

Assessment of the Relationship Between Prevalence of Reporting Fatty Liver Disease by Ultrasound and Body Mass Index in Children

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Abstract

Background: Obesity is the major cause of nonalcoholic fatty liver disease (NAFLD) as the most common form of chronic liver disease. Prevention of obesity can be useful in reducing the incidence of NAFLD.

Objectives: This study evaluated the prevalence of fatty liver in relation with body mass index (BMI) by means of ultrasound in high school students of Zanjan.

Methods: In this cross-sectional study, three hundred high school students aged 12 to 18 years, from Zanjan city were selected randomly and divided to three groups with one hundred children in each group, based on body mass index. Only 240 of them participated in the study. The participants were examined by a pediatrician. Weight, height and waist circumferences were measured at baseline. Liver ultrasound was performed for all children and grade of fatty liver was determined.

Results: There was a significant correlation between grade of fatty liver with BMI, gender and age ($P=0.000$, $P=0.000$ and $P=0.006$, respectively). Boys had higher rates of fatty liver than girls. Our study showed a strong association between BMI and prevalence of fatty liver on ultrasound. However, there was no relation between severity of fatty liver and waist circumference ($P=0.067$). The waist circumference was greater in boys, and it increased with age. The mean BMI in children with grade 1 and 2 fatty liver was 26.79 and 30.5, respectively.

Conclusions: According to the study hypothesis, based on BMI, the degree of NAFLD in children was predictable. Ultrasound of liver is one of the assessment methods of fatty liver but it is not a diagnostic method; it is useful for prevention in order to reduce BMI.

Keywords: Body Mass Index, Nonalcoholic Fatty Liver Disease, Children, Ultrasound

1. Background

Nonalcoholic fatty liver disease (NAFLD) is the most common form of chronic liver disease. It has a wide spectrum of clinical symptoms from simple steatosis up to end stage liver disease and cirrhosis (1). Nonalcoholic fatty liver disease occurs due to excessive deposition of triglycerides (more than 5% of liver weight) in the cytoplasm of hepatocytes (2). Currently, NAFLD is recognized as the most common chronic liver disease in children and adults (3). The prevalence of NAFLD is 25 to 30% of the general population in developed countries and in children it is estimated as 3 to 10%, all over the world (4, 5). Fatty liver disease was identified for the first time by Ludwig et al. in 1980 (6) and in 1983 it was reported in children (7). Although the real cause of the disease is still unclear (8), the main risk factors are obesity, insulin resistance, hyperlipidemia, hypertension and cardiovascular disease. Genetic factors, ethnicity, age, drugs and inactivity can influence the incidence of fatty liver (9-12). Previous studies showed that prevalence of NAFLD increases with obesity and sedentary lifestyle (13). Therefore, the main treatment is focused on physical ac-

tivity and weight loss (14). Obesity in children is a global problem (15). Iran is one of seven countries where obesity in children is common (16). In our country, a rapid increase since 1990 was reported in BMI as well as prevalence of overweightness and obesity (17). On the other hand, these problems in children and adolescents have doubled between 1993 and 1999 (18).

2. Objectives

According to the increased prevalence of childhood obesity, the aim of this study was to investigate the relationship between prevalence of fatty liver and BMI using ultrasound in high school students in Zanjan.

3. Materials and Methods

Three-hundred high school students aged 12 to 18 years in Zanjan city were randomly selected and divided to three groups with one hundred children in each group based on body mass index: normal weight (body mass index 85th

percentile or less), overweight (body mass index between 85th and 94th percentile), and obese (body mass index 95th percentile or more). Given that the prevalence of fatty liver is about 25%, with confidence of 95% and accuracy of 6%, the required sample size was calculated in 200 individuals. Cluster sampling was done in this study. According to this type of sampling and correction factor of 1/2, the final sample size consisted of 240 patients and was considered enough (120 individuals from each gender). Due to probability of withdrawal, we selected three hundred samples but 240 of them participated in the study, thus there were 60 dropouts. Parental consent was obtained from all children enrolled in the study. They were examined by one pediatrician.

