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Features of the Liver Sonoelastography Findings in Patients with Type 1 Diabetes Mellitus in Childhood

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ABSTRACT

Introduction: The prevalence and association of type 1 diabetes mellitus (T1D) and non-alcoholic fatty liver disease (NAFLD) have been explored; however, no study has examined liver parenchyma elasticity in pediatric T1D patients without NAFLD. Two-dimensional shear wave sonoelastography (2D-SWE) can effectively detect and grade fibrosis in liver diseases that can be seen in T1D patients. The aim of this study was to analyze the 2D-SWE results of the liver in T1D children without NAFLD to identify any potential effects early.

Methods: This prospective case-control study included 53 T1D patients (11.4±3.2 years) and 50 healthy children [12.5 (6) years]. None of the individuals were obese. Both groups had normal grayscale echogenicity, lipid profiles, and liver enzyme levels, ruling out NAFLD. The mean elasticity value was calculated as kiloPascal (kPa) by measuring in the right lobe of the liver. Correlations between elasticity and aspartate aminotransferase (AST), alanine aminotransferase, fasting blood glucose (FBG), duration of diabetes mellitus, and hemoglobin A1c (HbA1c) were evaluated and compared. $P<0.05$ indicates statistical significance.

Results: T1D had a higher liver 2D-SWE [5.4 (2.5) kPa] than controls (4.5±0.8 kPa) ($p<0.05$). T1D had a lower AST and a higher FBG than controls ($p<0.05$). The mean HbA1c of T1D was 8.3(2.4) mmol/mol and correlated with the duration of diabetes. FBG values and kPa values were correlated ($p<0.001$). There was no correlation between other variables and liver kPa (all; $p>0.05$).

Conclusion: Although liver function tests, lipid profiles, and grayscale ultrasonography showed no abnormalities in our pediatric T1D patients, increased liver parenchymal stiffness detected by 2D-SWE compared with the healthy group indicated hepatic involvement. Therefore, 2D-SWE follow-up may help detect liver involvement and NAFLD before grayscale and laboratory findings arise. Long-term follow-up studies involving a larger population of T1D patients would be beneficial in establishing quantitative reference values for 2D-SWE and will enhance the literature on this topic.

Keywords: Shear wave elastography, type 1 diabetes mellitus, liver, NAFLD, pediatric

Introduction

Type 1 diabetes mellitus (T1D) is frequent among wealthy children and is associated with metabolic dysregulation and liver abnormalities. The primary cause is autoimmune damage to pancreatic insulin-secreting beta cells (1). Organ-specific autoantibodies in patients with T1D indicate several immunological disorders (2). The autoimmune mechanism that leads to this disease may potentially produce autoimmune hepatitis (AIH), according to the literature (1). AIH type 2 liver/kidney microsomal autoantibodies target cytochrome *P4502D6*, whereas T1D carboxypeptidase *H3351* shares an amino acid motif. Other organs with comparable protein sequences can be affected by tissue-specific autoantibodies. This cross-reactive immunological mechanism can induce autoimmune illness in susceptible individuals (2). Non-alcoholic fatty liver disease (NAFLD) (3), the most common pediatric liver disease, is expected to become a clinical problem as T1D patients become more obese. In patients with T1D, blood sugar and insulin fluctuations inhibit glycogenesis and glycogenolysis and cause glycogenic hepatopathy, whereas insulin treatments promote glycogenic accumulation. Tight glycemic control can suddenly improve or regress GH. On ultrasound (US), hyperechogenic liver and/or hepatomegaly may be seen in children with T1D due to excess glycogen or fat. In T1D, they can mimic each other and confuse the diagnosis (1,4). Steatosis, a precursor to fibrosis, may have different Two-dimensional shear wave sonoelastography (2D-SWE) elasticity than reversible GH. Non-invasive quantitative data can distinguish these two illnesses and be used alongside clinical data to diagnose and treat them. NAFLD-type liver disease has been identified as an early indicator of metabolic disorders. Chronic hyperglycemia, poor glycemic management, high-fat, low-carbohydrate diets, and hypoglycemia phobia in patients with T1D may contribute. Normal-weight T1D patients should be tested for NAFLD to reduce cardiometabolic risk (5). Liver biopsy,

