Hepat Mon. 2018 December; 18(12):e83525. doi: 10.5812/hepatmon.83525.

Published online 2018 December 16. **Research Article**

Prevalence of Non-Alcoholic Fatty Liver Disease (NAFLD) and its Clinical Characteristics in Overweight and Obese Children in the South East of Iran, 2017

Kokab Namakin [1], Mahya Hosseini [2,*], Mahmoud Zardast [3] and Mahyar Mohammadifard [4]

[1] Cardiovascular Research Center, Birjand University of Medical Sciences, Birjand, Iran
[2] Pediatric Department, Student Research Center, Birjand University of Medical Sciences, Birjand, Iran
[3] Infectious Research Center, Birjand University of Medical Sciences, Birjand, Iran
[4] Fellowship of Interventional Radiology, Birjand University of Medical Sciences, Birjand, Iran

[*] *Corresponding author*: Pediatric Department, Student Research Center, Birjand University of Medical Sciences, Birjand, Iran. Email: hosseini.mahia66@gmail.com

Received 2018 August 21; **Revised** 2018 November 17; **Accepted** 2018 December 01.

Abstract

Background: During the last decade, lifestyle changes considerably leading to an increase in non-communicable diseases such as nonalcoholic fatty liver disease (NAFLD) accounted as the most common cause of chronic liver disease in children.
Objectives: The present study aimed to assess the prevalence and clinical characteristics of NAFLD overweight and obese children.
Methods: This is a cross-sectional study. A total of 200 overweight and/or obese children aged 12 to 18 years were enrolled by a multi-stage sampling method. All participants underwent an abdominal ultrasound after six hours of fasting. Beside liver function tests, lipid profile, and fasting blood glucose were measured after 12 hours of fasting.
Results: The NAFLD was reported in 108 individuals (54%). The prevalence of NAFLD was significantly higher in obese children compared to overweight ones (69.1% vs. 35.6%, $P < 0.001$). The logistic regression results show that there was a significant relationship between age, sex, and BMI and the prevalence of NAFLD ($P < 0.001$).
Conclusions: The results indicate that NAFLD is present in approximately half of the overweight and/or obese adolescents. Therefore being overweight and/or obese could be considered as main risk factors in development of NAFLD.

Keywords: Non-Alcoholic Fatty Liver Disease, Metabolic Syndrome, Childhood Obesity, Childhood Overweight

1. Background

Over the last decades, life-style has been changed dramatically including sedentary behaviors and unhealthy diet leading to a sharp rise in the incidence of obesity affecting children and adolescents as well (1). The prevalence of childhood obesity has been rising globally and has become a major childhood health problem in many countries causing several subsequent medical conditions including cardiovascular disease, Type 2 diabetes, hypertension, hyperlipidemia, and non-alcoholic fatty liver disease (2, 3).

Today, with a prevalence of 20% to 70%, the non-alcoholic fatty liver disease (NAFLD) is considered as the most common liver disease during childhood with a rapid increasing number (4-6). The NAFLD is defined based on paraclinical investigations due to lack of symptoms including abdominal ultrasonography and liver function tests (7). Liver steatosis, at abdominal ultrasonography, beside a mild elevation of liver function tests (including serum glutamic-oxaloacetic transaminase and glutamic pyruvic transaminase), are usually the main criteria of NAFLD. Occurrence of NAFLD during childhood affects the quality of life and these patients suffer higher level of emotional and behavioral problems (8). In addition, NAFLD causes several serious comorbidities (6).

There are several articles concerning the prevalence of NAFLD during childhood in Iranian children reporting a prevalence of 7% - 86% with large geographic variation in distribution of it (9-13). Based on search, there is no new report regarding the prevalence of NAFLD in the south east of Iran. Considering the dynamic of changes in human behaviors as well as need for up to date data, this study aimed to assess the prevalence of fatty liver in obese and overweight children aged 12 - 18 years in Birjand city.