Inclusion criteria included high school healthy children aged 12 to 18 years and exclusion criteria included individuals with

- History of endocrine and metabolism disorders including diabetes mellitus, hypothyroidism, galactosemia, tyrosinemia type I, Wilson disease, etc.

- Primary liver disease such as viral infections (hepatitis A virus, hepatitis B virus, hepatitis C virus, hepatitis D virus and other infectious organisms)

- Other secondary liver involvement due to systemic disease such as collagen-vascular disorders

- Use of hepatotoxic medications, including anticonvulsive agents

From the selected one hundred individuals in each group, 95 children in the group with normal weight, 59 in the overweight group and 86 in the obese group were willing to undergo ultrasound examination. Sixty of the 300 did not accept undergoing ultrasound. The children's weight, height and waist circumference were measured. Body mass index was calculated as weight (kg)/Height (m²). Liver Ultrasound was performed by a single radiologist, without knowledge of the children's BMI. Each patient's demographic data and ultrasound results were recorded in separate questionnaires. The data were analyzed by SPSS statistical software version 11.5. The descriptive results were expressed as frequencies, percentages, mean and standard deviation. We used chi-square and variance test for analysis of results. The P values less than 0.05 were considered statistically significant. The study was approved by the ethical committee of Zanjan University of Medical Sciences.

4. Results

The study enrolled 240 children aged 12 to 18 years with an equal number (120 patients) of boys and girls in each group; 95 (39.6%) with normal weight, 59 (24.6%) overweight and 86 (35.8%) obese. The highest and lowest BMI

was 37.6 and 12.6, respectively. Lowest BMI for grade I fatty liver was observed at 14.36 and for grade II was observed at 26.2. This means that with increasing BMI, the degree of fatty liver increases. Mean BMI was 26.79 in children with grade I fatty liver and mean BMI was 30.5 in grade II fatty liver. There was no significant correlation between BMI and gender with the chi-square test ($P = 0.123$). Fatty liver was reported in 40% of girls and 59.2% of boys in these three groups. There was a significant relationship between grades of fatty liver on ultrasound. Gender analysis, using chi-square test, showed that the boys had higher incidence ($P = 0.000$) of fatty liver. The ultrasound detected normal liver in 121 children and fatty liver in all the remaining 119. These children had a fatty liver grade I or II. None of the children had fatty liver with grade III. Table 1 shows that 80 of 95 individuals with normal weight had normal liver; grade I fatty liver was found in 31 of 59 overweight children and 51 of 86 obese children. Grade II fatty liver was seen in one overweight child and in 21 obese children. There was a significant correlation between BMI and fatty liver involvement using the chi-square test ($P = 0.000$). This means that, when body mass index increases the degree of fatty liver increases as well. Also there was a statistically significant association between age and gender with grade of fatty liver seen in ultrasound ($P = 0.006$ and $P = 0.003$ respectively). Boys had higher rates of fatty liver. In patients with normal liver, the mean and standard deviation of waist circumference were 77.1 cm and 16.2, respectively. Patients with grade I fatty liver measured 81.1 and 16.1 cm, respectively and those with grade II fatty liver measured, 81.6 and 15.7 cm respectively. The t-test showed that there was no statistically significant correlation between waist and grade of fatty liver ($P = 0.067$), while between waist circumference and gender there was a significant relationship ($P = 0.001$). The waist circumference was greater in boys.

5. Discussion

Children and adolescents with higher BMI have higher degrees of fatty liver seen on ultrasound. A highly significant relationship was observed between BMI and fatty liver ($P = 0.000$). A Chinese study (2004) reported that 77% of obese children had evidence of hepatosteatosis on ultrasound but further investigations proved that only 24% of these individuals had fatty liver disease (19). Younesian (2015) showed that high prevalence of obesity and anthropometric measurements are independent predicting factors for Non-Alcoholic Fatty Liver Disease (NAFLD) (20). In 2015, Ardakani et al. proved a high prevalence of fatty liver on ultrasound in obese children aged 5 to 15 years (21). Adibi showed that the prevalence of fatty liver on ultrasound in obese children was 54.4%. This rate is signifi-

