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ORIGINAL PAPER

Non-alcoholic fatty liver disease (NAFLD) spectrum in children with type 1 diabetes mellitus evaluated with non-invasive fibrosis score and instrument: A cross-sectional study

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ABSTRACT

The aim of the study was to evaluate NAFLD spectrum in children with type 1 of diabetes mellitus (T1DM) by simple fibrosis scores and advanced biochemical markers in association with abdominal ultrasonography (US), Acoustic radiation force impulse elastography (ARFI) and comparing their results.

Material and methods: A case-control study was conducted on 142children and adolescents with T1DM and79 subjects as controls. Through medical history, clinical examination, and laboratory assessment including glycosylated hemoglobin (HbA1c) levels and liver enzymes including AST and ALT were carried out. Calculation of simple fibrosis scores (AST/ALT ratio, AST to platelet ratio index (APRI), fibrosis (FIB)-4 index, paediatric NAFLD fibrosis index (PNFI) were done. Assessment of advanced biochemical markers including hyaluronic acid (HA) , amino terminal pro peptide of type III collagen (PIIINP) and tissue inhibitor of metalloproteinase 1 (TIMP-1) levels. Also, ELF test were calculated.

Results: Data of non-invasive fibrosis score, there were statistically significant difference between cases and controls in fibrosis 4 score, Discriminant score also ratio of AST to ALT value (p = 0.009, 0.000 and 0.019) respectively. Also, regarding advanced biochemical markers and ELF score, there were a high statistically significant difference in TMP, Hyaluronic acid and ELF(p = 0.00, 0.044 and 0.00) respectively.

Conclusions: Our results support that there are available non-invasive biomarkers for hepatic affection in children with T1DM. Obtained results support that there is a going on process in diabetic children could be assessed by AST/ALT ratio, FIB-4 index and ELF Score with performing abdominal sonography while ARFI needed in more advanced stage.

KEY WORDS:

nonalcoholic fatty liver disease (NAFLD), type 1 diabetes mellitus, fibrosis (FIB)-4 index, paediatric NAFLD fibrosis index (PNFI)

INTRODUCTION

In childhood, non-alcoholic fatty liver disease (NAFLD) is one of the main cause of chronic hepatic disease [1]. NAFLD includes a wide range of changes ranging from inflammation, fibrosis, and cirrhosis according fat accumulation steatosis to non-alcoholic steatohepatitis (NASH) [2]. The natural history of paediatric NAFLD is not fully known; children with NAFLD show a range of fibroses and to a lesser extent cirrhosis [3, 4]. In children,

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early diagnosis of this condition is crucial because this may help to decrease the occurrence of chronic liver disease later in life [3, 5]. The relation between liver disease and diabetes mellitus is increasing all over the world [6].

Diabetes mellitus type 1 (T1DM) is characterized by deficiency of insulin; also, obesity and correlated insulin resistance can present in those patients, and they may be the cause of occurrence of NAFLD [7]. The pathophysiology of steatosis in DM type 1 is not fully understood [8]. Updated data show contradicting results without increased prevalence of NAFLD in type 1 DM adults in some studies, compared to normal subjects [9], while other studies showed that adults with type 1 DM are at increased risk for NAFLD, with a prevalence of up to 44% [10-12].

Several scores for diagnosis have been developed to determine the occurrence of fibrosis using clinical and laboratory results. These scores are to integrate routine markers of liver injury (e.g. transaminase activity, platelet count) and risk characteristics (e.g. obesity, age, diabetes) [13].

So, there is an instant requirement to evaluate simple noninvasive tests to diagnose children with fibrosis. Many noninvasive scoring systems of fibrosis that depend on variable measurements have been developed in people with NAFLD to identify patients with marked stage of fibrosis, including the AST/ALT ratio, NAFLD fibrosis score (NFS), the AST/platelet ratio index (APRI), and the FIB4 score [14]. Hepatic fibrosis biomarkers, consisting of tumour growth factor-β (TGF-β), hyaluronic acid, laminin, type IV collagen, and extracellular matrix components, have been suggested, with some limitations [15]. Tissue inhibitor of matrix metalloproteinases-1(TIMP1), hyaluronic acid (HA), and amino-terminal propeptide of type III procollagen (PIIINP) assessment to calculate the non-invasive enhanced liver fibrosis (ELF) score for liver fibrosis diagnosis accurately [16] also to detect its degree [17] in those subjects with non-alcoholic fatty liver disease (NAFLD). The paediatric NAFLD fibrosis score result is less accurate and to be evaluated [18]. Some reports suggest that the paediatric NAFLD fibrosis index (PNFI) and the enhanced liver fibrosis (ELF) score are clearer in detecting fibrosis in children with NAFLD; the PNFI only and the paediatric NAFLD fibrosis score are less accurate [18-20].

