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Nonalcoholic fatty liver diseases in obese children and adolescents

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Summary

Aim: To determine the prevelance of the non-alcoholic fatty liver in obese children.

Material and Method: Medical records of 161 obese children (age 4-18 yrs) who were investigated for non-alcoholic fatty liver by USG were analysed retrospectively. Their findings of physical examination and antropometric measurements, presence of acanthosis nigricans, pubertal status and results of laboratory analysis were evaluated. The study protocol was approved by the Osmangazi University Ethical Committee (2010/13).

Results: Hepatosteatosis was found in 40% of the patients by ultrasonography. Elevation of serum alanine aminotransferase (≥40 U/L) was found in 35% of the patients with steatosis. These patients had higher body mass index, HOMA-IR (Homeostasis model of assessment-insulin resistance) and aspartat aminotransferase, alanine aminotransferase, insulin and triglyceride levels and lower HDL-C levels and higher acanthosis nigricans prevalences than the patients without steatosis. Patients with elevated alanine aminotransferase levels had significantly higher trygliceride and lower HDL-C levels than the patients with normal alanine aminotransferase levels. Steatosis prevalences were 32% in girls and 54% in boys ($p<0.01$). The prevalence of elevated alanine aminotransferase was found higher in prepubertal children ($p<0.05$), but, the steatosis prevalences were not different between prepubertal-pubertal children and between prepubertal girls and boys. Pubertal boys had higher steatosis prevalence than pubertal girls ($p<0.05$). The prevalence of steatosis was higher in children with acanthosis nigricans ($p=0.001$). The prevalences of steatosis and elevated alanine aminotransferase levels were not different between children with and without insulin resistance. In a logistic regression model, sex, body mass index and HDL-C were the determinants of steatosis and only HDL-C were related with alanine aminotransferase levels.

Conclusions: High prevalences of hepatosteatosis and elevated alanine aminotransferase levels are found in obese children and adolescents. Gender, the degree of obesity and dyslipidemia are more important determinants of steatosis than insulin resistance. *(Turk Arch Ped 2012; 47: 172-178)*

Key words: Children, insulin resistance, non-alcoholic hepatosteatosis, obese, steatohepatitis

Introduction

Nonalcoholic fatty liver disease (NFLD) is defined as histological presence of lipid deposits in the liver in individuals who do not consume alcohol and who have negative congenital, viral and autoimmune liver disease findings and variables. Although fatty liver disease generally has a benign prognosis, steatohepatitis (SH) characterized by steatosis and/or inflammation and/or accompanied by fibrosis may develop in these patients. SH may result in cirrhosis and hepatocellular carcinoma (1,2,3,4,5,6).

Fatty liver disease has been shown to be the most common cause of chronic liver disease both in adults and children (1,2,3,4,5,6,7,8). It has been reported that the prevalence of NFLD is 20-30%, SH develops in 20-30% of these patients and cirrhosis and mortality related to liver disease occur in 3-8% of the patients with SH (3,7). There are very few population studies investigating the prevalence of nonalcoholic fatty liver disease in the childhood. In studies performed in Asia and USA, it was found that the prevalence of NFLD was 2.6-9.6% in children and adolescents (5) and increased ALT level was found in 8% of the age group of 12-19 years after other causes were excluded (9,10).

The cause of fatty liver disease is not known. It has been reported that obesity is the most important risk factor for NFLD (1,2,3,4,5,6,7). The prevalence of NFLD is considerably high in obese children and adolescents and increases in parallel with the increase in the prevalence of obesity. In a population study

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performed in Italy, the prevalence of NFLD was found to be 16% in children and 76% in obese children (6). In a study, 90% of the individuals who were found to have NFLD/SH with biopsy were found to be overweight or obese and especially abdominal obesity was found to affect NFLD (8).

Patients with fatty liver disease are usually asymptomatic. Hepatosteatosis is shown by ultrasonography (USG), tomography and magnetic resonance imaging methods. Hepatic transaminases are elevated in individuals with steatohepatitis. However, the definite differentiation between simple steatosis and SH is done by biopsy (1,2,4,6,11).

NFLD is being investigated continuously by hepatobiliary USG and transaminase levels in obese children and adolescents referring to our endocrinology outpatient clinic. In this study, it was aimed to determine the prevalence of NFLD and related risk factors in obese children and adolescents who were being followed up in our clinic.

