# The Prevalence of Nonalcoholic Fatty Liver Disease and Its Risk Factors in Children and Young Adults with Type 1 Diabetes Mellitus

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**Objectives** To determine the prevalence of nonalcoholic fatty liver disease (NAFLD) and its associated risk factors in children and young adults with type 1 diabetes (T1D).

**Study design** A cross-sectional study was conducted at a tertiary care center in children and young adults with T1D. Liver fat quantification and hepatic fibrosis were assessed by magnetic resonance imaging proton density fat fraction and magnetic resonance elastography (MRE). Logistic regression analysis was performed to examine the associated risk factors for NAFLD.

**Results** Fifty patients with T1D (28 females, 13 with overweight/obesity) were included. The median age and duration of T1D were 16.9 years (IQR, 13.6-20 years) and 6.5 years (IQR, 4-11 years), respectively. The prevalence of NAFLD was 10%. Four out of 5 patients with NAFLD were overweight/obese, and 2 had an and elevated alanine aminotransferase (ALT) level. None had liver fibrosis (defined as MRE >2.9 kPa). Compared with patients without NAFLD, patients with NAFLD had significantly higher body mass index standard deviation score (BMI-SDS) (median, 0.94 [IQR, 1.30-2.62] vs 0.13 [IQR, −0.69 to 0.84]; $P$ = .01), ALT (median, 17 IU/L [IQR, 16-52 IU/L] vs 12 IU/L [IQR, 10-14 IU/L]; $P$ = .02), and lower high-density lipoprotein cholesterol (median, 49 mg/dL [IQR, 41-51 mg/dL] vs 57 mg/dL [IQR, 52-69 mg/dL]; $P$ = .039). Multivariate logistic regression analysis identified high BMI-SDS as the sole independent risk factor associated with NAFLD (OR, 5.79; 95% CI, 1.04-32.18).

**Conclusion** The prevalence of NAFLD in children and young adults with T1D was comparable to that in the general population. Our study suggests that routine screening for NAFLD in patients with T1D might not be necessary but should be performed in those patients with T1D who are overweight/obese. *(J Pediatr 2021;230:32-7)*.

Nonalcoholic fatty liver disease (NAFLD) is a spectrum of progressive liver disease ranging from simple steatosis to nonalcoholic steatohepatitis with advanced fibrosis and cirrhosis.[1,2] Obesity, metabolic syndrome, and type 2 diabetes (T2D) are the well-known risk factors for NAFLD.[3,4] The prevalence of NAFLD varies widely depending on geographic area and diagnostic methods. The estimated global prevalence of NAFLD is 24%.[5] A recent study demonstrated a pooled mean NAFLD prevalence of 7.6% in the general pediatric population and up to 34.3% in those with obesity.[6] The prevalence of NAFLD is approximately 60%-70% in pediatric patients with T2D. The coexistence of T2D and NAFLD increases the risk of severe forms of NAFLD, as well as chronic vascular complications of diabetes.[7,8]

In contrast to T2D, type 1 diabetes (T1D) is characterized by insulin deficiency due to progressive destruction of pancreatic beta cells and is not associated with adipocyte dysfunction.[3,9-11] The relatively low prevalence of NAFLD in patients with T1D may be explained by the lack of portal hyperinsulinism, which inhibits hepatic lipogenesis and the suppression of lipolysis by insulin.[10,12] On the other hand, patients with T1D with obesity and/or insulin resistance could also progressively develop features of T2D. The combined presentation of T1D and T2D, referred to as "double diabetes," may also increase the risk of NAFLD.[13,14]

The prevalence of NAFLD in patients with T1D ranges from 4.7% to 50% in adults[10,12,15-17] and from 0 to 27% in children and young adults.[18-21] One possible major reason for this variation is the different methods used to diagnose NAFLD. Ultrasound is inaccurate for detecting mild hepatic steatosis (<33%) and unable to differentiate NAFLD from glycogenic hepatopathy. Liver biopsy, the gold