2. Methods

2.1. Population of Study

This is a cross-sectional study conducted on 200 adolescents aged 12 to 18 years who are overweight and obese in Birjand, the capital of South Khorasan, south east of Iran. The inclusion criteria was the body mass index (BMI) of 85% or higher percentile (according to the Centers for Disease Control and Prevention, CDC, chart in terms of male and female gender). The exclusion criteria included known thyroid dysfunction (hypothyroidism and hypoparathyroidism), diabetes and Cushing's syndrome, as well as chronic consumption of any kind of drugs, such as corticosteroids, weight reducing or increasing agents, a history of alcoholism, and hepatitis caused by other factors (hereditary diseases, viruses, etc.). In multi-stage sampling, Birjand was first divided into five geographical regions (west, east, south, north, and center), and two schools were selected from each region; i.e. a total of 10 schools were selected from the entire city, and the number of girls' and boys' schools was the same (five boys' and five girls' schools). After determining the schools, we randomly selected and examined the adolescents who were obese or overweight from different grades in each school. The weight of the subjects was measured and recorded using a German digital Seca scale, while they were not wearing shoes and had the least amount clothes on. The height of the subjects was measured in meter twice, as they were standing without shoes. The BMI was then calculated by dividing the weight (in kilograms) into height squared (in meters), and the BMI with a percentile of 85 - 94 was considered as overweight with 95 $\leq$ considered as obese.

2.2. Methods

The protocol of the study was approved by the Ethics Committee of Birjand University of Medical Sciences. Written informed consent was obtained from participants and their parents. There are different imaging and laboratory measurements in order to diagnose the presence of fatty liver, including noninvasive assessment of parenchyma of liver using abdominal ultrasonography with an appropriate sensitivity and specificity (14, 15). Therefore, to determine the presence of fatty liver in adolescents who were obese or overweight an abdominal ultrasound was performed by a radiologist after six hours of fasting. The ultrasound method was as follows: in order to calculate the liver span along the midclavicular line, the superior and inferior limits of the liver were determined and the distance was measured with a regular fixed ruler. The liver parenchyma was then evaluated using two subcostal windows in the right upper quadrant (RUQ) and at the coronal section along the Axilary lines. To identify the presence of fatty liver, an increase in the echogenicity of liver parenchyma was determined at the level of fat echo and the detection of portal and hepatic veins. The ultrasound criteria for fatty liver severity include:

Grade 1 (mild): Echogenicity of the liver increases slightly, and the limits of diaphragm and intra-hepatic arteries are normal.

Grade 2 (moderate): Echogenicity of the liver increases moderately, and the limits of diaphragm and intra-hepatic arteries are slightly faded.

Grade 3 (severe): Echogenicity of the liver increases severely, and the limits of diaphragm and intra-hepatic arteries and the posterior part of the right lobe of the liver are faded or hardly observed (16).

Then in second stage , 5 mL of venous blood samples were taken for each subject that had NAFLD for laboratory tests including TG, cholestrol, HDL, LDL, ALT, AST, FBS, CRP, insulin, PLT, uric acid, and 25 OH Vitamin D .The blood samples were sent to the reference laboratory affiliated to Birjand University of Medical Sciences.

2.3. Statistical Analyzing

The data on demographic and clinical observations were analyzed using the SPSS version 22. The descriptive statistical methods including measures of central tendency, dispersion, and frequency distribution were used to describe the subjects' data. The chi-square test was also used to determine the difference in frequencies of fatty groups and the groups under study as well as determine the relationship between age groups and obesity and overweight in adolescents aged 12 to 18 years. We used the Fischer's exact test to determine the relationship between the prevalence of fatty liver in the age groups. To study the effects of age, sex, and BMI on the prevalence of non-alcoholic fatty liver, the forward multivariate logistic regression (conditional) was used based on selection of possible factors if $P < 0.2$ in univariate analysis. In all tests, $P \leq 0.05$ was considered as the significant level.

3. Results

A total of 108 adolescents who were overweight and or obese suffered from NAFLD (i.e. prevalence of this disease was 54%, 95% CI 47 - 61). The frequency of NAFLD in boys and girls was 69.8% and 42.1%, respectively ($P < 0.001$). There was a considerable number of NAFLD in adolescents aged 12 - 13 years and also obese individuals (for both $P < 0.001$) (Table 1). Of the 108 adolescents with NAFLD, grade I, II, and III with 83.3%, 14.8%, and 1.9% had the highest frequency, respectively. Table 2 presents biochemical parameters of blood in adolescents with NAFLD.