Acoustic radiation force impulse imaging (ARFI) is a non-invasive study identifying tissue stiffness with ultrasound examination. Data in the paediatric age group are available [21], so this can be used to grade the extent of liver stiffness [22].

The aim of our study was to evaluate the NAFLD spectrum in children with type I DM by simple fibrosis scores and advanced biochemical markers in association with conventional abdominal ultrasonography (US) and acoustic radiation force impulse elastography (ARFI), and to compare their results.

MATERIAL AND METHODS

A cross-sectional study involving 142 type 1 diabetes mellitus (T1DM) children in the age range 6–18 years, who were referred to the Paediatric Clinic in the Centre of Excellence in the National Research Centre between January 2018 and December 2019. A control group of 79 participants were included in the study; they were age- and sex-matched healthy subjects. The study protocol was approved by the Human Ethics Committee of National Research Centre Approval no. (16-334), and written informed consent was obtained from all parents/legal guardians of the children. A conventional insulin regimen was followed for all cases. Exclusion criteria were as follows: children with secondary DM and any chronic-related diseases like hypothyroidism or hypo-adrenalism; also, children with any previous hepatic involvement, especially viral hepatitis, were excluded from the study. Complete history taking and thorough clinical examination including anthropometric measurements (height and weight) were done following the International Biological Program (IBP) [23]. BMI was calculated as usual (kg/m^2). Pertinent laboratory investigations were performed for all patients and controls including glycosylated haemoglobin (HbA1C) levels, lipid profile (cholesterol, triglyceride, HDL, and LDL), complete blood picture (CBC) including (haemoglobin, total and differential WBC count and platelets), and liver enzymes including AST and ALT, using an Olympus AU 400 supplied from Olympus Life and Material Science (Europe GmbH, Wendenstraße, Hamburg, Germany). Viral Markers (HB s Ag, HCV Ab, and HIV Ab) were done to exclude viral hepatitis in our cases using the PRECHECK Kit (USA).

NON-INVASIVE FIBROSIS SCORE

Calculation of simple fibrosis scores (AST/ALT ratio, AST to platelet ratio index [APRI]) [24], fibrosis (FIB)-4 index, and paediatric NAFLD fibrosis index (PNFI) was performed in our cases and controls.

FIBROSIS 4 SCORE

(Age × AST) / [platelets × (square root (ALT))] [25, 26].

PAEDIATRIC NAFLD FIBROSIS INDEX (PNFI)

1) Calculation of the linear predictor:
$lp = -6.539 \times \log_e$ [age (years)] + 0.207 × waist (cm) + 1.957 × $\log_e$ [tryglicerydes (mg/dl)] – 10.074

2) Transformation of the linear predictor into the PNFI:

$$\text{PNFI} = \frac{1}{1 + e^{-lp}} \times 10 \quad [17].$$

Assessment of advanced biochemical markers of extracellular matrix turnover hyaluronic acid (HA), amino terminal pro peptide of type III collagen (PIIINP), and tissue inhibitor of metalloproteinase 1 (TIMP-1) levels in our cases and controls.

The ELF test is used for the diagnosis of liver fibrosis. ELF is an algorithm involving 3 direct markers of fibro genesis and extracellular matrix turnover, HA (hyaluronic acid), amino terminal pro peptide of type III collagen (PIIINP), and tissue inhibitor of metalloproteinase 1 (TIMP-1) levels. To calculate this equation

ELF Score*T = 2.278 + 0.851 In (CHA) + 0.751 In (CPIIINP) + 0.394 In (CTIMP-1) [27].

For the diagnosis of significant fibrosis in cases with chronic liver disease [28].

Blood sample collection:

Peripheral venous blood samples after 12 hrs of fasting were withdrawn from all participants by venepuncture under complete aseptic conditions: 2 mL EDTA blood for CBC and HbA_{1c} estimation, and finally 5 ml of blood was left to clot then sera were separated and aliquoted. Part of the sera were used immediately for measurement of fasting glucose, lipid profile, AST, ALT, and albumin using an Olympus AU 400 autoanalyser, and the remaining sera were uniquely labelled and stored at –20°C for further assessment of the selected parameters (Insulin, C-peptide , hyaluronic acid [HA], amino terminal pro peptide of type III collagen [PIIINP], and tissue inhibitor of metalloproteinase levels by ELISA technique). HBA1c levels were determined by Stanbio kit.