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the gold standard for identifying fibrosis, is invasive, expensive, and less common in children because it may cause pain or bleeding. Practical, non-invasive methods are essential in daily practice (6). Standard US is the first imaging modality used to diagnose fatty liver, but it is insensitive in identifying mild steatosis, differentiating it from steatohepatitis, or staging fibrosis (7). 2D-SWE, transient elastography (TE), and point shear wave sonoelastography (pSWE), as well as MR elastography, have been used to non-invasively measure liver stiffness (8-10). TE, commonly known as FibroScan, is a promising radiographic approach for staging hepatic fibrosis that resembles liver biopsy in predicting liver-related outcomes across chronic liver disorders. These include chronic viral hepatitis, NAFLD, non-alcoholic steatohepatitis, AIH, and primary biliary cirrhosis (1). Diagnostic distinguishing of T1D liver illnesses such as AIH and glycogenic hepatopathy can be helped by 2D-SWE (11). SWE can effectively evaluate liver fibrosis in juvenile patients with NAFLD. Guidelines support this reliable, non-invasive method for the detection of steatohepatitis and hepatic fibrosis (9,12).

Unlike TE, 2D-SWE analyzes tissue elasticity simultaneously with B-mode assessment and based on anatomy. 2D-SWE uses targeted US scanning to collect strain images of tissue responses generated by local mechanical compression (13). SWE predicts hepatic fibrosis (14). Quantitative maps and hardness-based elastography colors can quantify 2D-SWE homogeneity (13). SWE includes vibration-controlled transient elastography, pSWE, and 2D-SWE. 2D-SWE generates liver tissue elasticity maps in real time using a large tissue area. 2D-SWE region of interest (ROI) gives a broad field of view, rapidity, high patient compliance, and good observer [intraclass correlation coefficient (ICC): 0.93-0.95] and interobserver (ICC: 0.88) coefficients (15).

Current guidelines indicate elastography for NAFLD suspicion, although there is inadequate data for children (15). pSWE and 2D-SWE were not mentioned in practice guidelines due to inadequate data (12). Further 2D-SWE research in pediatric patients is required.

There are no studies evaluating the normal elasticity of the liver parenchyma in pediatric T1D patients. In addition, parenchymal elasticity may have begun to be affected during the subclinical period when NAFLD gray scale US and laboratory findings are not established. Considering these factors, we aimed to evaluate liver findings and clinical data with 2D-SWE in children with T1D without NAFLD and to obtain data for early detection of possible changes in liver elasticity.

Methods

This study was conducted in accordance with the Helsinki Declaration's standards. University of Health Sciences Turkey, Kartal Dr. Lütfi Kırdar City Hospital's Ethics Committee approved the study (approval number: 2022/514/225/5, date: 11.05.2022). Written informed consent was obtained from the patients' parents.

Study Design and Population

This study was conducted as a prospective case-control study in a single centre.

The study involved 65 pediatric patients aged 4 to 17 diagnosed with T1D under the care of a pediatric endocrinologist. Key parameters assessed included age, gender, fasting blood glucose (FBG), aspartate aminotransferase (AST), alanine aminotransferase (ALT), hemoglobin A1c (HbA1c), duration of diabetes mellitus, gray-scale US, and sonoelastography findings (kPa values). The inclusion criteria comprised individuals diagnosed with T1D by a pediatric endocrinologist for at least 6 months, with a C-peptide level <1 mmol/L at diagnosis, and at least one positive diabetes antibody (anti-insulin, anti-islet, or anti-glutamic acid decarboxylase). In the case group, 3 patients were excluded because of elevated body mass index (BMI) standard deviation score (SD score) (>1) during elastography measurement; 4 patients were excluded because current blood tests could not be obtained; 2 patients were excluded because of concomitant hypothyroidism and celiac disease; and 3 patients were excluded because of suspicious hyperechogenicity in grayscale US evaluation. Consequently, the study included a total of 53 patients. Lipid panels were available for all patients with T1D in the study, and none exhibited hyperlipidemia.