Table 3 shows results of the Logistic regression. There was a significant relationship between age, sex, and BMI and the prevalence of non-alcoholic fatty liver ($P < 0.001$). The results clearly indicate the high vulnerability of low-aged adolescents from non-alcoholic fatty liver compared

Table 1. Comparison of Relative Frequency of NAFLD in Overweight and Obese Children in Terms of Gender, Age, and Body Mass Index[a]

Variables	Inflicted with Fatty Liver		P Value	Chi-Square
	No	Yes		
Gender			< 0.001	$\chi^2 = 15.10$
Male	26 (30.2)	60 (69.8)		
Female	66 (57.9)	48 (42.1)		
Age group, y			< 0.001	$\chi^2 = 25.59$
12 - 13	17 (23.3)	56 (76.7)		
14 - 15	45 (64.3)	25 (35.7)		
16 - 18	30 (52.6)	27 (47.4)		
Body mass index, kg/m^2			< 0.001	$\chi^2 = 25.59$
Overweight	58 (64.4)	32 (35.6)		
Obese	34 (30.9)	76 (49.1)		

[a] Values are expressed as No. (%).

Table 2. Biochemical Parameters of Blood in Patients with Fatty Liver

Biochemical Parameters of Blood	Mean ± Standard Deviation	Minimum Value	Maximum Value
WBC	8.24 ± 2.07	4.80	15.50
HB	14.91 ± 1.34	8.40	18.80
PLT	302.03 ± 71.41	184	577
FBS (mg/dL)	92.74 ± 7.04	75	108
Uric acid (mg/dL)	5.65 ± 1.40	2.90	9.40
Chol (mg/dL)	162.47 ± 30.21	95	250
TG (mg/dL)	143.40 ± 63.59	41	340
HDL-c (mg/dL)	38.28 ± 6.89	19	63
LDL-c (mg/dL)	99.60 ± 26.54	46	196
Insulin	24.72 ± 10.71	4.97	62.70
Alb	4.54 ± 0.32	3.80	6.10
AST (IU/mL), median	24.63 ± 7.32	13	46
ALT (IU/mL), median	28.42 ± 14.09	7	84
ALK	220.64 ± 97.40	53	663
CRP	2.26 ± 2.37	0.10	13
Vit D	10.52 ± 5.94	2.10	28.40

to adults (P < 0.001). In addition, the BMI of obese individuals increased the risk of non-alcoholic fatty liver 3.5 times more than that of overweight people, which could well indicate the role of obesity in the prevalence of non-alcoholic fatty liver (OR = 3.57, 95% CI: 1.87 - 6.81). Furthermore, studying the relationship between the prevalence of fatty liver in sex groups clearly showed that the risk of non-alcoholic fatty liver in men was higher than in women, and being a girl significantly reduced their risk of the disease (OR girl = 0.21, 95% CI: 0.10 - 0.43).

Table 3. Logistic Regression Results Between Prevalence of NAFLD and Age, Sex, and Body Mass Index

Groups	OR	95% CI	P Value
Age	0.692	0.579 - 0.828	< 0.001
Gender (girls)	0.214	0.105 - 0.433	< 0.001
BMI (obese)	3.57	1.87 - 6.81	< 0.001

4. Discussion

The present study aimed to assess the prevalence of non-alcoholic fatty liver in obese and overweight adoles-

cents (12 to 18 years) and describe its clinical features. The overall prevalence of NAFLD in obese and overweight adolescents in this study was 54%. Similarly, in a study by Fattahi et al. (17), the NAFLD was reported in approximately half of the patients suffering from metabolic syndrome, where obesity and hypertriglyceridemia are two of its criteria (comparing 25.7% in the general population). The present study clearly shows that obesity at an early life increased the risk of non-alcoholic fatty liver by 3.5 times. Accordingly, Jimenez-Rivera et al. (2), reported that adolescents with NAFLD were at a greater risk of liver-associated disease and a significantly shorter survival than those of similar sex and age. Previous studies by Kazemi et al. (18), Taghavi Ardakani et al. (12), Abangah et al. (19), and Adibi et al. (20), confirmed the findings.

