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Original Article

Elevated 1-h post-load plasma glucose levels in normal glucose tolerance children with obesity is associated with early carotid atherosclerosis

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ABSTRACT

Context: Evidence suggests that the 1-h post-load plasma glucose (1-h PG) ≥155 mg/dL during an oral glucose tolerance test (OGTT) predicts development of type 2 diabetes (T2DM) and associated complications, among adults with normal glucose tolerance (NGT), but relevant data on children is scarce.
Objectives: To investigate whether NGT children with obesity whose 1-h PG is ≥155 mg/dL have an increased carotid intima-media thickness (IMT) and exhibit non-alcoholic fatty liver disease (NAFLD) diagnosed by ultrasonography, as compared with NGT subjects with 1-h PG <155 mg/dL and impaired glucose tolerance (IGT).
Methods: Cardio-metabolic profile, OGTT, measurements of carotid IMT and liver ultrasonography were analyzed in 171 non-diabetic children with obesity. Subjects were divided into 3 groups: NGT subjects with a 1-h PG <155 mg/dL, NGT subjects with a 1-h PG ≥155 mg/dL, and IGT subjects.
Results: As compared with NGT individuals with a 1-h PG <155 mg/dL, NGT individuals with a 1-h PG ≥155 mg/dL exhibited higher carotid IMT (0.75 ± 0.15 mm vs. 0.68 ± 0.15 mm; $p < 0.05$). No significant differences were observed in carotid IMT between IGT and NGT subjects with a 1-h PG ≥155 mg/dL (0.75 ± 0.18 mm vs 0.75 ± 0.15 mm; $p > 0.05$). Of the three glycemic parameters, 1-h and 2-h PG, but not fasting glucose, were significantly correlated with carotid IMT. There were no significant differences for increased risk of having NAFLD between the three groups.
Conclusions: These data suggest that a value of 1-h PG ≥155 mg/dL in children and adolescents with obesity is as important as IGT with respect to cardiovascular risks.

Introduction

The incidence of type 2 diabetes mellitus (T2DM) and related dysglycemic conditions at risk for diabetes (called as prediabetes) are gradually increasing worldwide mostly due to the continuously increasing prevalence of obesity [1]. In adolescence, obesity has been associated with increased risk of coronary vascular disability in later life [2]. It is known that T2DM is an independent risk factor for cardiovascular disease (CVD) and non-alcoholic fatty liver disease (NAFLD) [3,4]. Common carotid artery intima-media thickness (IMT) is a well-established measure of early atherosclerosis and is broadly used as a surrogate marker for CVD [5]. Several studies reported thicker carotid walls in diabetic patients than in individuals with normal glucose tolerance (NGT) [6]. Also, there is a clear association between diabetes and NAFLD [7]. Besides to all of these, an increasing number of emerging studies have determined that prediabetes status, which includes impaired fasting glucose (IFG), impaired glucose tolerance (IGT) and/or glycated hemoglobin (HbA1c), were found to be associated with an increased risk of NAFLD and play a vital role in atherosclerotic CVD [8,9].

However, some reports indicate a significant risk for CVD and NAFLD even in subjects with NGT [10,11,12]. Hanefeld et al. evalu-

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ated the risk factors for carotid IMT in a non-diabetic risk population and found that postprandial plasma glucose was an independent risk factor for increased carotid IMT [10]. Kimura et al. investigated whether secretion patterns of glucose and insulin could influence the histological severity in NAFLD patients without prior known T2DM. They found that postprandial hyperinsulinemia (but not glucose levels) was associated with advanced fibrosis [11]. In a recent report, NGT individuals with 1-h post-challenge plasma glucose ≥155 mg/dL have increased blood viscosity comparable to that observed in subjects with IFG and/or IGT. Blood viscosity has been found to be associated with left ventricular hypertrophy, atherosclerosis, vascular stiffness and NAFLD [12]. Additionally, prospective epidemiological studies have also demonstrated that 30–40% of individuals who develop T2DM have NGT at baseline, indicating that prediabetic conditions are limited in their ability to identify individuals at future risk for developing diabetes [13]. Therefore, for preventing diabetes and its associated complications it would be important to detect the individuals who carry the highest risk at NGT. Recently, a cutoff point of 155 mg/dL (8.6 mmol/L) for the 1-h post-load plasma glucose (PG) during an oral glucose tolerance test (OGTT) has been suggested to be able to identify individuals with NGT at high risk for future T2DM [14,15]. Also several observational studies, such as CATAMERI (Catanzaro metabolic risk factors) study, clearly demonstrated that NGT adults with 1-h PG ≥155 mg/dL were predisposed to an increased risk for developing T2DM over a 5 years period [16]. In this CATAMERI study, they also found a strong association between elevated 1-h post-load PG levels in adults with NGT with carotid IMT and NAFLD [17,18]. In a most recent study, Tanaka et al. showed that PG at 60 min was associated with increased carotid IMT more strongly than PG at 120 min by 75gOGTT suggested that PG at 60 min could be considered as a predictor of atherosclerosis [19]. In children, it has been demonstrated that 1-h post-load PG ≥155 mg/dL during an OGTT is correlated with an unfavorable metabolic and inflammatory profile [20]. According to this study a cutoff value of 1-h post-load PG ≥155 mg/dL could be used as an additional marker to identify children and adolescents with obesity at increased risk of developing obesity complications [20]. Because, there is no data regarding the impact of the 1-h post-load PG on the risk of atherosclerosis and NAFLD in asymptomatic children, we designed this study to address the question if glucose tolerance status, and in particular 1-h post-load PG levels, may affect carotid IMT and NAFLD in a group of children with obesity.