IMAGING MODALITIES

Abdominal ultrasonography was performed, by the same expert, for liver size and echogenicity. Normal liver parenchyma has a homogeneous echotexture with echogenicity equal to or slightly greater than that of the renal cortex and spleen. The liver reveals echogenicity more than the kidney and spleen due to fatty infiltration [29]. Various (0-3) grades of steatosis have been proposed based on analysis of the intensity of the echogenicity [30]. The model of ultrasound apparatus is SA –R3 (No S06YM3 HDC00012F) SAMSUNG MEDISON Company –South Korea.

Acoustic radiation force impulse elastography (ARFI): Acoustic radiation force impulse elastography was performed for all subjects with a Siemens Acuson S3000 Virtual Touch ultrasound system (Siemens AG, Erlangen, Germany) with a 6CI transducer [31].

STATISTICAL ANALYSIS

Analysis of our results was carried out using the standard computer program Statistical Package for the Social Sciences (SPSS) for Windows, release 17.0 (SPSS Inc., USA). All numerical variables were expressed as mean ± standard deviation (SD). The intergroup comparisons were performed by using an independent-sample t test and a one-way analysis of variance and chi-square tests for categorical variables. Pearson's and Spearman's correlation tests (r = correlation coefficient) were used for the correlation of normal and nonparametric variables, respectively. For all tests, a $p < 0.05$ was considered significant and $p < 0.01$ was considered highly significant.

RESULTS

A total of 142 children with T1DM were included in our study. Their mean age was 12.98 ±3.66 years, 86 were females (60.6%) and 56 (39.4%) were male. The control group comprised 79 age- and sex-matched children. The mean duration of diabetes in our cases was 5.52 ±3.23 years. Descriptive data (clinical and basic laboratory parameters) of the studied T1DM cases and controls are summarized in Tables 1 and 2.

According to the results of abdominal sonar there were 32 cases (22.4%) with enlarged liver and 53 (37.3%) cases of increased echogenicity grade (NAFLD). Comparing ultrasonography results between our cases and controls, there was a highly significant difference in liver span, $P = 0.000$. Also echogenicity grades difference in cases and control, normal echogenicity in 89cases (62.6%) and in 72 control (91.1%), while grade I 25 cases (17.6%), one control (1.3%), in addition grade II in 28 cases (19.7%) and 6 controls (7.6%). There was a highly statistically significant difference between cases and controls ($p = 0.000$).

TABLE 1. Comparative data of some clinical parameters between cases and controls

	1 = T1DM 2 = Controls	Mean	Std. Deviation	Sig. (2-tailed)
SYS	1	106.07	10.08	0.021*
	2	102.28	10.04	
DIAS	1	69.23	7.02	0.026*
	2	66.58	7.91	
BMI	1	20.79	4.87	0.001**
	2	18.51	4.00	
WC/ HIP	1	0.84	0.066	0.667
	2	0.83	0.057	
WC/ HT	1	0.48	0.075	0.042*
	2	0.51	0.124	
% Body Fat	1	22.30	6.90	0.012*
	2	19.84	5.987	

BMI – body mass index; SBP – systolic blood pressure; DPB – diastolic blood pressure; WC – waist circumference; HIPC – hip circumference

** Significant p < 0.05; **highly significant p < 0.01*

TABLE 2. Comparative data of some related laboratory parameters between cases and controls

	1 = T1DM 2 = Controls	Mean	Std. deviation	Sig. (2-tailed)
Fasting G mg/ml	1	161.00	36.28	0.000**
	2	78.00	7.89	
Glycated Hb	1	8.03	0.954	0.000**
	2	5.41	0.692	
Cholesterol mg/ml	1	156.16	18.46	0.001**
	2	146.89	19.84	
Triglyceride mg/ml	1	58.15	15.32	0.253
	2	60.46	12.20	
HDL mg/ml	1	38.50	6.66	0.245
	2	40.07	13.48	
LDL mg/ml	1	61.50	11.22	0.000**
	2	56.06	7.091	
AST U/l	1	16.77	3.27	0.307
	2	16.27	3.77	
ALT U/l	1	18.16	4.00	0.013*
	2	16.75	4.04	
C peptide ng/ml	1	0.2728	0.449	0.000**
	2	1.05	844	

