Fatty liver in obese children: prevalence and correlation with anthropometric measurements and hyperlipidemia

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SUMMARY: Arslan N, Büyükgebiz B, Öztürk Y. Fatty liver in obese children: prevalence and correlation with anthropometric measurements and hyperlipidemia. Turk J Pediatr 2005; 47: 23-27.

The aim of this study was to evaluate the correlation of ultrasonography-proven fatty liver with liver functions, serum lipid levels and anthropometric measurements in children with exogenous obesity. Three hundred and twenty-two patients (183 girls, 56.8%) with a mean age of 11.4±3.2 years (4-18 years) who presented with the complaint of obesity were enrolled. In 38 (11.8%) patients, increased liver echogenicity resembling fatty liver was found (Group 1). The body mass index percentages of group 1 patients were significantly higher than of those without fatty liver (Group 2) (157.7±18.0 vs 151.3±17.8, p=0.038). Alanine and aspartate aminotransferase levels of group 1 patients were significantly higher than of group 2 (p=0.002 vs p=0.028, respectively). Triglyceride levels were significantly higher in group 1 patients (120.8±88.8 vs 100.5±58.5 mg/dl, p=0.044). In conclusion, ultrasonography is an easy and noninvasive method for the diagnosis of fatty liver in children with obesity. Body mass index and serum lipids were higher in group 1 patients. The diagnosis and early treatment of obesity in childhood is important for the prevention and better treatment of related complications. Thus, ultrasonography should be a part of the early evaluation of obese children.

Key words: fatty liver, child, obesity, aminotransferase, lipids.

Non-alcoholic fatty liver disease has been described as permanent hepatic damage and elevated serum alanine aminotransferase levels (ALT) in the patients with no hereditary, toxic or infectious causes or alcohol usage[1,2]. Even though the etiology of the disease is unknown, its relationship with hyperlipidemia, obesity and diabetes has been reported[1-4]. Asymptomatic liver diseases like steatosis and steatohepatitis are frequently seen in adult obese patients[5]. In recent years, physicians have become increasingly interested in childhood obesity and accompanying steatohepatitis, and many trials have been published about these topics[6-9]. Non-alcoholic fatty liver disease may not be easily recognized since obese children usually have no symptoms and only hepatomegaly. In most instances, an incidental finding of abnormal serum aminotransferases leads to the diagnosis of fatty liver in adults and children.

The histopathologic features of non-alcoholic fatty liver disease include steatosis that is primarily macrovesicular, inflammation that is usually mild, and variable degrees of fibrosis[10,11]. The gold standard tool for diagnosis is liver biopsy. Liver biopsy findings are effective as a prognostic indicator, but liver biopsy is invasive and costly. Although imaging techniques have been helpful in assessing non-alcoholic fatty liver and steatosis, they lack the ability to identify fibrosis[11,12].

The aim of this study was to evaluate the correlation of ultrasonography (US)-proven fatty liver with liver enzymes, serum lipids and anthropometric measurements in children with exogenous obesity.

Material and Methods

The study population consisted of 355 patients who were admitted to Dokuz Eylül University Medical Faculty, Pediatric Gastroenterology, Hepatology and Nutrition Department, with complaint of excess body weight. Of these, one patient had Cushing's syndrome, 23 patients used steroids, one patient had complete gonadal dysgenesis, six patients had growth hormone

deficiency and two patients had diabetes, and they were excluded. The remaining 322 patients (183 girls, 56.8%) were enrolled into the study.

Physical examinations and anthropometric measurements of all the patients were performed. The calculated body mass indexes (BMI: weight/height^2) of the patients were proportioned to the BMI of age- and sex-matched children in the 50th percentile, then multiplied by 100. The ratio above 120 was accepted as obesity[13]. Hepatomegaly was defined as a liver edge greater than 2 cm below the right costal margin[14].