The control group comprised children aged 4 to 17, matched for age and gender with the case group. These healthy individuals were admitted to our clinic for various reasons, had no diagnosed diseases, showed no abnormalities in laboratory tests, and were not on any medication. Written informed consent was obtained from the subjects' parents before inclusion in the study. The exclusion criteria encompassed any history of diseases or medication use affecting liver parenchyma and the presence of hepatomegaly or hepatosteatosis on grayscale evaluation. Neither the T1D patients nor the control group were obese.

Grayscale and Shear Wave Elastography Techniques

A Samsung RS85 F4N/WR device with a convex probe (CA1-7A/FR43Hz/16 cm) was used for grayscale and elastography measurements. We evaluated liver size and the presence of steatosis using gray-scale ultrasonography. We measured the liver size at the midclavicular line and assessed hepatomegaly using reference values (16). We assessed steatosis using visual analysis with optimal gain adjustment (17). Measurements were performed blindly by a single radiologist with at least 5 years of expertise in sonoelastography. All measurements were performed under optimal fasting conditions. All measurements were performed with the patient in the supine position, with the right arm in maximal abduction and in the mid-respiratory phase. No pressure was applied to the probe, and the operator's hand was kept steady during the SWE measurements. An adequate US gel was used for elasticity measurements. The 2D-SWE technique employed in our study generates real-time tissue elasticity maps, with harder tissues depicted in red and softer tissues in blue (15). Shear wave speed measurements were algebraically converted to Young's modulus (kPa) to evaluate tissue stiffness. Measurements were taken using a 10 mm ROI, positioned 2 cm away from vascular structures and the subcapsular region in the right lobe of the liver, which is less susceptible to respiratory artifacts and offers better imaging (Figure 1). Each patient underwent 10 acceptable measurements, with an interquartile range (IQR)/median of 30%. The mean was recorded as the modulus of elasticity (kPa).

Analysis Technique

From the files of T1D patients, HbA1c, diabetes age, and laboratory data were noted. In both groups, NAFLD was excluded because of the

presence of normal echogenicity, normal lipid profile, and normal liver enzyme values on gray scale ultrasonography. The correlation between SWE kPa values and diabetes age, ALT, AST, and FBG in the last 6 months before the study and mean HbA1c% in the last year was studied. AST and ALT levels lower than 35 U/L were deemed normal. The SWE kPa values of the liver were compared between the T1D and healthy groups.

Statistical Analysis

The SPSS version 25 statistical package program was used for statistical analyses. Descriptive statistical methods (mean, SD, number of units, minimum-maximum, percentage) were used to summarize the data. The Shapiro-Wilk test was used for normality tests of continuous variables. In the case group, age, AST, and FBG variables showed a normal distribution ($p>0.05$), whereas in the control group, liver size, liver kPa, AST, and FBG variables showed a normal distribution. Statistical tests were performed according to normality. In cases of normality, two-group variables were analyzed by an Independent samples t-test, and in cases of non-normality, Mann-Whitney U tests were used to investigate the significance of differences between means. To find the relationships between two continuous variables, Pearson correlation coefficients were obtained in cases of normality, and Spearman-Rho correlation coefficients were obtained in cases of non-normality. The Fisher's exact test was used for the independence test between two categorical variables with two groups. The significance level was set at 0.05 for all tests.

Results

Considering the exclusion criteria, we included 103 children: 53 with T1D and 50 healthy controls aged 4-17 years. In the case group, age, AST, and FBG variables were normally distributed, whereas in the control group, liver size, liver kPa, AST, and FBG variables were normally distributed (all; $p>0.05$).