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|---|---|---|---|
| ALT | Alanine aminotransferase | LDL-c | Low-density lipoprotein cholesterol |
| AST | Aspartate aminotransferase | | |
| BMI-SDS | Body mass index standard deviation score | MRE | Magnetic resonance elastography |
| GGT | Gamma-glutamyl transferase | MRI | Magnetic resonance imaging |
| HbA1c | Hemoglobin A1c | NAFLD | Nonalcoholic fatty liver disease |
| HDL-c | High-density lipoprotein cholesterol | PDFF | Proton density fat fraction |
| | | T1D | Type 1 diabetes |
| | | T2D | Type 2 diabetes |

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standard for diagnosis of NAFLD and glycogenic hepatopathy, is an invasive procedure.[2,22] Magnetic resonance imaging (MRI)-proton density fat fraction (PDFF)[20] detects triglycerides (TG) in the liver, and the PDFF [PDFF = fat/(fat + water)] is used to measure the fat content. It is not interfered with patient factors or concomitant liver abnormalities, such as glycogen, iron overload, or necroinflammation. MRI-PDFF has shown diagnostic accuracy for detection and quantification hepatic steatosis throughout the liver.[23-26] Magnetic resonance elastography (MRE) is an accurate noninvasive technique for measurement of liver fibrosis, which can assess the severity of NAFLD in both children and adults.[26,27]

In this study, we evaluated the prevalence of NAFLD among children and young adults with T1D using the MRI-PDFF and simultaneously assess the degree of hepatic fibrosis using MRE. Clinical measures were analyzed to determine the associated risk factors for NAFLD in T1D.

## Methods

The study protocol was reviewed and approved by the Institutional Review Board of Faculty of Medicine, Chulalongkorn University (COA 322/2019). Informed consent was obtained from all subjects. A cross-sectional study was conducted between March and September 2019. Subjects with pediatric-onset T1D (diagnosed before age 15 years) were enrolled from the pediatric diabetic clinic at King Chulalongkorn Memorial Hospital, Bangkok, Thailand. Inclusion criteria were children and young adults aged 8-30 years who were diagnosed with T1D according to American Diabetes Association criteria for >1 year. Exclusion criteria included a preexisting hepatic disease (eg, chronic viral hepatitis, autoimmune hepatitis, genetic-metabolic liver disease), a history of drug use known to induce hepatic steatosis, and alcohol drinking. We also excluded children who had an uncertain type of diabetes or other endocrine diseases, such as hypothyroidism or adrenal insufficiency.

Baseline demographic data and clinical characteristics were collected. These data included age, sex, duration of diabetes, family history of liver disease and NAFLD, other complications (eg, diabetic retinopathy, diabetic nephropathy, diabetic neuropathy, hypertension), current medications, and current insulin regimen and daily dose. All subjects were examined for weight, height, body mass index standard deviation score (BMI-SDS), blood pressure, signs of insulin resistance (acanthosis nigricans), and signs of chronic liver disease and hepatomegaly. The BMI-SDS was calculated and categorized as underweight (BMI-SDS <−2 SD), normal weight (−2 SD ≤ BMI-SDS ≤ +1 SD), overweight (+1 SD < BMI-SDS ≤ +2 SD), and obesity (BMI-SDS > +2 SD) according to the World Health Organization growth chart. For subjects aged ≥20 years, overweight and obesity were defined using cutoff BMIs for adults of ≥25.0 kg/m$^2$ and ≥30.0 kg/m$^2$, respectively.[28] Biochemical measures were collected including the mean of hemoglobin A1c (HbA1C) over the previous 12 months, lipid profile (total cholesterol, TG, high-density lipoprotein cholesterol [HDL-c], and low-density lipoprotein cholesterol [LDL-c]), and liver function tests (aspartate aminotransferase [AST], alanine aminotransferase [ALT], and gamma-glutamyl transferase [GGT]). ALT >26 IU/L in males and >22 IU/L in females were used to define elevated liver enzyme levels.[2] Liver enzymes and lipids were measured by standard enzymatic methods.