Biochemical tests of patients were performed after a 12-hour fasting period. The levels of fasting serum glucose, alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma glutamyl transpeptidase (GGT), total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) and triglycerides were measured. ALT and AST normal limits were 5-45 U/L[15]. Total protein, albumin, total bilirubin and prothrombin time were tested if the patients' AST and ALT levels were above the accepted value. Hepatotropic viruses and TORCH serologies, serum copper and ceruloplasmin levels, serum alpha 1-antitrypsin level (9/15 patients), and autoantibodies against nuclear, smooth muscle, liver and kidney microsomal type-1 antigens (8/15 patients) were screened to eliminate infectious, metabolic and immunologic liver pathologies.

Liver ultrasonographies of all patients were performed by the same radiologist. Three ultrasonographic criteria are used to diagnose fatty liver[7,16]. For each criterion a score was assigned as an indicator of the level of fatty infiltration. A score of two (++) indicated a definitive positive finding of fatty infiltration. A score of one (+) indicated a probable fatty infiltration. When fatty infiltration was negative (–), a score of zero was assigned. The sum of the scores for the three criteria was considered to be an indicator of severity of fatty infiltration. Thus, the fatty liver indicator ranged from zero to six, with fatty liver indicated by a total score of three or more. The criteria and scoring assignments are described below.

1. The ECHO levels for the liver and kidney parenchyma were compared. An evaluation was made of the relative increase in the liver versus kidney surface ECHO level accompanied by a high contrast between liver and kidney parenchyma (liver-kidney ECHO discrepancy). A large discrepancy between hepatic and renal echoes resulted in a ++ finding. A slight increase in liver echogenecity, that is, a slight increase of liver and kidney ECHO discrepancy, was assigned a + evaluation. A negative (–) evaluation of fatty liver was made when the ECHO level was homogeneous and the contrast between the liver and the kidney parenchyma was unclear.

2. An assessment was made of ECHO penetration into the deep portion of the liver. Penetration of US at the deepest portion of the liver is low due to interference from enhanced liver surface echogenecity. This results in an opacity of the lower part of the liver and the loss of visibility of the diaphragm. A ++ evaluation was given when both indications were definitely present. The probable presence of both indications resulted in a + score, while a – evaluation meant that the liver structure was clearly defined from the surface of the liver to the diaphragm.

3. The clarity of the hepatic vessels in the sonography, especially the veins, was evaluated. When hepatic vessel structures were not clear and the identification of the vessel walls could not be made, a ++ evaluation was assigned. If loss of echoes from the vessel wall was observed, a + score was given. A-score resulted when the vessel structures and vessel walls could be clearly defined.

Ages, %BMIs, hepatic function tests, serum glucose and lipid levels of the patients with fatty liver (group 1) and the patients with normal liver echogenicity at US (group 2) were compared.

Data were analyzed by SPSS software 10.0. Chi-square test and Student's t test were used for comparing group ratios and group averages, respectively. A p value less than 0.05 was considered significant.

Results

The mean age of patients was 11.4±3.2 years (range 4-18 years). Hepatomegaly and acanthosis nigricans were detected in 8 and 53 patients, respectively, but none had splenomegaly or signs of chronic liver disease. All tests used to eliminate chronic hepatic diseases due to metabolic, infectious and immunologic etiologies were negative. At admission, the mean %BMI

was found as 152.1±17.9. Demographic properties and biochemical values of patients are shown in Table I.

Table I. The Demographic, Physical and Biochemical Parameters at Admission

	Mean±SD (Range)
Age (year)	11.4±3.2 (4-18)
Sex (F/M)	183/139
Weight for height (%)	151.5±17.9 (121-212)
%BMI	152.1±17.9 (121-214)
Serum glucose (mg/dl)	94.3±9.7 (58-121)
ALT (U/L)	23.1±9.8 (5-77)
AST (U/L)	24.6±9.3 (9-77)
GGT (U/L)	15.7±6.4 (5-45)
Total cholesterol (mg/dl)	168.7±34.35 (110-358)
HDL-C (mg/dl)	46.6±13.4 (35-204)
LDL-C (mg/dl)	103.0±29.6 (60-304)
Triglyceride (mg/dl)	102.9±47.2 (35-388)

BMI: body mass index; ALT: alanine aminotransferase; AST: aspartate aminotransferase; GGT: gamma glutamyl transpeptidase; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol.