In addition, our study showed that being male was predominantly affected by the NAFLD, similar to the results of the studies by Di Sessa et al. (21), Schwimmer et al. (22), and Tominaga et al. (23), yet opposed to the findings of Fu et al. (24), and Adibi et al. (20). It seems that a difference in sex-hormones and presence of high estrogen levels in younger-aged women during pre-menopause period protects them from NAFLD (25). Anti-oxidative effects of estrogen have been proven leading to inhibition of development of fibers and proliferation of hepatic stellate cell (26, 27). Beside the absence of anti-oxidative effects of estrogen, higher speed of accumulation of visceral adipose tissue in obese men increase the susceptibility of men to NAFLD (28).

Regarding age, the relative prevalence of NAFLD in adolescents aged 12 - 13 years was 76.7%, which is due to the fact that a higher percent of 12 - 13 year-old adolescents were obese. Of the 108 adolescents with NAFLD, 90 (83.3%) had grade 1 NAFLD, 16 (14.8%) had grade 2, and two (1.9%) had grade 3 NAFLD, with grade 1 as the dominant type of NAFLD; this finding is similar to those of Di Sessa et al. (21), Kazemi et al. (18), and Taghavi Ardakani et al. (12).

In this study, various metabolic disorders were found in the adolescents with NAFLD including increased blood sugar and lipid blood levels. It seems that NAFLD is a component of metabolic syndrome.

Another noteworthy finding in this study was that 100% of the adolescents with NAFLD had vitamin D deficiency. Vitamin D deficiency stands as a risk factor for metabolic syndrome; yet interestingly, both are of a high prevalence in the Iranian population (29, 30). Vitamin D holds anti-inflammatory and regulatory properties. It can reduce insulin resistance and increase insulin secretion.

One of the limitations of this study was the technique employed, although the same method, i.e., liver ultrasonography was applied in most studies (16). Nonetheless, the golden diagnostic standard is biopsy, which is invasive. Other imaging techniques that have been employed comprise of magnetic resonance (MR) and computed tomography (CT). Whilst arguably the most precise test to evaluate liver fatty infiltration, MR is nevertheless costly and at times inaccessible in many situations (31, 32). CT, which is more accurate when diagnosing fatty liver, is usually accompanied by radiation exposure; hence, it is not generally applied. Moreover, to quantify the amount of fat and water in the liver, spectroscopy has proven more accurate than the conventional MR images (32, 33). Nonetheless, whereas such tests are accurate, there are limiting parameters including cost and accessibility. Meanwhile, transient elastography is employed as a non-invasive measure that evaluates the extent of fibrosis in chronic liver diseases such as NAFLD (2).

4.1. Conclusions

The results of this study showed that obesity and being male were associated with an increased risk of non-alcoholic fatty liver and, on the other hand, a low BMI and being female significantly reduced it. However, given the inadequacy of causal studies in this area, the generalization of the results of this study should be done with caution. In addition, further studies in this regard can lead to finding out the role of the factors affecting the prevalence of obesity and non-alcoholic fatty liver in adolescents, and implementing preventive and interventional programs in lifestyle and diets that can help reduce the burden of non-alcoholic fatty liver disease in adolescents and therefore, in adults.

Footnotes

Conflict of Interests: None declared.

Ethical Considerations: The study was approved by the Ethics Committee of Birjand University of Medical Sciences (ir.bums.REC.1396). Written informed consent was obtained from participants and their parents.

Funding/Support: Birjand University of Medical Sciences.

References

1. Azizi-Soleiman F, lMotlagh ME, Qorbani M, Heshmat R, Ardalan G, Mansourian M, et al. Dietary habits and health related behaviors in Iranian children and adolescents: The CASPIAN-IV study. *Int J Pediatr*. 2016;**4**(7):2087–97. doi: 10.22038/IJP.2016.6975.
2. Jimenez-Rivera C, Hadjiyannakis S, Davila J, Hurteau J, Aglipay M, Barrowman N, et al. Prevalence and risk factors for non-alcoholic fatty liver in children and youth with obesity. *BMC Pediatr*. 2017;**17**(1):113. doi: 10.1186/s12887-017-0867-z. [PubMed: 28446162]. [PubMed Central: PMC5406891].
3. 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. [PubMed: 22395188].
4. 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].