Table 1. Distribution of Body Mass Index Based on the Grade of Fatty Liver on Ultrasound

	Ultrasound			Total
	Normal Liver	Grade I Fatty Liver	Grade II Fatty Liver	
BMI				
Normal Weight	80 (84.2%)	15 (15.8%)	0 (0%)	95 (100%)
Overweight	27 (45.8%)	31 (52.5%)	1 (1.7%)	59 (100%)
Obese	14 (16.3%)	51 (59.3%)	21 (24.4%)	86 (100%)
Total	121 (50.4%)	97 (40.4%)	22 (9.2%)	240 (100%)

Abbreviation: BMI, body mass index.

cantly higher in normal weight and overweight children (22). Kruger (2010) reported that fatty liver could be seen on ultrasound of half of overweight or obese people (23). In our study, the rate of ultrasound reports of fatty liver in children and adolescents with higher BMI were significantly higher. Most epidemiological studies, similar to ours showed a strong association between BMI and fatty liver on ultrasound (24-26). Nowadays, due to the rise in global prevalence of overweightness and obesity (15, 27, 28), fatty liver is seen more frequently. Panah believed that the risk of steatohepatitis was positively non-linearly correlated with BMI so that with every five-unit increase in BMI, the risk of developing steatohepatitis increased more than four folds (29). Bahrami proposed that BMI is a strong indicator for steatohepatitis (30). The results of the above-mentioned studies are consistent with our findings. In different countries, the actual prevalence of fatty liver in children is estimated between 3 and 10% (4, 5). Alavian estimated the prevalence of NAFLD in Iranian children at 7.1% (31). Childhood obesity is common in Iran (16) and BMI has shown a rapid increase in the recent years (17). Therefore, the high percentage of fatty liver disease in Iranian children and adolescents can be predicted. In our study, the gender distribution in the samples was identical and there was no significant relation in terms of BMI between boys and girls. Fatty liver was found in 40% of girls and 59.2% of boys in these three groups, and this difference was statistically highly significant. We agree with Schwimmer that fatty liver is significantly higher in boys than in girls (32). In our study, waist circumference was higher in boys, and its size increased with age. There was no significant correlation between waist size and the degree of fatty liver on ultrasound. The number of cases of fatty liver on ultrasound increased with age. According to our findings, there was an association between overweightness and/or obesity and fatty liver. It is recommended to study the relationship between fatty liver, overweightness and obesity, especially in patients with definitive diagnosis of fatty liver. To reduce

the risk of fatty liver disease, physical activity, reasonable diet and weight loss, should be recommended.

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Footnote

Authors' Contribution: All authors have equally contribution to this study, including study design, collection of the data and results, interpretation of data, drafting the article, statistical analysis and study supervision.