Methods

Study design and participants

The study was carried out over a period of 12 months from Jan 2018 to Jan 2019. The subjects were selected from the patients aged between 10–18 years that presented to our outpatient clinic to assess their metabolic status for obesity. After a 12-h fasting, all subjects underwent thorough a physical examination and a biochemical evaluation. Patients with diabetes were excluded from the study. Additionaly, patients who have a chronic gastrointestinal and/or cardiovascular disease, any hematologic disease, which could alter HbA1c values, a history of drug use, an endocrine pathology or suspected syndromes associated with obesity were also excluded. Except those, patients who have a body mass index (BMI) greater than 95th percentile according to the standards of the Centers for Disease Control and Prevention (CDC2000) were consecutively enrolled in the study. Thereafter, after a 12-h fasting 1.75 g/kg (max75 g) OGTT was carried out in order to determine glucose status of 178 eligible participants. Glucose and insulin levels measured 5 time points (0-,30-,60-,90-,120-min) during a 2-h OGTT. Among 178 patients, 7 patients were excluded because they have diagnosed with diabetes after the OGTT had been performed. Carotid IMT was measured and liver ultrasonography were performed in all patients on the same day with OGTT.

Clinical and biochemical measurements

After a 12-h fasting, all individuals underwent anthropometrical evaluation including assessment of BMI, blood pressure (BP) obtained in the left arm of the supine position, after 10 min of quiet rest. A biochemical evaluation including thyroid function tests and serum cortisol measurements for probable endocrine pathology were performed in all subjects. Height was measured using a Seca stadiometer with a sensitivity of 0.1 cm. Weight was measured using a Seca scale with a sensitivity of 0.1 kg. Height and weight were obtained with participants in light clothes and without shoes. Serum concentrations of fasting plasma glucose (FPG), triglyceride, total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C) concentrations were measured enzymatically using DP Modular Systems (Roche Diagnostic Corp., Indianapolis, IN). Fasting insulin was measured using sandwich electrochemiluminescence immunoassay (ECLIA) techniques (Elecsys Insulin, Roche Diagnostics Corp., Indianapolis, IN). High performance liquid chromatography (HPLC) was employed to determine the percentage of HbA1c.

Calculation

BMI was calculated by dividing weight (kg) by height squared (m^2). Patients with a BMI over 95th percentile were defined as obese [21]. Glucose tolerance status was evaluated according to ADA criteria [22]: individuals were thus classified as NGT when FPG was less than 100 mg/dL and 2-h post-load PG was less than 140 mg/dL, and IGT when 2-h post-load PG was 140 −199 mg/dL. Then, individuals in the NGT group were further divided into two subgroups based upon their 1-h post-load PG concentration (NGT with a 1-h post-load PG < 155 mg/dL, NGT with a 1-h post-load PG ≥ 155 mg/dL, respectively).

Measurement of carotid IMT

High resolution B-mode ultrasound imaging was used to measure IMT of the common carotid artery (CCA) by a 7.5 MHz linear array transducer (Aplio 500, Toshiba, Japan). IMT was measured from plaque-free 10 mm linear arterial segment at the far wall of the CCA, 10 mm proximal to the carotid bifurcation. For each patient two measurements were performed bilaterally, the values were averaged, and presented as the mean of IMT of the common carotid artery. Ultrasound assessment was performed by an experienced radiologist who was unaware of the subjects' clinical and laboratory findings.