### Magnetic Resonance Imaging Examination

Patients underwent magnetic resonance imaging (MRI) examination on a 3.0-T whole-body scanner (Discovery MR750w; GE Healthcare) equipped with a 12-channel torso phased array coil. Patients were required to fast for at least 4 hours before MRI examination. The MRI examination included routine sequences (gradient echo [GRE] T1-weighted imaging with dual echo images and T2-weighted imaging), as well as proton density fat fraction (PDFF) and MRE. An IDEAL-IQ MRI sequence was acquired to estimate the PDFF with the following protocol: fractional anisotropy, 25°; repetition time, 32.5 msec; 8 echo times: 1.25, 2.76, 4.27, 5.78, 7.30, 8.81, 10.32, and 11.83 msec; slice thickness, 8 mm; field of view 192 × 160 matrix; total scan time, 20 seconds. PDFF maps were then generated on the scanner console. Regions of interest were placed in the right hepatic lobe on the PDFF maps while avoiding large vessels and bile ducts. Measurements were obtained as percentage of fat in the tissue. Breath-hold 2-dimensional GRE-based MRE acquisition with the 60-Hz passive acoustic driver was performed with the following protocol: repetition time, 1000 msec; echo times, 63 msec; fractional anisotropy, 90°; field of view, 38 × 46.5 cm; matrix, 64 × 64; slice thickness, 7 mm; total scan time, 24 seconds. The MRE elastogram was then obtained on the scanner console using MR-Touch (GE Healthcare). Regions of interest were placed in the right hepatic lobe, excluding nonhepatic parenchyma such as intrahepatic vessels.

The PDFF cutoff value of hepatic steatosis for NAFLD was ≥6.4% in children and adolescents aged <18 years[25,29] and ≥5.5% in young adults aged 18-30 years.[30] These cutoff values were based on published studies in large children and adult populations. A shear stiffness >2.9 kPa detected on MRE performed at a frequency of 60 Hz was considered to indicate fibrosis. Previous studies have shown comparable shear stiffness cutoff values in children and adults.[27,31]

All patients with hepatic steatosis detected by MRI-PDFF were reevaluated to exclude other common causes of hepatic steatosis and confirm the diagnosis of NAFLD. Further tests excluded viral hepatitis B and C infection, autoimmune hepatitis (eg, antinuclear antibodies, anti-smooth muscle antibodies, immunoglobulin G), and Wilson disease (eg, serum ceruloplasmin, urine copper, examination for Kayser-Fleischer ring by an ophthalmologist).

### Statistical Analyses

Data analysis was performed using SPSS version 22.0 (IBM). Descriptive statistics were recorded as number, percentage,

mean, or median. The Mann-Whitney *U* test and Fisher exact test were used for comparisons between the NAFLD group and non-NAFLD group. Logistic regression analysis was used to assess risk factors associated with NAFLD. Variables included in the univariate logistic regression analysis were sex, age, diabetes duration, daily insulin dose, BMI-SDS, diabetes nephropathy, diabetes neuropathy, HbA1c, total cholesterol, TG, HDL-c, LDL-c, AST, ALT, and GGT. In multivariate logistic regression analysis, the variables included BMI-SDS and ALT. A *P* value <.05 was considered to indicate statistical significance.

## Results

A total of 50 patients (28 females) were included in the study. Baseline clinical and demographic data are presented in **Table I**. The median age was 16.9 years (IQR, 13.6-20 years), and 31 patients (62%) were children and adolescents aged <18 years. Of the 50 subjects, 49 patients (98%) had entered puberty. The median duration of diabetes was 6.5 years (IQR, 4-11 years). Most of the patients (92%) had been diagnosed for more than 2 years. The median daily insulin dose was 1.09 U/kg/day (IQR, 0.81-1.25 U/kg/day). The median HbA1c was 8.7% (IQR, 7.9%-10.1%). In accordance with the International Society for Pediatric and Adolescent Diabetes guidelines, an HbA1c of 7.5% was chosen to define good glycemic control for T1D.[32] Nine patients (18%) were considered to have good control (mean HbA1c, 7.2 ± 0.3%), and the other 41 patients had poor control (mean HbA1c, 9.7 ± 1.8%). The median BMI-SDS was 0.21 (IQR, −0.61 to 1.06). According to World Health Organization charts, 11 subjects were overweight, 2 had obesity, and only 1 was underweight. Thus, the prevalence of subjects who were overweight/obese in our cohort was 26%. Abnormal ALT was found in only 2 patients (1 had obesity and 1 had overweight) at the time of examination. There was no significant difference between the overweight/obese group and the normal BMI group in all measures except acanthosis nigricans ($P = .015$) (**Table II**; available at www.jpeds.com).