The mean fasting serum glucose level was 94.3±9.7 mg/dl at admission. In 13 patients, fasting serum glucose levels were higher than 110 mg/dl and found normal in repeated tests.

In 38 (11.8%) patients, increased liver echogenicity resembling fatty liver was found. Fatty liver was found. Fatty liver was more frequent in boys than girls (15.1% and 9.3%, respectively), but the difference was not significant (p=0.153). Age of the patients with fatty liver was 11.6±2.9 years (range 5-18 years). Weight for height values and %BMIs of the patients with fatty liver were 156.2±17.4 (range 129-207) and 157.7±18.0 (range 121-206), respectively.

Serum ALT levels in seven patients, AST levels in five patients and both AST and ALT levels in three patients (totally 15 patients, 4.6%) were higher than normal values. None of these patients had steroid or other medication usage, malignancy or hepatic diseases in their family. Moreover, serum total protein, albumin, total bilirubin levels and prothrombin times of these patients were all within normal limits.

Aminotransferase levels of nine patients with fatty liver were elevated. ALT levels in five, AST levels in two, and both AST and ALT levels in two were higher than normal values.

The mean GGT level was 15.7±6.4 U/L (range 5-45) at admission. GGT levels of 12 patients were higher than normal limits for their ages (1-10 years: <32; older than 10 years: <24 U/L)[15]. At US, fatty liver was found in eight patients of 12; six of these patients' aminotransferase levels were also high.

Ages, %BMIs, hepatic functions, serum glucose and lipid levels of the patients with fatty liver and the patients with normal liver echogenicity at US were compared (Table II). The mean %BMI of patients with fatty liver was significantly higher than of the others (157.7±18.0 vs 151.3±17.8, p=0.038). Likewise, mean ALT and AST levels were significantly higher in patient group 1 versus

Table II. Demographic, Physical and Biochemical Parameters of the Patients with Fatty Liver (group 1) Versus Those with Normal Liver Echogenicity at US (group 2)

	Mean±SD		
	Group 1 38 (11.8%)	Group 2 284 (88.2%)	P
Age (year)	11.6±2.9	11.4±3.2	0.618
Sex (F/M)	17/21	166/118	0.153
Weight for height (%)	156.2±17.4	150.9±17.9	0.084
%BMI	157.7±18.0	151.3±17.8	0.038
Acanthosis nigricans (positive/patients)	10/38	43/284	0.081
Serum glucose (mg/dl)	96.8±11.0	94.0±9.5	0.142
ALT (U/L)	31.3±16.6	22.0±7.9	0.002
AST (U/L)	29.8±15.5	23.9±7.9	0.028
GGT (U/L)	20.2±12.2	15.1±6.9	0.001
Total cholesterol (mg/dl)	176.0±41.9	187.7±33.6	0.163
HDL-C (mg/dl)	44.8±8.4	46.8±13.9	0.396
LDL-C (mg/dl)	110.2±44.0	102.0±27.1	0.274
Triglyceride (mg/dl)	120.8±88.8	100.5±58.5	0.044

US: ultrasonography; BMI: body mass index; ALT: alanine aminotransferase; AST: aspartate aminotransferase; GGT: gamma glutamyl transpeptidase; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol.

group 2 (p=0.002) and p=0.028, respectively). Moreover, fasting triglyceride levels were significantly higher in group 1 (120.8±88.8 vs 100.5±58.5 mg/dl, respectively, p=0.044).

Discussion

In this study, increased liver echogenicity resembling fatty liver at US in 11.8% and elevated serum aminotransferase levels in 4.6% of the obese patients were found. Vajro[17] and Tazawa[18] have determined that the prevalences of the elevated aminotransferase level in obese patients were 10% and 24%, respectively. Highest normal limit of ALT was 30 U/L in the second study, but this was 45 U/L in our study. A study with a large number of school-aged children showed a prevalence of fatty liver at US in 22.5% of cases with BMI>20[7]. In another study in Italy, the children between 4.5 and 15 years old were screened for steatohepatitis with US, and the prevalence of fatty liver was found as 52%. In the same study, elevated serum aminotransferases were found in 25%[8]. In that study, both fatty liver and elevated aminotransferase frequencies were found higher than ours, but those differences may be due to higher weight for height ratio (159.9±20.9) than in our study (151.5±17.9).