Liver ultrasonography

Ultrasonography of the liver executed by the same experienced radiologist who was blind to participants' clinical characteristics. Right intercostal, right subcostal longitudinal-transverse and epigastric longitudinal-transverse scanning were carried out using a 3.5 MHz convex transducer (Aplio 500, Toshiba, Japan). The ultrasonographic criteria used to diagnose fatty liver included liver and kidney echogenicity discrepancy, the presence of diffusely increased hepatic echogenicity, indistinct periportal echogenicity and/ or disturbed visibility of deeper portions of the liver. Since semiquantitative evaluation of the degree of fatty liver by ultra-

sound was not available participants were categorized as subjects with or without fatty liver.

Ethics

This study was conducted in accordance with the declaration of Helsinki and initiated after the approval of the local Ethics Committee of Medipol University (approvel number: 2018-619). Data were collected from the participants attending at endocrinology outpatient clinic in University of Health Sciences Istanbul Bagcılar Training and Research Hospital after the nature of the study was explained to them and written informed consent of the subjects and parents was obtained before the study.

Statistical analysis

In addition to descriptive statistics (mean, standard-deviation), one-way analysis of variance (ANOVA) test was used for group comparisons of normally distributed variables. Kruskal–Wallis test was used for intergroup comparisons of non-normally distributed variables, Dunn's multiple comparison test was utilized in the comparison of subgroups, and Chi-square test was performed for the evaluation of qualitative data. A correlation analysis was performed using Spearman's correlation analysis. All variables were included in a multiple linear regression analysis to assess the independent determinants. A P-value of <0.05 was considered statistically significant. Statistical analysis was performed using the program NCSS 2007 (Number Cruncher Statistical System, Kaysville, Utah, USA).

Results

A total of 171 non-diabetic subjects with obesity (97 females, 74 males, mean age: 13.1 ± 1.9 years) were included in the study. Among 171 patients, 69 had impaired glucose tolerance (IGT). A 1-h post-load PG cutoff point of 155 mg/dL during OGTT was used to divide subjects with NGT into two groups: 73 subjects with 1-h post-load PG <155 mg/dL, and 29 subjects with 1-h post-load PG ≥155 mg/dL. Table 1 shows the clinical characteristics and laboratory findings of the three study groups.

No statistically significant difference was found between the groups in terms of age, gender, height and BMI ($p > 0.05$). As shown in Table 1, IGT subjects had a worse metabolic and cardiovascular risk profile exhibiting significantly higher triglycerides, insulin (1-h and 2-h post-challenge insulin), glucose (fasting, 1-h and 2-h post-load PG) and carotid IMT as compared with NGT individuals with 1-h post-load PG <155 mg/dL ($p < 0.05$). By contrast, no significant differences were observed in metabolic and cardiovascular risk factors between IGT subjects and NGT individuals with 1-h post-load PG ≥155 mg/dL ($p > 0.05$), with the exception of 2-h post-challenge glucose levels which were increased in the IGT group ($p < 0.05$). As compared with individuals with 1-h post-load PG <155 mg/dL, NGT individuals with 1-h post-load PG ≥155 mg/dL exhibited significantly higher FGP, 1-h post-challenge insulin levels and carotid IMT ($p < 0.05$). There were no significant differences between the two groups in terms of other clinic and metabolic parameters.

The ultrasonography revealed NAFLD in a total of 71(41.5%) of the subjects; of these, 26 (36.6%) had NGT with a 1-h post-load PG <155 mg/dL, 11 (15.4%) had NGT with a 1-h post-load PG ≥155 mg/dL, and 34 (47.8%) had IGT. It is notable that individuals with IGT exhibit an increased risk to have NAFLD, but in comparison of three groups, no significant differences were observed in relation to presence of NAFLD (Table 1). But patients with NAFLD had significantly increased carotid IMT (0.76 ± 0.16 mm vs. 0.69 ± 0.15 mm; $p = 0.003$) than the patients without NAFLD.

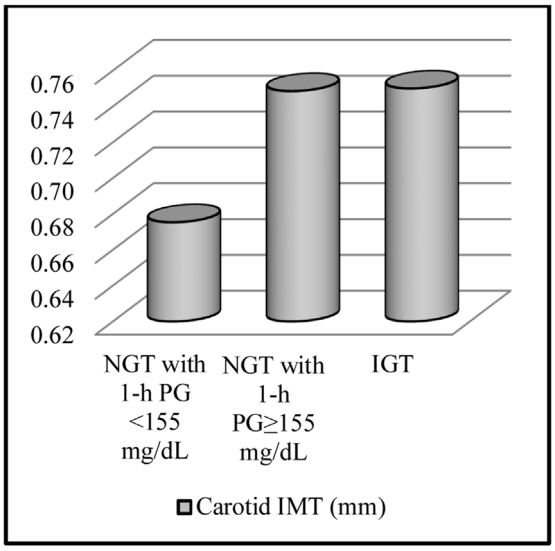

Fig. 1. Carotid IMT in the study population stratified according to glucose status.