Five of the 50 patients (10%) were diagnosed with NAFLD. All the patients with NAFLD had no signs of chronic liver disease and no hepatomegaly. The characteristics of the patients with NAFLD are summarized in **Table III**. Of the 5 patients with NAFLD, 2 were overweight, 2 were obese, and 3 had acanthosis nigricans. The prevalence of NAFLD in patients with T1D with overweight/obesity was relatively high (26%; 4 of 13). Only 2 of the 5 patients with NAFLD had an elevated ALT level (52 and 60 mg/dL). Three patients had PDFF values slightly above the cutoff, and 1 patient (patient 4) had a very high PDFF value of 40.4%, compatible with hepatic steatosis grade 3. In addition, 2 patients had focal fat infiltration at hepatic segment IVb, but their PDFF values (1.9% and 3.8%) did not exceed the cutoff value, and their ALT levels were normal. None of the patients with NAFLD demonstrated hepatic fibrosis as assessed by MRE. The **Figure** shows representative MRI-PDFF and MRE study results in patients 1 and 4.

**Table IV** compares clinical and biochemical characteristics of the NAFLD and non-NAFLD groups. Patients with NAFLD had significantly higher median BMI-SDS (1.94 [IQR, 1.3-2.62] vs 0.13 [IQR, −0.69 to 0.84]; $P = .006$), ALT level (17 IU/L [IQR, 16-52 IU/L] vs 12 IU/L [IQR, 10-14 IU/L]; $P = .015$), and GGT level (25 IU/L [IQR, 24-30 IU/L] vs 16 IU/L [IQR, 13-20 IU/L]; $P = .005$). HDL-c levels were significantly lower in the NAFLD group

**Table I. Demographic and baseline clinical characteristics of the study subjects (N = 50)**

| Characteristics | Values |
|---|---|
| Age, y, median (IQR) | 16.9 (13.6-20) |
| Female, n (%) | 28 (56) |
| Age at diagnosis of diabetes, y, median (IQR) | 9 (7-12) |
| Duration of diabetes duration, y, median (IQR) | 6.5 (4-11) |
| Daily insulin dose, U/kg/d, median (IQR) | 1.09 (0.81-1.25) |
| BMI-SDS, median (IQR) | 0.21 (−0.65 to 1.06) |
| Overweight/obesity, n (%) | 13 (26) |
| Normal weight, n (%) | 36 (72) |
| Hypertension, n (%) | 1 (2) |
| Acanthosis nigricans, n (%) | 3 (6) |
| Diabetic retinopathy, n (%) | 1 (2) |
| Diabetic nephropathy, n (%) | 5 (10) |
| Diabetic neuropathy, n (%) | 5 (10) |
| HbA1c, %, median (IQR) | 8.7 (7.9-10.1) |
| Total cholesterol, mg/dL, median (IQR) | 202 (170-218) |
| TG (mg/dL) | 68 (56-88) |
| HDL-c, mg/dL, median (IQR) | 56 (49-69) |
| LDL-c, mg/dL, median (IQR) | 125 (102-139) |
| AST, IU/L, median (IQR) | 16 (14-18) |
| ALT, IU/L, median (IQR) | 12 (10-16) |
| GGT, IU/L, median (IQR) | 16 (13.5-21.5) |