Material and Method

File records of 161 obese children (105 female and 56 male) aged 1-18 years old in whom the presence of NFLD was investigated by ultrasonography in our Pediatric Endocrinology Outpatient Clinic between January 2007 and January 2010 were examined retrospectively. Children who had a systemic disease and who used drugs were not included in the study. None had a history of alcohol consumption. Examination performed at the time of investigation of steatosis by USG and simultaneous test records were evaluated. Approval was given by the ethics committee of our university for the study protocol (2012/13).

Records related to history, physical examination findings, antropometric measurements, acanthosis nigricans (AN), hepatomegaly, adolescence state and laboratory investigations were obtained from the files. A body mass index (body weight/height^2) of ≥the 95th percentile (p) was considered as obese (12).

The records of serum glucose, insulin, lipid and lipoprotein, alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels were evaluated. The cut-off value for ALT was considered as ≥40 U/L. Comparing with source values a triglyceride (TG) value of > the 95th percentile was accepted as hypertriglyceridemia and a HDL-C level of <the 10th percentile was accepted as low HDL-C (13). HOMA-IR (Homeostasis model of assessment-insulin resistance) values were calculated using the formula of glucose (mmol/L) x insulin (μU/ml)/22.5 (14). For insulin resistance HOMA-IR treshold value was considered as 2.22 in prepubertal girls, 2.67 in prepubertal boys, 3.82 in pubertal girls and 5.22 in pubertal boys (15).

For statistical analysis SPSS package program (SPSS, Chicago, IL, Versiyon 13) was used. Shapiro-Wilks test was used for compatibility with normal distribution, independent samples T, Mann-Whitney U and chi-square tests were used for comparisons and Pearson and Spearman correlation analyses were used for correlations. In our study, it was observed that data were lacking for all variables. Therefore, values of the variables (n) lacking data were given in tables. In statistical evaluation of each variable, the variable's own universe was used. In addition, the rates of sensitivity, specificity and negative-positive predictive values of AN, IR (insulin resistance) and ALT level were calculated in determining the presence of steatosis.

In tables, data which showed normal distribution were given as mean±SD, data which did not show normal distribution were given as median (the min-the max). A p value of <0.05 was considered as statistically significant.

Results

When patient files were examined, it was found that ALT and AST levels were measured in 134 patients, TG level was measured in 136 patients and HDL-C level was measured in 124 patients and presence of AN was found to be recorded as positive-negative in 142 patients in examination notes. HOMA-IR could be calculated in 152 patients.

The findings of the patients by presence of steatosis and serum ALT level are shown in Table 1. In 40% of our patients, hepatosteatosis was found by USG. Mild steatosis was found in 61% of these patients, moderate steatosis was found in 31% and severe steatosis was found in 8%. Since the number of patients with severe steatosis was low, the data of these patients were examined together with the data of the patients with moderate steatosis. There was no difference between mild steatosis and moderate-severe steatosis groups in terms of presence of AN, increased ALT level and IR frequencies (p>0.05). In patients with moderate-severe steatosis, AST, TG and total cholesterol (TC) levels were higher compared to the patients with mild steatosis (p<0.05, for all).

In patients with steatosis, median HOMA-IR and AN frequency (68%) were higher compared to the patients without steatosis (p=0.001). The frequency of IR was different according to presence of steatosis (p>0.05).

ALT level was high in 17.5% of the patients in whom ALT was measured and in 35% of the patients with steatosis. Steatosis was found in all patients who had high ALT levels. ALT was not high in any of the patients without steatosis. In patients with normal ALT level, the rate of steatosis was found to be 32%. The frequencies of AN and IR did not differ by the level of ALT (p>0.05).

IR was found in 53% of the patients. The frequencies of steatosis and increased ALT did not differ according to presence of IR (p>0.05). The frequency of acanthosis nigricans was higher in patients with IR (66%) compared to the patients without IR (34%) (p<0.001). IR was found in 49% of the patients who were found to have AN. The frequency of steatosis in patients with and without AN were found to be 54% and 25%, respectively and the frequencies of increased ALT were found to be 21% and 8.5%, respectively (Table 2). While the frequencies of steatosis and ID differed according to presence of AN (p<0.001), the frequency of increased ALT did not differ (p>0.05).