Table 1 shows the AST, ALT, FBG, gender, age, liver size, liver SWE, HbA1c, diabetes duration, and BMI values for the subjects. Significant differences were observed in AST, FBG, and liver kPa values between the case and control groups (all; $p<0.05$), with the case group showing higher FBG and liver kPa values. Gender distribution was similar between the study and control groups ($p=0.207$), and mean age did not significantly differ between groups ($p=0.247$). The mean HbA1c (mmol/mol) in T1D cases was 8.3 (2.4) mmol/mol. The distribution of HbA1c levels in T1D patients (n=53) was as follows: HbA1c <7 (n=10), 7≤ HbA1c <9 (n=26), 9≤ HbA1c <11 (n=9), and HbA1c ≥11 (n=8). None of the T1D patients or the control group were obese, with no statistically significant difference in BMI values between the groups ($p=0.60$).

When we evaluated the correlations between age, duration of diabetes, and HbA1c and FBG values in the T1D group, 38% correlation between duration of diabetes and HbA1c values was significant ($p<0.05$), whereas the correlations between age and FBG and HbA1c and between duration of diabetes and FBG, which were negatively correlated, were not significant ($p=0.4$, $p=0.06$, $p=0.9$, respectively).

There was no statistically significant difference in the mean values of FBG, HbA1c, and liver kPa based on gender ($p=0.274$, $p=0.169$, and $p=0.884$, respectively).

When we evaluated the correlation between liver kPa values and AST, ALT, FBG, HbA1c, diabetes duration, and liver size; we found a significant correlation between liver kPa and FBG (CC=0.311; $p=0.001$). We did not find a significant correlation between other variables and liver kPa value (all; $p>0.05$).

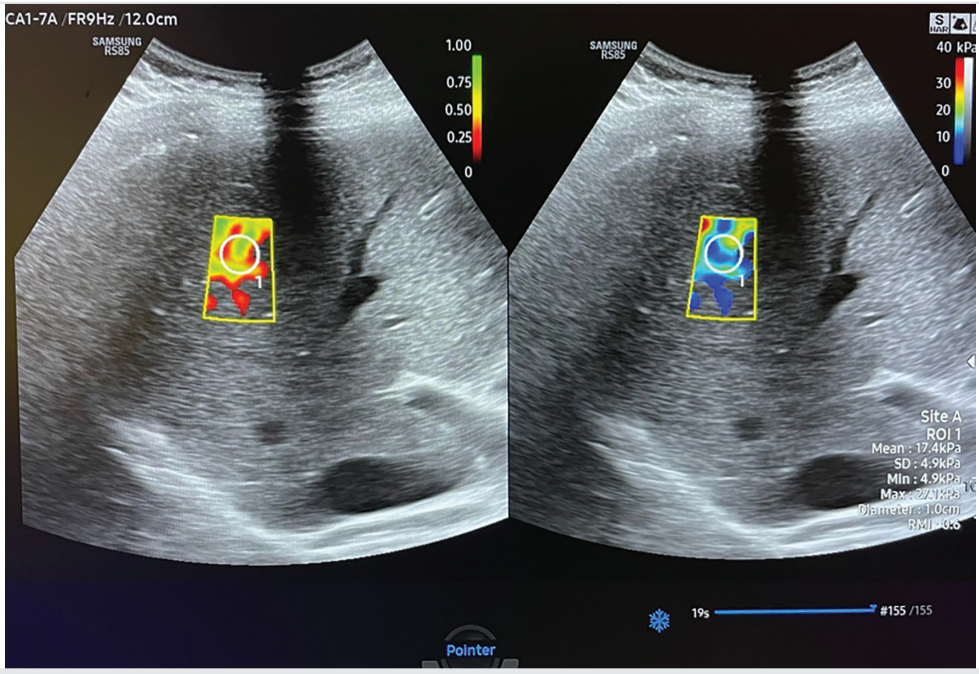

Figure 1: ROI selection and 2D-SWE map of SWE measurements of the liver
ROI: Region of interest, 2D-SWE: Two-dimensional shear wave sonoelastography

Table 1. Distribution of AST, ALT, FBG, gender, age, liver size, liver SWE, HbA1c, and duration of diabetes in the groups