**Table III. Characteristics of patients with T1D and NAFLD (N = 5)**

| | Patients with NAFLD | | | | |
|---|---|---|---|---|---|
| Characteristics | 1 | 2 | 3 | 4 | 5 |
| Sex | F | M | F | F | F |
| Age, y | 20 | 19 | 15 | 14 | 22 |
| Duration of diabetes, y | 7 | 7 | 6 | 8 | 9 |
| Daily insulin dose, U/kg/d | 1.73 | 0.95 | 1.33 | 1.12 | 0.86 |
| BMI-SDS | 0.07 | 1.3 | 2.62 | 2.98 | 1.94 |
| Waist circumference (cm) | 70 | 93 | 88.5 | 95 | 86 |
| Hypertension (+ yes, - no) | - | + | - | - | - |
| Acanthosis nigricans (+ yes, - no) | - | - | + | + | + |
| Diabetic retinopathy (+ yes, - no) | - | - | - | - | - |
| Diabetic nephropathy (+ yes, - no) | - | + | - | - | - |
| Diabetic neuropathy (+ yes, - no) | - | + | - | - | - |
| Average HbA1c, % | 10.9 | 9.4 | 8 | 9 | 8.6 |
| Total cholesterol, mg/dL | 152 | 203 | 185 | 176 | 220 |
| TG, mg/dL | 69 | 103 | 72 | 108 | 74 |
| HDL-c, mg/dL | 49 | 51 | 41 | 36 | 62 |
| LDL-c, mg/dL | 89 | 135 | 127 | 136 | 147 |
| AST, IU/L | 10 | 28 | 19 | 26 | 17 |
| ALT, IU/L | 12 | 52 | 17 | 60 | 16 |
| GGT, IU/L | 30 | 24 | 25 | 30 | 20 |
| PDFF value, % | 12.2 | 6 | 6.9 | 40.4 | 5.6 |
| MRE fibrosis, kPa | 1.4 | 2.3 | 2.5 | 1.5 | 1.3 |

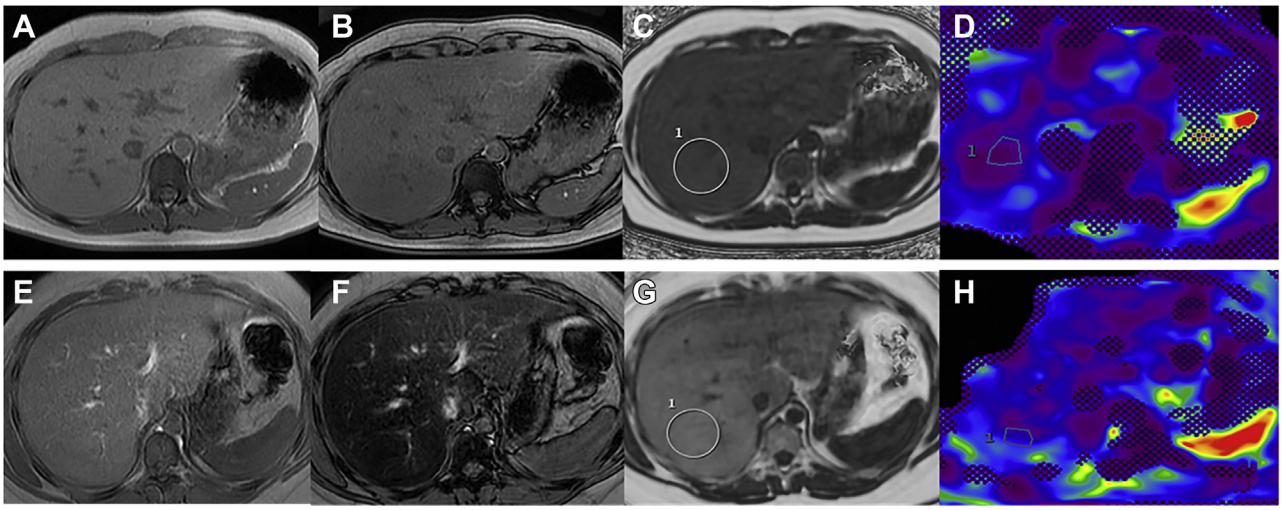


**Figure.** Axial MRI of the liver, **A** and **E,** dual GRE T1 in-phase and **B** and **F,** opposed-phase; **C** and **G,** PDFF; and **D** and **H,** color MRE in patients 1 and 4. In patient 1, MRI revealed decreased parenchymal signal intensity on the opposed-phase image (**B**) compared with the in-phase image (**A**), PDFF confirmed fatty liver (PDFF 12%) (**C**), and color MRE showed normal liver stiffness (mean, 1.4 kPa) (**D**). In patient 4, MRI showed decreased parenchymal signal intensity on the opposed-phase image (**F**) compared with the in-phase image (**E**), PDFF confirmed severe fatty liver (PDFF 40.4%) (**G**), and color MRE showed normal liver stiffness (mean, 1.5 kPa) (**H**).