FG – fasting glucose; HDL – high density lipoprotein; LDL – low density lipoprotein; AST – aspartate aminotransferase; ALT – alanine aminotransferase

** Significant p < 0.05; **highly significant p < 0.01*

TABLE 3. Correlations between Abdominal Sonar with ARFI in our cases

		Liver eugenicity	Liver span	Stiffness
Liver eugenicity				
	Pearson Correlation	1	0.600**	0.290**
	Sig. (2-tailed)		0.000	0.000
	N	203	203	141
Liver span				
	Pearson Correlation	0.600**	1	0.179*
	Sig. (2-tailed)	0.000		0.033
	N	203	204	142
Stiffness				
	Pearson Correlation	0.290**	0.179*	1
	Sig. (2-tailed)	0.000	0.033	
	N	141	142	148

** Correlation is significant at the 0.05 level (2-tailed); ** Correlation is significant at the 0.01 level (2-tailed)*

ARFI results in cases and controls: there were 93 cases (65.5%) with normal results, 11 (7.7%) with various degrees of fibrosis, and 38 cases were dropped. Also, 24 controls (30.4%) were dropped, 52 controls (65.8%) were normal, and 3 controls (3.8%) had various degrees of fibrosis. Positive correlation was revealed of liver echogenicity with liver span and degree of stiffness evaluated by ARFI in our cases, as shown in Table 3. Also, in different degrees of fibrosis there was a positive correlation in our cases with enlarged liver ($p = 0.044$; Table 4).

Regarding results of non-invasive fibrosis score, there were statistically significant differences between cases and controls in fibrosis 4 score, discriminant score, and ratio of AST to ALT; $p = 0.009$, 0.000, and 0.019, respectively (Table 5).

Comparing results of cases with controls, regarding advanced biochemical markers and ELF score, there was a high statistically significant difference in TMP, hyaluronic acid, and ELF; $p = 0.00$, 0.044, and 0.00, respectively (Table 6).

Non-invasive score results of our cases when divided into NAFLD and non-NAFLD showed statistically significant differences in the following scores: fibrosis 4 score, APRI score, and discriminant score ($p = 0.049$; 0.031, and 0.042, respectively; Table 7).

DISCUSSION

Excess triglyceride accumulation in the liver in the absence of excessive alcohol consumption occurred in non-alcoholic fatty liver disease (NAFLD) [32]. NAFLD consists of a range of liver diseases from simple steatosis progressing through non-alcoholic steatohepatitis (NASH) and fibrosis to cirrhosis, ending in liver failure. The definition of simple steatosis pathologically is more than 5% hepatic steatosis with lack of inflammation or hepatocellular injury, whereas NASH constitutes inflammation and liver cell injury with different fibrosis stages [33]. While NASH has the potential to advance to fibrosis, liver failure, and hepatic cancer, simple steatosis rarely progresses to more advanced liver disease [34].

Our results regarding ALT, there was a statically significant difference between cases and controls ($p = 0.013$). There were 6 females of our cases with > 22 IU/l. ALT levels in boys ≥ 26 IU/l and in girls ≥ 22 IU/l were used as the upper limit of normal (ULN). The criteria of potential NAFLD with ALT was more than twice the ULN. [35, 36]. In a previous article by Nagwa *et al.* [37] only 3 female patients (4.2%) had mild elevation of ALT level. Various studies found that NAFLD could occur in individuals with normal ALT values [38-40].

In our study regarding liver span and hyper echogenicity in abdominal US in diabetic cases compared to a control group, there was a statistically significant difference ($p = 0.000$). Our result is in concordance with that of El-Karaksy *et al.*[41], who showed that 4.5% had abnormal hyperechogenic liver and/or hepatomegaly on ultrasound in children with type I DM cases. Also, Abdulrahman *et al.* [42] reported that hyperechogenicity with or without hepatomegaly are common in children

TABLE 4. Correlations between cases with enlarged liver and ARFI

		ARFI								Total	
Enlarged liver		Missed	F0	F0-F1	F1	F1-F2	F2	F3	F4		Sig. (2-tailed)
No		26	48	0	23	5	4	2	0	108	
	24.1%	44.4%	.0%	21.3%	4.6%	3.7%	1.9%	.9%	100.0%	0.044*	
Enlarged liver		12	10	1	5	1	1	1	2	34	
	35.3%	29.4%	2.9%	14.7%	3.1%	2.9%	2.9%	5.9%	100.0%	142	
Total		38	58	1	28	6	5	4	2		

**. Correlation is significant at the 0.05 level (2-tailed)*

with type 1 diabetes and tend to be more prevalent among children with less glycaemic control.