	Case (T1D)	Control	p-value
AST (U/L)	18.5±5.4	21.4±6	0.011[1]
ALT (U/L)	12 (5.5)	11.5 (6)	0.307[2]
FBG (mg/dL)	247.8±69.4	88.6±6.12	0.000[2]
Gender, n (%)			
Female	32 (60.4)	35 (70)	0.207[3]
Male	21 (39.6)	15 (30)	
Age (year)	11.4±3.2	12.5 (6)	0.247[2]
Liver size (cm)	120.7 (18.3)	118.1±11.2	0.228[2]
Liver SWE (kPA)	5.4 (2.5)	4.5±0.8	0.000[2]
HbA1c (mmol/mol)	8.3 (2.4)		
Duration of diabetes (years)	2 (2)	-	-
Body mass index (kg/m^2)	17.7±3.09	17.98±2.37	0.60

Numeric data are presented as median (interquartile range), mean ± standard deviation, [1]: T-test, [2]: Mann-Whitney U test, [3]Fisher's exact test, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, FBG: Fasting blood glucose, SWE: Shear wave sonoelastography, HbA1c: Hemoglobin A1c, T1D: Type 1 diabetes mellitus

Discussion

In this study, we evaluated the clinical findings and 2D-SWE liver stiffness changes in pediatric T1D patients with normal BMI and no abnormalities in gray scale US, liver function tests, and lipid profile. We found that liver tissue stiffness was increased in our patients compared to the healthy controls. In this respect, we believe that our study contributes to the literature as a first.

In the literature, liver disease incidence in patients with T1D ranges from 20% to 31%, whereas NAFLD incidence in the pediatric population varies from 0% to 27% (18,19). Patients with T1D are at risk of developing long-term liver damage, necessitating costly and invasive investigations and treatments. Thus, the use of imaging for the early diagnosis and monitoring of hepatopathy, along with its incorporation into guidelines, is crucial. SWE has been reported as an effective quantitative imaging biomarker for assessing liver parenchymal stiffness and detecting NAFLD and is included in adult screening guidelines because of its high sensitivity and specificity (7,9,12,20-22). Elastography is recommended for suspected NAFLD, but 2D-SWE data in the pediatric population are limited (23). Our findings suggest that 2D-SWE can detect liver involvement early and accurately in pediatric T1D patients. In our study, our 2D-SWE findings were not correlated with biopsy, but there is a biopsy-referenced study in the literature stating that 2D-SWE is an alternative reference standard to TE, and there is also a study reporting that it is more effective than TE (15,24). In healthy children, TE (FibroScan) studies reported mean liver elasticity values of 4.4-5.6 (mean 4.7) kPa (25). In the literature, reference 2D-SWE liver stiffness values for healthy children were found to be 4.29±0.59 kPa by Galina et al. (26) and 6.58±1.46 by Franchi-Abella et al. (27). We found a 2D-SWE liver stiffness value of 4.5±0.8 kPa in healthy children. Our findings will contribute to the literature because of the novelty of 2D-SWE and limited pediatric data.

Harman et al. (28) reported that T1D is associated with an unrecognized burden of chronic liver disease, which may be caused by oxidative damage, lipid accumulation, glycogenosis, autophagy, and apoptotic factors, and that age and gender may affect the severe inflammatory response in patients (18). However, we found no effect of gender on the mean values of FBG, HbA1c and hepatic kPa ($p>0.005$). This may be due to differences in the chronic burden of the disease or the severity of the inflammatory response in our patients.

In the literature, there are studies that detected fatty liver in patients with T1D (1). Chronic hyperglycemia, poor glucose control, oxidative stress, and exogenous insulin administration are effective in intrahepatic fat homeostasis (29). In fact, it was reported by Al-Hussaini et al. (30) that 60% of patients with abnormal sonographic findings improved in 6 months with successful glucose management. In our study, no fatty liver was detected sonographically in any of our T1D patients; however, liver stiffness was increased on 2D-SWE compared with that in healthy subjects. This may be an early imaging finding of impaired intrahepatic fat homestasis; therefore, long-term follow-up data may be useful.