(median, 49 mg/dL [IQR, 41-51 mg/dL] vs 57 mg/dL [IQR, 52-69 mg/dL]; $P = .039$). Of note, GGT levels were within the normal range in both groups. Acanthosis nigricans was seen more frequently in patients with NAFLD. There were no significant differences in age, sex, duration of diabetes, daily insulin dose, diabetic complications, and levels of total cholesterol, TG, or LDL-c between the NAFLD and non-NAFLD groups.

Factors associated with NAFLD analyzed by logistic regression analysis (**Table V**; available at www.jpeds.com). Univariate logistic regression analysis showed that BMI-SDS, ALT, and GGT were associated with an increased risk of NAFLD. Multivariate logistic regression analysis identified high BMI-SDS as the sole risk factor associated with NAFLD (OR, 5.79; 95% CI, 1.04-32.18) after adjustment by ALT level.

## Discussion

Despite the well-established relationship between NAFLD and T2D, there are conflicting data regarding the prevalence and the consequences of NAFLD in patients with T1D, especially in pediatric population. Previous studies in pediatric and adult patients with T1D showed wide variations in the

**Table IV. Clinical and biochemical characteristics of patients with and without NAFLD**

| Variables | NAFLD | No NAFLD | *P* value |
|---|---|---|---|
| Total cases, n (%) | 5 (10) | 45 (90) | — |
| Female sex, n (%) | 4 (80) | 24 (53.3) | .368 |
| Age, y, median (IQR) | 18.8 (15.3-20) | 16.8 (13.4-19.5) | .529 |
| Duration of diabetes, y, median (IQR) | 7 (7-8) | 6 (4-11) | .683 |
| Daily insulin dose, U/kg/d, median (IQR) | 1.1 (1.0-1.3) | 1.1 (0.8-1.2) | .267 |
| BMI-SDS, median (IQR) | 1.94 (1.3-2.62) | 0.13 (−0.69 to 0.84) | .006* |
| Hypertension, n (%) | 1 (20) | 0 (0) | .1 |
| Acanthosis nigricans, n (%) | 3 (60) | 0 (0) | .001* |
| Diabetic retinopathy, n (%) | 0 (0) | 1 (2.2) | 1 |
| Diabetic nephropathy, n (%) | 1 (20) | 4 (8.9) | .423 |
| Diabetic neuropathy, n (%) | 1 (20) | 4 (8.9) | .423 |
| HbA1c, %, median (IQR) | 9 (8.6-9.4) | 8.7 (7.8-10.1) | .615 |
| Total cholesterol, mg/dL, median (IQR) | 185 (176-203) | 203 (170-218) | .43 |
| TG, mg/dL, median (IQR) | 74 (72-103) | 63 (54-87) | .14 |
| HDL-c, mg/dL, median (IQR) | 49 (41-51) | 57 (52-69) | .039* |
| LDL-c, mg/dL, median (IQR) | 135 (127-136) | 123 (102-139) | .469 |
| AST, IU/L, median (IQR) | 19 (17-26) | 16 (14-17) | .227 |
| ALT, IU/L, median (IQR) | 17 (16-52) | 12 (10-14) | .015* |
| GGT, IU/L, median (IQR) | 25 (24-30) | 16 (13-20) | .005* |

*$P$ values from the Mann-Whitney $U$ test and Fisher exact test.