5. Lavine JE, Schwimmer JB. Nonalcoholic fatty liver disease in the pediatric population. *Clin Liver Dis*. 2004;**8**(3):549–58. viii-ix. doi: 10.1016/j.cld.2004.04.010. [PubMed: 15331063].
6. Malespin M, Sleesman B, Lau A, Wong SS, Cotler SJ. Prevalence and correlates of suspected nonalcoholic fatty liver disease in Chinese American children. *J Clin Gastroenterol*. 2015;**49**(4):345–9. doi: 10.1097/MCG.0000000000000121. [PubMed: 24667593].
7. 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**(7):877–83. doi: 10.1038/sj.ejcn.1602588. [PubMed: 17151586].
8. Mazzone L, Postorino V, De Peppo L, Della Corte C, Lofino G, Vassena L, et al. Paediatric non-alcoholic fatty liver disease: Impact on patients and mothers' quality of life. *Hepat Mon*. 2013;**13**(3). e7871. doi: 10.5812/hepatmon.7871. [PubMed: 23745129]. [PubMed Central: PMC3669678].
9. Alavian SM, Mohammad-Alizadeh AH, Esna-Ashari F, Ardalan G, Hajarizadeh 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].
10. Amirkalali B, Poustchi H, Keyvani H, Khansari MR, Ajdarkosh H, Maadi M, et al. Prevalence of non-alcoholic fatty liver disease and its predictors in north of Iran. *Iran J Public Health*. 2014;**43**(9):1275–83. [PubMed: 26175982]. [PubMed Central: PMC4500430].
11. Moghaddasifar I, Lankarani KB, Moosazadeh M, Afshari M, Ghaemi A, Aliramezany M, et al. Prevalence of non-alcoholic fatty liver disease and its related factors in Iran. *Int J Organ Transplant Med*. 2016;**7**(3):149–60. [PubMed: 27721961]. [PubMed Central: PMC5054138].
12. Taghavi Ardakani A, Sharif MR, Kheirkhah D. Fatty liver disease in obese children in Kashan, Iran. *Caspian J Pediatr*. 2015;**1**(1):17–21.
13. Namakin K, Mohammadifard M, Zardast M, Ebrahimabadi N. The relationship between non-alcoholic fatty liver disease and metabolic syndrome in children. *Int J Sch Health*. 2017;**4**(1). e38135. doi: 10.17795/intjsh-38135.
14. Alizadeh A, Mansour-Ghanaei F, Roozdar A, Joukar F, Sepehrimanesh M, Hojati SA, et al. Laboratory tests, liver vessels color doppler sonography, and fibroscan findings in patients with nonalcoholic fatty liver disease: An observation study. *J Clin Imaging Sci*. 2018;**8**:12. doi: 10.4103/jcis.JCIS_93_17. [PubMed: 29692949]. [PubMed Central: PMC5894278].
15. Uchil D, Pipalia D, Chawla M, Patel R, Maniar S; Narayani, et al. Non-alcoholic fatty liver disease (NAFLD)–the hepatic component of metabolic syndrome. *J Assoc Physicians India*. 2009;**57**:201–4. [PubMed: 19588647].
16. 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**(11):3120–3. doi: 10.1016/j.ejrad.2012.06.020. [PubMed: 22817846].
17. Fattahi MR, Niknam R, Safarpour A, Sepehrimanesh M, Lotfi M. The prevalence of metabolic syndrome in non-alcoholic fatty liver disease: A population-based study. *Middle East J Dig Dis*. 2016;**8**(2):131–7. doi: 10.15171/mejdd.2016.18. [PubMed: 27252820]. [PubMed Central: PMC4885612].
18. Kazemi SA, Kamali K, Asgari L, Eftekhari K. Assessment of the relationship between prevalence of reporting fatty liver disease by ultrasound and body mass index in children. *Iran J Pediatr*. 2017;**27**(1). doi: 10.5812/ijp.8028.
19. Abangah G, Yousefi A, Asadollahi R, Veisani Y, Rahimifar P, Alizadeh S. Correlation of body mass index and serum parameters with ultrasonographic grade of fatty change in non-alcoholic fatty liver disease. *Iran Red Crescent Med J*. 2014;**16**(1). e12669. doi: 10.5812/ircmj.12669. [PubMed: 24719704]. [PubMed Central: PMC3964422].