Exogenous insulin use and obesity double the risk of NAFLD in T1D patients with poor glycemic control (HbA1c >7%) (31). Subcutaneous insulin injections do not reach the liver via the portal vein, similar to endogenous insulin production, suggesting insulin resistance and increased insulin demand (29). Recent studies have also shown that patients with T1D have higher insulin sensitivity than non-diabetics (5). Hyperglycemia and impaired insulin clearance saturate glycogen synthesis pathways and redirect them to lipogenic pathways, leading to NAFLD. In our patients, high HbA1c values (median/IQR: 8.3/2.4), a significant correlation between diabetes duration and HbA1c, and a significant correlation between liver kPa and FBG may support early hepatic involvement. However, while a strong correlation between liver stiffness and HbA1c has been reported in the literature (31); we could not detect a significant correlation with kPa despite our high HbA1c values. However, the strong correlation between diabetes duration and HbA1c in our patients ($p<0.05$) supports long-term poor glycemic control.

In the literature, it has been reported that NAFLD can be seen in normal weight subjects, and this may be an early warning sign of metabolic disorder (18,19). This may be due to chronic hyperglycemia, high-fat

low-carbohydrate diet and sedentary life with concern of hypoglycemia in T1D patients. It has also been reported in animal studies that the fatty acid translocase CD 36, which is tightly linked to the development of fatty liver, is significantly increased in T1D livers (18). Early diagnosis is also important for the prevention of metabolic diseases. Therefore, 2D-SWE can be used as a quantitative imaging biomarker in the liver follow-up of T1D patients, especially those with poor glycemic control, even if they have normal BMI values, as in our study population, for early diagnosis due to the risk of NAFLD development.

GH, which is a sonographic mimicking condition, may be a factor in the variability in the incidence of NAFLD reported in the literature in pediatric-juvenile T1D cases. Although biopsy is the gold standard for the detection of fat content and fibrosis in the liver, its invasiveness is a major problem in diagnosis and especially in follow-up in the pediatric population. Steatosis, a precursor to fibrosis, may result in higher 2D-SWE liver stiffness values than GH, a reversible condition. The quantitative data provided by 2D-SWE in diagnosis and response to treatment can be easily used in the pediatric population to differentiate between reversible GH.

The increased degree of liver parenchymal stiffness on 2D-SWE in our pediatric T1D patients compared with the healthy group may be due to one or more of the processes mentioned above. What is important here is to determine non-invasive methods that can be used in harmony with the clinic in the follow-up of the cases and can also be standardized by providing quantitative data. In the literature, it has been reported that differences in diagnostic and identification methods play a role in the heterogeneity in the incidence of NAFLD and that AST and ALT values are unreliable in the detection of NAFLD (31). In this context, 2D-SWE can be used in pediatric patients as an easily accessible imaging method with high reproducibility and patient compliance.

Study Limitations

Our study had several limitations. First, its cross-sectional design prevented us from establishing causal relationships because of the lack of long-term follow-up. Additionally, the absence of histological confirmation via liver biopsy, considered the gold standard diagnostic method for excluding NAFLD, posed a limitation. Furthermore, the small sample size, absence of comparative evaluation with T1D patients with NAFLD, limited existing literature on this group, and the inability to draw conclusions about long-term liver involvement and NAFLD development among our patients further restricted our study's scope.

Conclusion

Although liver function tests, lipid profiles, and grayscale ultrasonography showed no abnormalities in our pediatric T1D patients, increased liver parenchymal stiffness detected by 2D-SWE compared with the healthy group indicated hepatic involvement. Therefore, we believe that 2D-SWE could serve as a valuable imaging method for the early detection and monitoring of potential hepatopathy in pediatric T1D patients. Long-term follow-up studies involving a larger population of T1D patients would be beneficial in establishing quantitative reference values for 2D-SWE.

Ethics Committee Approval: University of Health Sciences Turkey, Kartal Dr. Lütfi Kırdar City Hospital's Ethics Committee approved the study (approval number: 2022/514/225/5, date: 11.05.2022).

Informed Consent: Written informed consent was obtained from the patients' parents.