References

- Vajro P, Lenta S, Socha P, Dhawan A, McKiernan P, Baumann U, et al. Diagnosis of nonalcoholic fatty liver disease in children and adolescents: position paper of the ESPGHAN Hepatology Committee. *J Pediatr Gastroenterol Nutr.* 2012;**54**(5):700-13. doi: [10.1097/MPG.0b013e318252a13f](https://doi.org/10.1097/MPG.0b013e318252a13f). [PubMed: [22395188](https://pubmed.ncbi.nlm.nih.gov/22395188/)].
- Kopec KL, Burns D. Nonalcoholic fatty liver disease: a review of the spectrum of disease, diagnosis, and therapy. *Nutr Clin Pract.* 2011;**26**(5):565-76. doi: [10.1177/0884533611419668](https://doi.org/10.1177/0884533611419668). [PubMed: [21947639](https://pubmed.ncbi.nlm.nih.gov/21947639/)].
- 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**(2):372-84. doi: [10.1016/j.jhep.2010.04.008](https://doi.org/10.1016/j.jhep.2010.04.008). [PubMed: [20494470](https://pubmed.ncbi.nlm.nih.gov/20494470/)].
- Nomura H, Kashiwagi S, Hayashi J, Kajiyama W, Tani S, Goto M. Prevalence of fatty liver in a general population of Okinawa, Japan. *Jpn J Med.* 1988;**27**(2):142-9. [PubMed: [3047469](https://pubmed.ncbi.nlm.nih.gov/3047469/)].
- Roberts EA. Non-alcoholic fatty liver disease (NAFLD) in children. *Front Biosci.* 2005;**10**:2306-18. [PubMed: [15970496](https://pubmed.ncbi.nlm.nih.gov/15970496/)].
- Ludwig J, Viggiano TR, McGill DB, Oh BJ. Nonalcoholic steatohepatitis: Mayo Clinic experiences with a hitherto unnamed disease. *Mayo Clin Proc.* 1980;**55**(7):434-8. [PubMed: [7382552](https://pubmed.ncbi.nlm.nih.gov/7382552/)].
- Moran JR, Ghishan FK, Halter SA, Greene HL. Steatohepatitis in obese children: a cause of chronic liver dysfunction. *Am J Gastroenterol.* 1983;**78**(6):374-7. [PubMed: [6859017](https://pubmed.ncbi.nlm.nih.gov/6859017/)].