20. 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):14–9. [PubMed: 19224500].
21. Di Sessa A, Umano GR, Miraglia del Giudice E. The association between non-alcoholic fatty liver disease and cardiovascular risk in children. *Children (Basel)*. 2017;**4**(7). doi: 10.3390/children4070057. [PubMed: 28686220]. [PubMed Central: PMC5532549].
22. Schwimmer JB, Middleton MS, Deutsch R, Lavine JE. A phase 2 clinical trial of metformin as a treatment for non-diabetic paediatric non-alcoholic steatohepatitis. *Aliment Pharmacol Ther*. 2005;**21**(7):871–9. doi: 10.1111/j.1365-2036.2005.02420.x. [PubMed: 15801922].
23. Tominaga K, Fujimoto E, Suzuki K, Hayashi M, Ichikawa M, Inaba Y. 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. doi: 10.1007/s12199-008-0074-5. [PubMed: 19568858]. [PubMed Central: PMC2684773].
24. Fu CC, Chen MC, Li YM, Liu TT, Wang LY. The risk factors for ultrasound-diagnosed non-alcoholic fatty liver disease among adolescents. *Ann Acad Med Singapore*. 2009;**38**(1):15–7. [PubMed: 19221666].
25. Summart U, Thinkhamrop B, Chamadol N, Khuntikeo N, Songthamwat M, Kim CS. Gender differences in the prevalence of non-alcoholic fatty liver disease in the northeast of Thailand: A population-based cross-sectional study. *F1000Res*. 2017;**6**:1630. doi: 10.12688/f1000research.12417.2. [PubMed: 29093809]. [PubMed Central: PMC5645706].
26. Florentino GS, Cotrim HP, Vilar CP, Florentino AV, Guimaraes GM, Barreto VS. Nonalcoholic fatty liver disease in menopausal women. *Arq Gastroenterol*. 2013;**50**(3):180–5. doi: 10.1590/S0004-28032013000200032. [PubMed: 24322188].
27. Ryu S, Suh BS, Chang Y, Kwon MJ, Yun KE, Jung HS, et al. Menopausal stages and non-alcoholic fatty liver disease in middle-aged women. *Eur J Obstet Gynecol Reprod Biol*. 2015;**190**:65–70. doi: 10.1016/j.ejogrb.2015.04.017. [PubMed: 25988514].
28. Ayonrinde OT, Olynyk JK, Beilin LJ, Mori TA, Pennell CE, de Klerk N, et al. Gender-specific differences in adipose distribution and adipocytokines influence adolescent nonalcoholic fatty liver disease. *Hepatology*. 2011;**53**(3):800–9. doi: 10.1002/hep.24097. [PubMed: 21374659].
29. Zardast M, Taheri F, Gholinejadan A, Namakin K, Javadinia S. The relationship between serum 25-hydroxyvitamin d levels and metabolic syndrome in Birjand children, east of Iran. *Int J Pediatr*. 2016;**4**(5):1759–66. doi: 10.22038/ijp.2016.6748.
30. Foroughi M, Maghsoudi Z, Ghiasvand R, Iraj B, Askari G. Effect of vitamin D supplementation on C-reactive protein in patients with nonalcoholic fatty liver. *Int J Prev Med*. 2014;**5**(8):969–75. [PubMed: 25489444]. [PubMed Central: PMC4258669].
31. Bydder GM, Chapman RWG, Harry D, Bassan L, Sherlock S, Kreel L. Computed tomography attenuation values in fatty liver. *J Comput Tomography*. 1981;**5**(1):33–5. [PubMed: 7273824].
32. Di Martino M, Pacifico L, Bezzi M, Di Miscio R, Sacconi B, Chiesa C, et al. Comparison of magnetic resonance spectroscopy, proton density fat fraction and histological analysis in the quantification of liver steatosis in children and adolescents. *World J Gastroenterol*. 2016;**22**(39):8812–9. doi: 10.3748/wjg.v22.i39.8812. [PubMed: 27818597]. [PubMed Central: PMC5075556].
33. Idilman IS, Keskin O, Celik A, Savas B, Elhan AH, Idilman R, et al. A comparison of liver fat content as determined by magnetic resonance imaging-proton density fat fraction and MRS versus liver histology in non-alcoholic fatty liver disease. *Acta Radiol*. 2016;**57**(3):271–8. doi: 10.1177/0284185115580488. [PubMed: 25855666].