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References

1. Elkabbany ZA, Elbarbary NS, Ismail EA, Mohamed NA, Ragab D, Abdel Alem S, et al. Transient elastography as a noninvasive assessment tool for hepatopathies of different etiology in pediatric type 1 diabetes mellitus. J Diabetes Complications 2017; 31: 186-94.
2. Al-Hussaini AA, Alzahrani MD, Alenizi AS, Suliman NM, Khan MA, Alharbi SA, et al. Autoimmune hepatitis related autoantibodies in children with type 1 diabetes. Diabetol Metab Syndr 2014; 6: 38.
3. Anderson EL, Howe LD, Jones HE, Higgins JP, Lawlor DA, Fraser A. The Prevalence of Non-Alcoholic Fatty Liver Disease in Children and Adolescents: A Systematic Review and Meta-Analysis. PLoS One 2015; 10: e0140908.
4. Singh Y, Gurung S, Gogtay M. Glycogen hepatopathy in type-1 diabetes mellitus: A case report. World J Hepatol 2022; 14: 471-8.
5. Serdarova M, Dimova R, Chakarova N, Grozeva G, Todorova A, Tsarkova P, et al. Metabolic determinants of NAFLD in adults with type 1 diabetes. Diabetes Res Clin Pract 2022; 186: 109819.
6. Marzuillo P, Grandone A, Perrone L, Miraglia Del Giudice E. Controversy in the diagnosis of pediatric non-alcoholic fatty liver disease. World J Gastroenterol 2015; 21: 6444-50.
7. Bohte AE, Koot BG, van der Baan-Slootweg OH, van Werven JR, Bipat S, Nederveen AJ, et al. US cannot be used to predict the presence or severity of hepatic steatosis in severely obese adolescents. Radiology 2012; 262: 327-34.
8. Sağlam NÖ, Aksoy S, Kazancı SY, Palabıyık F, Hatipoğlu SS, İnci E. The performance of shear wave elastography on evaluating liver changes in obese and overweight children. Turk J Pediatr 2021; 63: 575-83.
9. Garcovich M, Veraldi S, Di Stasio E, Zocco MA, Monti L, Tomà P, et al. Liver Stiffness in Pediatric Patients with Fatty Liver Disease: Diagnostic Accuracy and Reproducibility of Shear-Wave Elastography. Radiology 2017; 283: 820-7.
10. Mandelia C, Kabbany MN, Worley S, Conjeevaram Selvakumar PK. Performance Characteristics, Intra- and Inter-operator Agreement of Transient Elastography in Pediatric Nonalcoholic Fatty Liver Disease. J Pediatr Gastroenterol Nutr 2021; 72: 430-5.
11. Jeong JY, Cho YS, Sohn JH. Role of two-dimensional shear wave elastography in chronic liver diseases: A narrative review. World J Gastroenterol 2018; 24: 3849-60.
12. European Association for the Study of the Liver (EASL); European Association for the Study of Diabetes (EASD); European Association for the Study of Obesity (EASO). EASL-EASD-EASO Clinical Practice Guidelines for the management of non-alcoholic fatty liver disease. J Hepatol 2016; 64: 1388-402.
13. Jeong JY, Kim TY, Sohn JH, Kim Y, Jeong WK, Oh YH, et al. Real time shear wave elastography in chronic liver diseases: accuracy for predicting liver fibrosis, in comparison with serum markers. World J Gastroenterol 2014; 20: 13920-9.

14. Friedrich-Rust M, Nierhoff J, Lupsor M, Sporea I, Fierbinteanu-Braticevici C, Strobel D, et al. Performance of Acoustic Radiation Force Impulse imaging for the staging of liver fibrosis: a pooled meta-analysis. J Viral Hepat 2012; 19: e212-9.

15. Honda Y, Yoneda M, Imajo K, Nakajima A. Elastography Techniques for the Assessment of Liver Fibrosis in Non-Alcoholic Fatty Liver Disease. Int J Mol Sci 2020; 21: 4039.

16. Konuş OL, Ozdemir A, Akkaya A, Erbaş G, Celik H, Işik S. Normal liver, spleen, and kidney dimensions in neonates, infants, and children: evaluation with sonography. AJR Am J Roentgenol 1998; 171: 1693-8.

