. Shapiro WL, Noon SL, Schwimmer JB. Recent advances in the epidemiology of nonalcoholic fatty liver disease in children. Pediatr Obes 2021;16:e12849.