Table 1. Findings according to presence of steatosis on USG and ALT level*

	Steatosis (+) (n=64)	Steatosis (-) (n=97)	p	ALT≥40 (n=20)	ALT<40 (n=114)	p
F/M	34/30	71/26	p<0.01	9/11	77/11	p>0.05
Prepubertal/pubertal	15/49	16/81	p>0.05	7/12	18/96	p>0.05
Age (Months)	151±36	145±37	p>0.05	150±37	130±29	p<0.05
BMI (kg/m^2)	30 (21-48)	27.4 (20-40)	p=0.001	30.7±5.8	28.4±6.1	p>0.05
Waist /hip ratio	0.89±0.07	0.87±0.06	p>0.05	0.88±0.07	0.87±0.06	p>0.05
Glucose (mg/dl)	83±13	84±10	p>0.05	84±21	84±9	p>0.05
Insulin (μıu/L)	21±15	15±10	p<0.01	20±14	17±12	p>0.05
HOMA-IR	3.5 (0.4-17.7)	2.7 (0.3-10.3)	p<0.05	4±4	4±3	p>0.05
AST (U/L)	35±18	21±6	p<0.001	52±14	22±8	p<0.001
ALT (U/L)	28 (10-148)	17 (10-35)	p<0.001	64±26	20±6	p<0.001
AST/ALT ratio	1.05±0.42	1.16±0.47	p>0.05	0.89±0.3	1.15±0.46	p<0.05
TC (mg/dl)	169±33	163±28	p>0.05	173±29	165±31	p>0.05
HDL-C (mg/dl)	42±11	52±25	p<0.001	36±9	50±23	p<0.05
LDL-C (mg/dL)	106±28	97±28	p<0.05	112±28	99±29	p>0.05
TG (ng/dl)	158±87	121±57	p<0.01	193±93	129±70	p=0.01
AN (+/-)(n)	38/18	32/54	p=0.001	12/5	45/54	p>0.05
IR (+/-) (n)	26/35	29/63	p>0.05	6/13	39/68	p>0.05
ALT≥40/ALT<40 (n)	20/37	0/67				
Steatosis (+/-) (n)				20/0	37/67	

*Data are given as median (min-max) or mean± SD according to the status of normal distribution

Steatosis was found in 54% of the boys and in 32% of the girls (p<0.01). 55% of the patients who had increased ALT level were male and 45% were female. The frequencies of AN, increased ALT level and IR did not differ by gender (p>0.05).

The frequency of IR was higher in pubertal children compared to prepubertal children (85% and 15%, respectively) (p>0.05). While the frequency of steatosis was 48% and 38% in prepubertal/pubertal children, respectively, the frequency of increased ALT was 28% and 14%, respectively. The frequency of increased ALT level differed by presence of puberty (p<0.05), whereas the frequency of steatosis did not differ (p>0.05). While the frequency of steatosis was not different in prepubertal boys and girls (p>0.05), it was higher in pubertal boys (52%) compared to pubertal girls (30%) (p<0.05). There was no difference between prepubertal and pubertal groups in terms of the frequencies of AN and IR (p>0.05). There was no difference between pubertal boys and girls in terms of the frequencies of IR, AN and increased ALT level (p>0.05).

In patients with steatosis, TG and LDL-C levels were statistically significantly higher compared to the patients without steatosis and HDL-C level was lower. Hypertriglyceridemia was present in 55% of the patients who had TG record. Steatosis was found in 45% of the patients with hypertriglyceridemia and in 37% of the patients who had normal TG level. The frequencies of steatosis, AN and increased ALT level were not different between these two groups (p>0.05). The frequencies of steatosis (71% and 29%, respectively, p<0.05) and increased ALT level (63% and 27%, respectively, p<0.001) were different between the patients with low HDL-C (n=17) and high HDL-C. Steatosis was found in 9 of 15 patients who had both hypertriglyceridemia and low HDL-C level.

In simple correlation analysis, a positive correlation was found between the degree of steatosis and insulin, ALT and AST (r=0.3, p<0.05, r=0.5, p<0.001 and r=0.3, p<0.05, respectively) and a negative correlation was found between HDL-C and AST and ALT (r=-0.3, p<0.01 and r=-0.2, p<0.05, respectively).