In our study, %BMIs of group 1 patients were significantly higher than of group 2 (157.7±18.0 and 151.3±17.8, respectively). In two previous studies, similar results were also found[7,8]. In one of them, by Franzese et al.[8], mean weight for height ratio in obese children with fatty liver was 167.3±22.3 and with normal liver was 152.0±16.2. Very similar findings were also found in adult studies[1,4].

In this study, there was no difference between the prevalence of fatty liver in obese boys and girls. Althought fatty liver was found more frequently in boys than girls, the difference was not significant (15.1% and 9.3%, respectively, p=0.153). In the studies of Franzese et al.[8] and Tominaga et al.[7], there was no difference between fatty liver prevalences between boys and girls. In the study of Baldridge et al.[19], 14 patients with steatohepatitis were found and 10 were boys.

Aminotransferase levels of nine patients with fatty liver were elevated. In adults with steatohepatitis, mild or moderately increased aminotransferase levels were found in 70-100% of cases[3,5]. In the studies, high ALT levels in obese were found more frequently as in our study[5,17,20]. But the cause is not clearly known. On the other hand, an AST:ALT ratio greater than 1 is found in adults with alcoholic fatty liver disease, but also in advanced liver fibrosis, possibly because of impaired clearance of AST by sinusoidal liver cells[11,21]. In the literature, a positive correlation was reported between the level of aminotransferases and degree of histological findings[22]. Aminotransferase levels of patients whose liver was found as severely fatty at magnetic resonance imaging (MRI) and US were also higher[8,9].

Hyperlipidemia is also frequently seen with steatohepatitis. Serum triglycerides and/or LDL-C levels might be elevated in patients with fatty liver. In our study, serum triglyceride levels were found significantly higher in patients with fatty liver than in the others. In other studies, which included children and adults, hyperlipidemia prevalence was detected as varying between 21-44% in the patients with fatty liver[1,3,23].

Fatty liver results from accumulation of fatty acids in various forms, predominantly triglycerides[3,19]. This accumulation occurs when there is a shift in fatty acid metabolism to favor net lipogenesis rather than lipolysis[5]. This can occur when the amount of fatty acid supplied to the liver from the gut or adipose tissue exceeds the amount needed for mitochondrial oxidation, phospolipid and cholesterol ester synthesis[5,11]. This is the presumed mechanism for steatosis in the setting of diabetes mellitus, obesity, malnutrition, acute starvation, total parenteral nutrition, steroid treatment and excessive dietary intake of fats[3,5,24]. Hyperinsulinemia and insulin resistance may be important components in the development of steatosis in these diseases[6,25]. In hyperinsulinemia, fatty acids are esterified to triglycerides[25]. In the study performed by Rashid et al.[6], acanthosis nigricans, which is a cutaneous marker of hyperinsulinemia, was detected in 13 of 36 patients with non-alcoholic fatty liver. Similarly, acanthosis nigricans was detected in 10 patients with fatty liver in our study.

The relation between diabetes and steatohepatitis is clearly known[25]. Therefore, we did not include diabetic patients in our study. There was no difference between mean blood glucose levels of the group 1 versus group 2, patients. The control blood glucose was found normal in the patients having levels higher than 110 mg/dl at

adminission; the first values were interpreted as a result of the test being performed before the passage of a sufficient starvation period.

In conclusion, US is an easy and noninvasive method for the diagnosis of fatty liver in children with obesity. As shown in our study, aminotransferase levels increased in only a portion of the patients with fatty liver and thus alone are not enough for the diagnosis of fatty liver. US should be a part of the early examination of obese children because diagnosis and treatment of obesity in childhood is important for the prevention and early treatment of related complications. Informing patients and their parents about clinically silent liver disease and the benefical effects of weight reduction might also help in compliance of patients, since it is hard for pediatricians to effectively persuade the children reagarding the benefits of dieting and exercise programs.

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