8. Day CP, James OF. Steatohepatitis: a tale of two "hits"? *Gastroenterology*. 1998;**114**(4):842-5. [PubMed: [9547102](#)].
9. Fraser A, Longnecker MP, Lawlor DA. Prevalence of elevated alanine aminotransferase among US adolescents and associated factors: NHANES 1999-2004. *Gastroenterology*. 2007;**133**(6):1814-20. doi: [10.1053/j.gastro.2007.08.077](#). [PubMed: [18054554](#)].
10. Hashimoto E, Yatsuji S, Tobari M, Taniai M, Torii N, Tokushige K, et al. Hepatocellular carcinoma in patients with nonalcoholic steatohepatitis. *J Gastroenterol*. 2009;**44 Suppl 19**:89-95. doi: [10.1007/s00535-008-2262-x](#). [PubMed: [19148800](#)].
11. Dubuquoy C, Burnol AF, Moldes M. PNPLA3, a genetic marker of progressive liver disease, still hiding its metabolic function?. *Clin Res Hepatol Gastroenterol*. 2013;**37**(1):30-5. doi: [10.1016/j.clinre.2012.06.014](#). [PubMed: [22884299](#)].
12. Hallsworth K, Thoma C, Moore S, Ploetz T, Anstee QM, Taylor R, et al. Non-alcoholic fatty liver disease is associated with higher levels of objectively measured sedentary behaviour and lower levels of physical activity than matched healthy controls. *Frontline gastroenterol*. 2014;2014-32.
13. Zelber-Sagi S, Ratzju V, Oren R. Nutrition and physical activity in NAFLD: an overview of the epidemiological evidence. *World J Gastroenterol*. 2011;**17**(29):3377-89. doi: [10.3748/wjg.v17.i29.3377](#). [PubMed: [21876630](#)].
14. Nseir W, Hellou E, Assy N. Role of diet and lifestyle changes in nonalcoholic fatty liver disease. *World J Gastroenterol*. 2014;**20**(28):9338-44. doi: [10.3748/wjg.v20.i28.9338](#). [PubMed: [25071328](#)].
15. Eells LJ, Campbell K, Lidstone J, Kelly S, Lang R, Summerbell C. Prevention of childhood obesity. *Best Pract Res Clin Endocrinol Metab*. 2005;**19**(3):441-54. doi: [10.1016/j.beem.2005.04.008](#). [PubMed: [16150385](#)].
16. Gurney M, Gorstein J. The global prevalence of obesity—an initial overview of available data. *World Health Stat Q*. 1988;**41**(3-4):251-4. [PubMed: [3232412](#)].
17. Dorosty AR, Siassi F, Reilly JJ. Obesity in Iranian children. *Arch Dis Child*. 2002;**87**(5):388-91. [PubMed: [12390907](#)].
18. Kelishadi R, Hashemipour M, Sarraf-Zadegan N, Amiri M. Trend of Atherosclerosis Risk Factors in Children of Isfahan. *Asian Cardiovascular Thoracic Ann*. 2001;**9**(1):36-40. doi: [10.1177/021849230100900110](#).
19. Chan DF, Li AM, Chu WC, Chan MH, Wong EM, Liu EK, et al. Hepatic steatosis in obese Chinese children. *Int J Obes Relat Metab Disord*. 2004;**28**(10):1257-63. doi: [10.1038/sj.ijo.0802734](#). [PubMed: [15278103](#)].
20. Younesian A, Morady H, Razavianzadeh N, Zahedi E. . Prevalence of fatty liver using ultrasound in male high-school pupils without history of liver disease and its relationship with liver enzymes, body mass index and waist-hip ratio. *RJMS*. 2015;**22**(132):79-86.
21. Taghavi Ardakani A, Sharif MR, Kheirkhah D. Fatty liver disease in obese children in Kashan, Iran. *Caspian J Ped*. 2015;**1**(1):17-21.
22. Adibi A, Kelishadi R, Beihaghi A, Salehi H, Talaei M. Sonographic fatty liver in overweight and obese children, a cross sectional study in Isfahan. *Endokrynol Pol*. 2009;**60**(1):4-9. [PubMed: [19224500](#)].
23. Kruger FC, Daniels C, Kidd M, Swart G, Brundyn K, Van Rensburg C, et al. Non-alcoholic fatty liver disease (NAFLD) in the Western Cape: a descriptive analysis. *S Afr Med J*. 2010;**100**(3):168-71. [PubMed: [20459941](#)].
24. Nouredin M, Loomba R. Nonalcoholic fatty liver disease: Indications for liver biopsy and noninvasive biomarkers. *Clinical Liver Dis*. 2012;**1**(4):104-7. doi: [10.1002/cld.65](#).
25. Festi D, Colecchia A, Sacco T, Bondi M, Roda E, Marchesini G. Hepatic steatosis in obese patients: clinical aspects and prognostic significance. *Obes Rev*. 2004;**5**(1):27-42. [PubMed: [14969505](#)].
26. Dixon JB, Bhathal PS, O'Brien PE. Nonalcoholic fatty liver disease: predictors of nonalcoholic steatohepatitis and liver fibrosis in the severely obese. *Gastroenterology*. 2001;**121**(1):91-100. [PubMed: [11438497](#)].
27. Davison KK, Birch LL. Weight status, parent reaction, and self-concept in five-year-old girls. *Pediatrics*. 2001;**107**(1):46-53. [PubMed: [11134433](#)].
28. Martorell R, Kettel Khan L, Hughes ML, Grummer-Strawn LM. Overweight and obesity in preschool children from developing countries. *Int J Obes Relat Metab Disord*. 2000;**24**(8):959-67. [PubMed: [10951533](#)].
29. Hossein-Panah F, Sadeghi L, Rambod M, Foroutan M, Naseri M. Assessing predicting factors in non-alcoholic fatty liver disease (NAFLD) in type 2 diabetes [in Persian]. *Pejouhesh*. 2006;**30**(1):9-15.
30. Bahrami H, Daryani NE, Mirmomen S, Kamangar F, Haghpanah B, Djalili M. Clinical and histological features of nonalcoholic steatohepatitis in Iranian patients. *BMC Gastroenterol*. 2003;**3**:27. doi: [10.1186/1471-230X-3-27](#). [PubMed: [14561231](#)].
31. Alavian SM, Mohammad-Alizadeh AH, Esna-Ashari F, Ardalan G, Harizadeh B. Non-alcoholic fatty liver disease prevalence among school-aged children and adolescents in Iran and its association with biochemical and anthropometric measures. *Liver Int*. 2009;**29**(2):159-63. doi: [10.1111/j.1478-3231.2008.01790.x](#). [PubMed: [18492015](#)].
32. 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**(5):561-5. doi: [10.1542/peds.2004-1832](#). [PubMed: [15867021](#)].