With regression analysis it was found that HOMA-IR alone affected presence of steatosis (p<0.05), presence of steatosis increased 1.14 fold (odds ratio) for HOMA-IR increase of one unit and AN alone increased presence of steatosis 3.56 fold (p<0.05). Body mass index was also found to affect presence of steatosis (p=0.01, odds ration=1.12). It was found that HOMA-IR, presence of AN and BMI alone did not affect ALT level (p>0.05). However, triglyceride and HDL-C affected presence of

Table 2. Findings according to presence of acanthosis nigricans and IR*

	AN (+) (n=70)	AN (-) (n=72)	p	IR (-) (n=78)	IR (+) (n=74)	p
F/M	44/26	50/22	p>0.05	49/29	48/26	p>0.05
Prepubertal/pubertal	13/57	13/59	p>0.05	19/59	11/63	p>0.05
Age(Months)	152±32	145±40	p>0.05	145 ±41	154±30	p>0.05
BMI (kg/m^2)	31.3±6	26.8±5	p<0.001	27±5	30.9±6	p<0.001
Waist/hip ratio	0.89±0.07	0.87±0.68	p>0.05	0.86±0.07	0.9±0.07	p<0.05
Glucose (mg/dl)	85±13	83±10	p>0.05	79±8	88±13	p<0.001
Insulin (μıu/L)	23±14	14±7	p<0.001	10±7	26±12	p<0.001
HOMA-IR	2.2 (0.34-10.4)	4.3 (0.5-17.7)	p<0.001			
AST (U/L)	30±17	24±11	p<0.05	27±12	26±15	p>0.05
ALT (U/L)	30±24	24±16	p>0.05	19 (10-85)	21 (10-148)	p>0.05
AST/ALT ratio	1.09±0.5	1.08±0.4	p>0.05	1.1±0.5	1.09±0.4	p>0.05
TC (mg/dl)	167±26	167±32	p>0.05	166±30	163±28	p>0.05
HDL-C (mg/dl)	47 (22-234)	45 (19-73)	p>0.05	46 (22-234)	45 (19-73)	p>0.05
LDL-C (mg/dL)	101±23	105±32	p>0.05	106±28	97±28	p>0.05
TG (ng/dl)	144±79	135±70	p>0.05	125±68	150±77	p<0.05
Steatosis (+/-) (n)	38/32	18/54	p=0.001	26/52	35/39	p>0.05
ALT≥40/ALT<40 (n)	12/45	5/54	p>0.05	6/39	13/68	p>0.05
AN (+/-)(n)				23/44	45/23	p<0.001
IR (+/-)	45/23	23/44	p<0.001			

* Data are given as median (min-max) or mean± SD according to the status of normal distribution

steatosis and ALT level. As TG increased one unit, steatosis increased 1.01 fold (138 patients) and ALT level increased (114 patients) 1.008 fold (p<0.01). As HDL-C decreased one unit, presence of steatosis increased 1.05 fold and ALT level increased 1.11 fold (p<0,01 and p<0.001, respectively) (125 patients). When the same regression analysis was done with gender, puberty, HOMA-IR, AN, HDL-C and TG, presence of steatosis was found to be affected by gender, HDL-C and BMI. It was found that presence of steatosis was increased 3.4 fold in male patients (p<0.05). As HDL-C decreased one unit, presence of steatosis increased 1.04 fold (p=0.05). As BMI increased one unit, presence of steatosis increased 1.21 fold (p<0.01). In the same regression model (79 patients), HDL-C alone affected ALT and a decrease of one unit in HDL-C increased ALT 1.15 fold (p=0.001).

The sensitivity of acanthosis nigricans, IR and increased ALT level in determining presence of steatosis was found to be 0.68, 0.43 and 0.35, respectively. The specificity of acanthosis nigricans, IR and increased ALT level in determining absence of steatosis was found to be 0.63, 0.69 and 1.0, respectively. Positive predictive values related to steatosis were found to be 0.54, 0.47 and 1.0, respectively and negative predictive values were found to be 0.75, 0.64 and 0.64, respectively. These results showed that AN and ALT levels were more sensitive in determining presence of steatosis and ALT level was found to be more specific.