prevalence of NAFLD in T1D. These differences might be related to variations across studies in the methods used to diagnose NAFLD and in other factors, such as age, duration of diabetes, and glycemic control of T1D.[10,16-21] In the present study, we evaluated the prevalence of NAFLD and hepatic fibrosis among Asian children and young adults with T1D diagnosed by MRI-PDFF/MRE. We found a 10% prevalence of NAFLD in our youths with T1D, which increased by 3-fold in those who were overweight/obese. These findings are comparable with previous studies in the general pediatric population.[6] Hepatic fibrosis was not detected in any of our subjects. In line with previous studies, high BMI-SDS was the independently associated risk factor for NAFLD.[10,16,33] HbA1c levels and daily insulin dose were not associated with NAFLD. Our results are consistent with previous studies in adults with T1D showing no correlation between liver fat content and HbA1c level.[10,16] Similarly, Cusi et al found that sex, duration of diabetes, HbA1c level, total daily insulin dose, TG level, and LDL-c level were not associated with NAFLD in patients with T1D.[10]

MRI-PDFF and MRE detect hepatic steatosis and liver stiffness and can provide accurate and reliable results independent of age, sex, BMI, and operator experience. Importantly, these techniques are able to differentiate hepatic steatosis from the glycogenic hepatopathy commonly found in patients with poorly controlled T1D.[23,25-27] It is important to distinguish NAFLD from glycogenic hepatopathy because of the risk for progressive liver disease, cirrhosis, and/or hepatocellular carcinoma in NAFLD. In contrast, glycogenic hepatopathy is generally a benign reversible condition caused by accumulation of excess glycogen in the hepatocytes. Achieving good glycemic control can result in resolution.[34]

In our study cohort, 26% of the youths with T1D were overweight or obese, as proportion similar to those in previous studies in pediatric patients with T1D by Pinhas-Hamiel et al (age 5-30 years),[35] and the SWEET study group (age 2-18 years).[36] NAFLD was detected in 10% of the patients with T1D, which is comparable to the rates in studies reported by Cusi et al (8.8%)[10] and Petit et al (4.7%),[16] which used MRI as a diagnostic tool. The prevalence of NAFLD in youths with T1D was relatively low compared with previous studies in adults with T1D (~30%-50%) diagnosed by ultrasound.[17,21,37] This discrepancy could be due to overdiagnosis by misinterpretation of glycogenic hepatopathy as NAFLD because of the limitations of ultrasound.[16] Farhan et al reported that 10% of nonobese children with T1D in Iraq had NAFLD.[18] In contrast, Kummer et al screened 93 children and adolescents with T1D in Germany and found that none met the NAFLD definition criteria based on ALT, ultrasound, and fibroscan.[19] Several studies have suggested that NAFLD may be less common in youths with T1D than in healthy controls.[12,33,38] Previous studies have shown a lower liver fat content, evaluated by either MRI or magnetic resonance spectroscopy, in patients with T1D compared with matched healthy controls irrespective of BMI[12] or the duration of diabetes.[38] Llaurado et al also showed that patients with T1D have greater insulin sensitivity to lipolysis than nondiabetic subjects, which might lead to restricted free fatty acid flux to the liver and reduced liver fat content.[12] Regnell et al reported a slightly lower median hepatic fat fraction measured by MRI in 22 children with T1D compared with controls, and no patients with T1D had NAFLD.[20] These results support the hypothesis that a lack of portal hyperinsulinemia in patients with T1D might inhibit hepatic lipogenesis. Suppression of lipolysis by insulin therapy may restrict free fatty acid flux to the liver and reduce intrahepatic TG synthesis in these patients.[12] Moreover, uncontrolled T1D mice did not have hepatitis and NAFLD, likely due to the reduced lipid synthesis in response to insulin deficiency.[39]

In the present study, we identified high BMI (overweight/obesity) as an independent risk factor for NAFLD, consistent with previous studies in adults and children.[2,10,16,38] Overweight and obesity are well-known risk factors for NAFLD and are closely related to insulin resistance.[4] We found acanthosis nigricans, a cutaneous manifestation of insulin resistance, in our patients with NAFLD. In addition, HDL-c levels were lower in the NAFLD group. Despite its low sensitivity and specificity in diagnosing NAFLD, ALT is the most common screening test for NAFLD in general practice.[2] In our study, more than one-half of patients with NAFLD had normal ALT levels. There was no association between the occurrence of NAFLD and HbA1c level, duration of diabetes, and total daily insulin dose. This is in line with previous studies using MRI to diagnose NAFLD[10,16] and a study in T1D mice.[39] These findings suggest that patients with T1D who are overweight/obese and have features of the metabolic syndrome are at risk for NAFLD. Notably, a limitation of our study is its relatively small sample size.