ARFI comparative results in this study showed no statistically significant difference between cases and controls.

Prospective paediatric studies have shown ARFI to be an accepted non-invasive method. Hanquinet *et al.* [43] studied 39 children with biopsy-proven chronic liver disease also 103 normal subjects, and revealed the mean value for ARFI to be 1.12 m/s in normal subjects and 1.99 m/s in those with chronic liver disease. Furthermore, to differentiate between children with mild and severe (F>2) fibrosis [43]. Also, the results of Kummur *et al*. did not show any significantly increased prevalence of NAFLD in a paediatric cohort using ALT, ultrasound, and liver stiffness measurements [44] .

Regarding the simple fibrosis score in our study, the results of cases showed no statistically significant difference in PNFI; the same results were shown by Nobili *et al.* [17]. This score includes simple available data consisting of age, waist circumference, and triglyceride levels.

In addition, other simple fibrosis score parameters, FIB-4 index, AST/ALT ratio. Our results showed a statistically significant difference ($p = 0.007$ and 0.15, respectively). The AST-platelet ratio index (APRI), which includes AST and platelet count, was used to predict fibrosis in different chronic hepatic involvement in both children and adults [45, 46]. The APRI score provides a number of results, ranging from 0.1 to 8.0, for the detection of significant fibrosis in those with chronic hepatitis C. According to the reviews, a cut-off level less than or equal to 0.5 provides a sensitivity of 81.0%

Our results of APRI showed no statistically significant difference between cases and controls, but when we subdivide our cases into NAFLD and non-NAFLD, there was a statistically significant difference; $p = 0.031$. The results of Alkhouri *et al.* [18] were in concordance with our results of FIB-4 index but not of APRI and AST/ALT ratio.

The assessment levels of 3 main parts directly involved in liver matrix metabolism: hyaluronic acid (HA), procollagen III amino terminal peptide (PIIINP), and tissue inhibitor of matrix metalloproteinase 1 (TIMP-1) for use in the enhanced liver fibrosis (ELF™) test, which is considered as a noninvasive test to measure the analyses, and the software calculates results and reports a unit numeric

TABLE 5. Comparative data of non-invasive scores between cases and controls

	1 = T1DM 2 = controls	Mean	Std. deviation	SIG
PNFI	1	0.88	1.75	0.820
	2	0.94	1.64	
Fibrosis 4 Score	1	0.19	0.095	0.009**
	2	0.15	0.102	
APRI score	1	0.12	0.05	0.825
	2	0.12	0.05	
Discriminant score	1	12.60	2.13	0.000**
	2	8.53	1.53	
ratio of AST to ALT Values.	1	0.93	0.136	0.019*
	2	0.98	0.17	
Linear Predictor	1	3.95	2.61	0.630
	2	4.15	3.16	

PNFI – pediatric NAFLD fibrosis index; APRI – AST to platelet ratio index

** Significant $p < 0.05$; **highly significant $p < 0.01$*

TABLE 6. Comparative data of advanced biochemical markers as markers of extracellular matrix turnover and ELF score between cases and controls

	1 = T1DM 2 = Control	Mean	Std. deviation	Sig. (2-tailed)
H P III PRO Peptide (ng /ml)	1	18.19	26.47	0.417
	2	27.27	80.60	
TIMP1 (ng/ml)	1	18.85	9.51	0.000**
	2	9.20	9.86	
Hyaluronic acid (ng/ml)	1	24.32	67.71	0.044*
	2	11.88	9.34	
ELF Score	1	10.22	3.171	0.000**
	2	7.79	1.473	

H P III PRO Peptide: amino terminal pro peptide of type III collagen (PIIINP)

TIMP1 – tissue inhibitor of metalloproteinase 1; ELF score – enhanced liver fibrosis score