Discussion

It has been reported that the prevalence of NFLD is high in obese children and adults and continues to increase (1,2,3,4,5,6). In a population study performed in Italy, the prevalence of NFLD was found to be 16%. It was found to be 76% in obese individuals (6). Schwimmer et al. (16) reported that 88% of 43 children who were diagnosed as NFLD with biopsy were found to be obese. Papandreou et al. (17) reported that they found steatosis in 42% of obese children on USG. In another study, 90% of individuals who were found to have NFLD/SH by biopsy were overweight or obese and especially abdominal obesity affected NFLD (8). Nobili et al. (18) found NFLD in 85% of 87 obese children by biopsy and SH in 58% of these patients after excluding the causes which may increase ALT level in 3280 children in whom increased ALT level was found in the emergency outpatient clinic. Loguercio et al. (19)

showed that 70% of the individuals who were being followed up for one year with increased ALT and/or GGT level were obese and mild fibrosis in the liver and steatosis accompanied by inflammation were found in 80% of these patients by biopsy.

In our country, the prevalence of NFLD in children and adults has not been investigated in a population-based study. In a study performed in Ankara in obese children, hepatosteatosis was found with a rate of 52% on USG and increased ALT level was found with a rate of 14% (20). In Denizli, steatosis was found on USG in 47% of 322 obese children and increased ALT was found in 8% (21).

In our study, hepatosteatosis was found in 40% of obese children and adolescents on USG and increased ALT level was found in 17.5%. Simple steatosis is considered in patients with normal alanine aminotransferase level, but presence of steatosis and SH is considered in patients with high ALT level and steatosis. However, liver biopsy is necessary for a definite diagnosis of SH. Biopsy was not performed in our patients. Simple steatosis has a benign prognosis. However, patients with steatosis carry a risk in terms of hepatic damage and inflammation and enter the adulthood with a risk of chronic liver disease.

In our study, obesity was found to be more severe in individuals with steatosis. In addition, our patients carried cardiovascular risk factors including IR and dyslipidemia and the characteristics of metabolic syndrome (MS). Fatty liver disease was found to be related to atherosclerosis and the risk of cardiovascular disease was found to be increased in these patients (7,22,23). The prevalence of NFLD was reported to be increased by 2-3 fold in individuals with metabolic syndrome and type 2 diabetes mellitus compared to the general population (7). Manco et al. (8) found that most of the patients with NFLD had hypertriglyceridemia and low HDL-C, 40% had hypertension, 10% had inadequate glucose tolerance and 65% has MS, 2% had type 2 diabetes at the time of diagnosis and 8% developed type 2 diabetes in the future and presence of more than one MS criteria in these patients increased the risk of SH. It has also been suggested that fatty liver disease reflects hepatic involvement of MS (3,4). Some investigators think that NFLD should be included in the diagnostic criteria of MS (24).

Insulin resistance is the most important pathophysiologic factor which is involved in development and progression of NFLD (1,2,3,4,5,7,23). HOMA-IR is high in patients with NFLD (2,16,25,26,27). In a study, it was found that all children who were found to have steatosis by biopsy had IR and fasting insulin levels, HOMA-IR and QUICKI (quantitative IS check index) were found to be compatible with hepatic histological findings (16). In another study, HOMA-IR was shown to be high in obese girls with increased ALT levels and ALT level increased by 0.27 as HOMA-IR increased for one unit (27). In individuals with prediabetes, insulin sensitivity decreased as the degree of steatosis increased and beta cell functions were disrupted independent of obesity (24). In patients with type 2 diabetes, the rate of NFLD has been reported to be 30-50% (28). It was shown that hepatic volume was reduced, transaminase levels decreased and hepatic histology was improved with use of antidiabetic drugs in patients with type 2 diabetes mellitus (28). These results suggest the role of NFLD in the pathogenesis of IR.

In our study, high prevalence of HOMA-IR and AN in patients with steatosis and the fact that presence of AN increased presence of steatosis suggested the correlation between steatosis and IR. However, the prevalences of steatosis and increased ALT level did not differ according to presence of IR.

Acanthosis nigricans is a finding of IR on the skin. AN was found in 30% of the patients with fatty liver disease and in 50% of the patients with SH (2,5,7,8). Rashid et al. (29) reported that AN was found in 13 of 36 children with NFLD. AN was found with a rate of 49% in our study group and with a rate of 68% in the patients with steatosis. In our study, it was shown that the prevalence of IR and steatosis was 2 fold higher in patients with AN compared to the patients without AN, ALT level was 2-3 fold higher and AN was more sensitive in determining the prevalence of steatosis. In addition, a strong correlation was found between AN and presence of steatosis. These results suggest that AN is a better marker in predicting presence of steatosis compared to HOMA-IR.