In conclusion, in our cohort of children and young adults with T1D, the prevalence of NAFLD diagnosed by MRI-PDFF and MRE was not increased. Overweight/obesity was a strong risk factor for NAFLD, especially in youths with features of metabolic syndrome, such as acanthosis nigricans and low HDL-c level. Our data suggest that routine screening for NAFLD in all young patients with T1D might not be necessary, but it should be considered in patients with overweight/obesity and features of metabolic syndrome. ■

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**Table II. Clinical characteristics and laboratory data of the overweight/obese and non-overweight/obese groups**

| Characteristics | Overweight/obese (N = 13) | Non-overweight/obese (N = 37) | *P* value |
|---|---|---|---|
| Female sex, n (%) | 9 (69.2) | 19 (51.4) | .339 |
| Age, y, median (IQR) | 11 (8-11) | 9 (7-12) | .607 |
| Duration of diabetes, y, median (IQR) | 4 (4-7) | 7 (4-12) | .081 |
| Daily insulin dose, U/kg/d, median (IQR) | 1.1 (0.94-1.2) | 1.08 (0.8-1.25) | .816 |
| Hypertension, n (%) | 1 (7.7) | 0 (0) | .260 |
| Acanthosis nigricans, n (%) | 3 (23.1) | 0 (0) | .015 |
| Diabetes retinopathy, n (%) | 1 (7.7) | 0 (0) | .260 |
| Diabetes nephropathy, n (%) | 1 (7.7) | 4 (11.1) | 1 |
| Diabetes neuropathy, n (%) | 1 (9.1) | 4 (14.8) | 1 |
| HbA1c, % | 9 (8.8-9.4) | 8.4 (7.8-10.2) | .135 |
| Total cholesterol, mg/dL, median (IQR) | 189 (170-209) | 203 (176-219) | .419 |
| TG, mg/dL, median (IQR) | 73 (69-103) | 62 (54-84) | .099 |
| HDL-c, mg/dL, median (IQR) | 55 (49-62) | 58 (51-69) | .232 |
| LDL-c, mg/dL, median (IQR) | 118 (102-135) | 126 (105-142) | .493 |
| AST, IU/L, median (IQR) | 17 (15-19) | 16 (14-18) | .609 |
| ALT, IU/L, median (IQR) | 12 (8-16) | 12 (10-16) | .764 |
| GGT, IU/L, median (IQR) | 17 (16-20) | 16 (13-23) | .303 |

**Table V. Factors associated with NAFLD analyzed by logistic regression analysis**

| Variables | Crude OR (95% CI) | *P* value | aOR (95% CI) | *P* value |
|---|---|---|---|---|
| Female sex | 3.5 (0.36-33.82) | .279 | | |
| Age, y | 1.04 (0.85-1.27) | .709 | | |
| Duration of diabetes, y | 0.99 (0.8-1.22) | .916 | | |
| Daily insulin dose, U/kg/d | 17.9 (0.36-896.52) | .149 | | |
| BMI-SDS | 6.58 (1.52-28.53) | .012* | 5.79 (1.04-32.18) | .045* |
| Diabetic nephropathy | 2.5 (0.22-28.13) | .458 | | |
| Diabetic neuropathy | 1.81 (0.16-20.54) | .631 | | |
| HbA1c, % | 0.99 (0.6-1.62) | .956 | | |
| Total cholesterol, mg/dL | 0.99 (0.95-1.02) | .459 | | |
| TG, mg/dL | 1 (0.99-1.02) | .673 | | |
| HDL-c, mg/dL | 0.91 (0.82-1.01) | .068 | | |
| LDL-c, mg/dL | 1.01 (0.97-1.05) | .586 | | |
| AST, IU/L | 1.11 (0.95-1.3) | .194 | | |
| ALT, IU/L | 1.15 (1.01-1.31) | .039* | 1.16 (0.94-1.43) | .157 |
| GGT, IU/L | 1.23 (1.04-1.44) | .015* | | |

**P* value by logistic regression analysis <.05.