** Significant $p < 0.05$; **highly significant $p < 0.01$*

TABLE 7. Comparative data of non-invasive scores in cases with & without NAFLD

	NAFLD without NAFLD	Mean	Std. deviation	SIG
PNFI	NAFLD	1.05	1.87	0.467
	without NAFLD	0.82	1.64	
Fibrosis 4 score	NAFLD	0.205	0.077	0.049*
	without NAFLD	0.175	0.103	
ELF score	NAFLD	9.99	3.61	0.259
	without NAFLD	9.20	2.77	
APRI score	NAFLD	0.110	0.038	0.031*
	without NAFLD	0.133	0.061	
Discriminant score	NAFLD	12.44	2.09	0.042*
	without NAFLD	11.15	2.81	
Ratio of AST to ALT values	NAFLD	0.92	0121	0.171
	without NAFLD	0.96	0.159	
Linear Predictor	NAFLD	3.36	2.02	0.081
	without NAFLD	4.25	2.93	

NAFLD — nonalcoholic fatty liver disease; PNFI — pediatric NAFLD fibrosis index; APRI — AST to platelet ratio index

** Significant $p < 0.05$*

score. There is a link between elevated ELF scores and biopsy-proven fibrosis/cirrhosis also in clinical prognosis. ELF has been widely investigated across various forms of chronic liver disease (CLD) [47].

Advanced biochemical marker results in our study revealed a statistically significant difference in tissue inhibitor of metalloproteinase and hyaluronic acid ($p = 0.000$ and 0.044, respectively). Also, the ELF score results showed a statistically significant difference. The same results were shown by Nobili *et al.* [17]; this study revealed the importance of the ELF test as a diagnostic marker of liver fibrosis in both children and adolescents.

In the present work there was a statistically significance greater increase in TMP1 levels in cases than in controls. Previous studies have reported the TIMP-1 level to be positively correlated with HbA1C in type 1 diabetic patients [48, 49]. TIMP-1 was used as a marker for abnormal regulation of matrix remodelling post cardiovascular event in patients with type 1 diabetes [50].

Also, findings by Wang *et al.* [51] showed a positive association between TIMP1 and type 2 diabetes, which concur with the results from several different studies.

Increase extracellular matrix deposition is the main feature of systemic fibrosis. TIMP1 is a considered a biomarker for systemic fibrosis. The mechanism of TIMP1 enhances fibrosis by preventing metalloproteinases in the breakdown of extracellular matrix [52]. Epidemiological findings in people with and without T2D have shown different levels of metalloproteinases, the target enzyme of TIMP1 inhibition [53, 54]. Also, TIMP1 promotes adipogenesis by accelerating lipid accumulation and adipocyte differentiation [55]. Hypoxia and inflammation in the adipose tissues, with aggravating adipose tissue fibrosis resulting from rapid expansion of adipose tissues [56].

The pathogenesis of T2D might be influenced with TIMP1 by its role in adiposity, systemic fibrosis, and inflammation, which have been correlated with metabolic disturbances resulting in insulin resistance [57]. In Wang *et al.* [51] found that increased TIMP1 levels, but not ELF score, PIIIMP, and HA, were associated with increased type 2 diabetes risk in adults [51].

NAFLD is mostly benign, whereas NASH can progress to cirrhosis, hepatic failure, and hepatocellular cancer. Hence, it is important to identify NASH in the early stages to initiate treatment. For early diagnosis of NASH, it is necessary to reveal NASH with no or mild fibrosis. While liver biopsy is the gold standard for the diagnosis of NAFLD, it is invasive and its reliability for detecting steatosis and fibrosis has limitations – sampling errors and variations in interpretation among pathologists may occur. Non-invasive methods are needed to diagnose NASH and to assess NASH progression or resolution without the need for liver biopsy.

In our study, there were statistically significant differences in many parameters for hepatic involvement, which reflect that a pathological condition was occurring that requires a meticulous follow-up for early diagnosis and prompt intervention for safe hepatic function and good prognosis of diabetic cases. To the best of our knowledge, our study included many non-invasive parameters to evaluate the NAFLD spectrum in type I DM children with limited studies that evaluate hepatic involvement affection in diabetic children.

A limitation of this study is the small sample size of included cases leading to difficulty in drawing solid conclusions. However, the findings from this study could lead to better organized larger studies. Liver biopsy as the gold standard for diagnosis of NAFLD was not done.

CONCLUSIONS

In conclusion, the obtained results support that there are suitable available non-invasive biomarkers for hepatic affection in children with type I diabetes mellitus. In addition of importance of performing abdominal sonography in children with type I DM for early non-invasive assessment of hepatic affection, also the AST/ALT ratio, FIB-4 index, and ELF scores should be measured to evaluate any ongoing process in diabetic children, while ARFI is needed in more advanced stages.

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DISCLOSURE

The authors declare no conflict of interest.

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