17. Saadeh S, Younossi ZM, Remer EM, Gramlich T, Ong JP, Hurley M, et al. The utility of radiological imaging in nonalcoholic fatty liver disease. Gastroenterology 2002; 123: 745-50.

18. Jiang S, Tang X, Wang K, Liang Y, Qian Y, Lu C, et al. Hepatic functional and pathological changes of type 1 diabetic mice in growing and maturation time. J Cell Mol Med 2019; 23: 5794-807.

19. Sae-Wong J, Chaopathomkul B, Phewplung T, Chaijitraruch N, Sahakitrungruang T. The Prevalence of Nonalcoholic Fatty Liver Disease and Its Risk Factors in Children and Young Adults with Type 1 Diabetes Mellitus. J Pediatr 2021; 230: 32-7.

20. Bailey SS, Youssfi M, Patel M, Hu HH, Shaibi GQ, Towbin RB. Shear-wave ultrasound elastography of the liver in normal-weight and obese children. Acta Radiol 2017; 58: 1511-8.

21. Tutar O, Beşer ÖF, Adaletli I, Tunc N, Gulcu D, Kantarci F, et al. Shear wave elastography in the evaluation of liver fibrosis in children. J Pediatr Gastroenterol Nutr 2014; 58: 750-5.

22. Kim JR, Suh CH, Yoon HM, Lee JS, Cho YA, Jung AY. The diagnostic performance of shear-wave elastography for liver fibrosis in children and adolescents: A systematic review and diagnostic meta-analysis. Eur Radiol 2018; 28: 1175-86.

23. Samir AE, Dhyani M, Vij A, Bhan AK, Halpern EF, Méndez-Navarro J, et al. Shear-wave elastography for the estimation of liver fibrosis in chronic liver disease: determining accuracy and ideal site for measurement. Radiology 2015; 274: 888-96.

24. Herrmann E, de Lédinghen V, Cassinotto C, Chu WC, Leung VY, Ferraioli G, et al. Assessment of biopsy-proven liver fibrosis by two-dimensional shear wave elastography: An individual patient data-based meta-analysis. Hepatology 2018; 67: 260-72.

25. Cailloce R, Tavernier E, Brunereau L, Fievet A, Falip C, Dujardin F, et al. Liver shear wave elastography and attenuation imaging coefficient measures: prospective evaluation in healthy children. Abdom Radiol (NY) 2021; 46: 4629-36.

26. Galina P, Alexopoulou E, Zellos A, Grigoraki V, Siahanidou T, Kelekis NL, et al. Performance of two-dimensional ultrasound shear wave elastography: reference values of normal liver stiffness in children. Pediatr Radiol 2019; 49: 94-8.

27. Franchi-Abella S, Corno L, Gonzales E, Antoni G, Fabre M, Ducot B, et al. Feasibility and Diagnostic Accuracy of Supersonic Shear-Wave Elastography for the Assessment of Liver Stiffness and Liver Fibrosis in Children: A Pilot Study of 96 Patients. Radiology 2016; 278: 554-62.

28. Harman DJ, Kaye PV, Harris R, Suzuki A, Gazis A, Aithal GP. Prevalence and natural history of histologically proven chronic liver disease in a longitudinal cohort of patients with type 1 diabetes. Hepatology 2014; 60: 158-68.

29. Memaj P, Jornayvaz FR. Non-alcoholic fatty liver disease in type 1 diabetes: Prevalence and pathophysiology. Front Endocrinol (Lausanne) 2022; 13: 1031633.

30. Al-Hussaini AA, Sulaiman NM, Alzahrani MD, Alenizi AS, Khan M. Prevalence of hepatopathy in type 1 diabetic children. BMC Pediatr 2012; 12: 160.

31. de Vries M, Westerink J, Kaasjager KHAH, de Valk HW. Prevalence of Nonalcoholic Fatty Liver Disease (NAFLD) in Patients With Type 1 Diabetes Mellitus: A Systematic Review and Meta-Analysis. J Clin Endocrinol Metab 2020; 105: 3842-53.