Hypertriglyceridemia has been defined as a risk factor for NFLD (10). It has been shown that hypertriglyceridemia is related with steatosis in children (1) and most children with NFLD have hypertriglyceridemia and low HDL-C (8). In our study, the prevalence of steatosis did not differ according to presence of hypertriglyceridemia. However, TG and HDL-C levels were found to affect both presence of steatosis and ALT levels. In addition, it was found that the prevalences of steatosis and increased ALT level were increased in individuals with low HDL-C and a negative correlation was found between HDL-C and ALT and AST. Our results show that dyslipidemia is one of the important factors related to NFLD.

In our study, it was observed that the patients with high ALT levels were younger, had high TG levels and low HDL-C levels. There was no difference between the patients with high ALT and normal ALT in terms of steatosis and IR variables. It was understood that lipid variables and especially HDL-C level affected ALT level.

In the pathogenesis of fatty liver disease, “double impact hypothesis” has been proposed. The first impact is accumulation of fat in the liver on the background of hyperinsulinemia and IR which are also related to diet. Our patients carried the risk factors of the first impact including obesity, IR and dyslipidemia. Hepatic damage (inflammation and fibrosis, SH) develops and progresses with the second impact. Mitochondrial dysfunction, increased oxidative stress, endotoxins and increased apoptosis have been accused for the second impact (3,5,8). These factors were not investigated in our study.

In our study, no difference was found between the prepubertal and pubertal groups in terms of prevalences of steatosis, AN and IR. Increased HOMA-IR and BMI found in pubertal patients can be evaluated to be compatible with

physiological increase in body weight and IR in this period. Increased prevalence of high ALT level in prepubertal children suggested that these children carried a risk of SH.

It has been reported that the prevalence of fatty liver disease is higher in women in the adulthood (2,6) and in boys in the childhood (2/1) (1,2,5,6,24). We found no difference between the girls and boys in terms of steatosis, lipid and IR variables in the whole of our study group. However, it was found that male gender increased presence of steatosis and steatosis was more prevalent in males. While the prevalence of steatosis was higher in pubertal boys compared to pubertal girls, it showed no difference between prepubertal girls and boys. No difference was found between pubertal girls and boys in terms of prevalences of IR, AN and increased ALT level. Thus, a protective factor is thought to be present in girls in the puberty. It has been reported that the prevalence of NFLD is increased in menopause (30). The difference in the prevalence of NFLD according to gender was proposed to be related to the level of sex steroids (estrogen/testosterone ratio), expression of sex steroid receptors in the liver or growth hormone release pattern (1,6,11).

In our study, positive correlation between the degree of steatosis and AST and ALT levels and high levels of AST in patients with moderate-severe steatosis suggested that these patients carried a risk of SH/fibrosis, because a ratio of AST/ALT>0.8-1 has been defined to be a risk in terms of hepatic fibrosis (1,6,9,16).

The facts that our study was a retrospective study and viral hepatitis markers which are needed in the differential diagnosis of NFLD were not tested were limitations of our study in terms of assessment of our results. However, hepatitis findings were not present in any of our patients. The patients who were included in our study were the ones who were expected to have developed hepatosteatosis while doing investigations because of obesity and who were investigated in this direction objectively.

Conclusively, hepatosteatosis and high ALT are found with a considerably high rate in obese children and adolescents. The prevalence of IR and AN is increased in patients with steatosis. Although IR is also an effective factor, AN is a better indicator of presence of steatosis. Gender, the degree of obesity and dyslipidemia are effective factors for presence of steatosis. Male gender is a risk factor for steatosis. The prevalence of steatosis is higher in boys and especially in pubertal boys. Dyslipidemia and especially HDL-C level affects serum ALT level.

Obese children with steatosis and high ALT carry a risk for development of diabetes and cardiovascular disease because of characteristics including IR and dyslipidemia as well as chronic hepatic disease. Therefore, obese children and adolescents should be investigated in terms of hepatosteatosis and MS and life-style changes including diet and exercise and/or pharmacological treatment plans in appropriate cases should be implemented.

Conflict of interest: None declared.

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