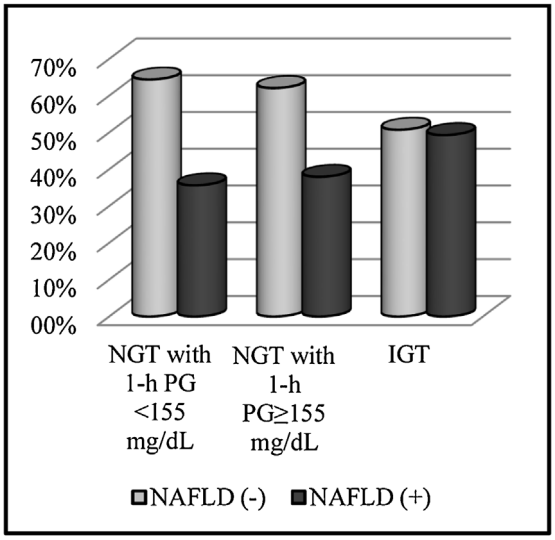

Fig. 2. Proportion of NAFLD diagnosed by ultrasonography among individuals stratified according to glucose status.

Carotid IMT in the study population and proportion of NAFLD among patients stratified according to glucose status is shown in Figs. 1 and 2 .

In Spearman's correlation analysis, of the three glycemic parameters, 1-h and 2-h post-load PG, but not fasting PG, were significantly positively correlated with carotid IMT ($r = 0.215$, $p = 0.005$ for 1-h post-load PG; $r = 0.189$, $p = 0.013$ for 2-h post-load PG). Additionally, carotid IMT was correlated with BMI-SDS ($r = 0.172$, $p = 0.026$), triglycerides ($r = 0.191$, $p = 0.013$) and ALT ($r = 0.183$, $p = 0.017$), while there was a negative correlation with HDL-C ($r = -0.190$, $p = 0.013$), (Table 2). To estimate the independent contribution of carotid IMT, and eliminate the influence of confounders, we conducted a multiple linear regression analyses (Table 3). The three variables that remained significantly associated with carotid IMT were BMI-SDS (β-coefficient = 0.155, $p = 0.040$), 1-h post-load PG (β-coefficient = 0.151, $p = 0.044$) and 2-h post-load PG (β-coefficient = 0.153, $P = 0.041$).

Table 1
Anthropometric and metabolic characteristics of study subjects stratified according to glucose tolerance.

Variables	NGT with 1-h PG < 155 mg/dL	NGT with 1-h PG ≥ 155 mg/dL	IGT	*P*	*P* NGT with 1-h PG < 155 mg/dL vs. NGT with 1-h PG ≥ 155 mg/dL	*P* NGT with 1-h PG < 155 mg/dL vs.IGT	*P* NGT with 1-h PG ≥ 155 mg/dL vs. IGT
Gender (n)(male/female)	73 (37/36)	29(9/20)	69 (28/41)	0.165	0.114	0.298	0.508
Age (years)	13.5 ± 1.8	14.0 ± 2.0	13.3 ± 1.8	0.257	0.448	0.822	0.226
Height-SDS	0.19 ± 1.03	0.08 ± 1.19	0.29 ± 0.97	0.634	0.875	0.833	0.624
BMI (kg/m2)	32.5 ± 3.5	33.1 ± 4.9	32.8 ± 3.3	0.700	0.699	0.853	0.919
BMI-SDS	2.8 ± 0.5	2.9 ± 0.5	2.9 ± 0.4	0.237	0.231	0.555	0.680
SBP (mmHg)	121 ± 12	122 ± 12	125 ± 11	0.131	0.953	0.123	0.416
DBP (mmHg)	75 ± 9	79 ± 8	78 ± 9	0.110	0.145	0.248	0.820
HbA1c	5.7 ± 0.1	5.8 ± 0.1	5.9 ± 0.2	0.311	0.781	0.557	0.318
Total cholesterol (mg/dL)	181 ± 30	187 ± 23	188 ± 37	0.365	0.698	0.350	0.969
HDL-C (mg/dL)	47 ± 8	46 ± 9	44 ± 7	0.159	0.948	0.147	0.512
LDL-C (mg/dL)	117 ± 25	123 ± 19	121 ± 28	0.512	0.567	0.642	0.940
Triglycerides (mg/dL)	126 ± 36	137 ± 55	150 ± 67	**0.044**	0.897	**0.047**	0.058
ALT (UI/L)	27 ± 19	27 ± 18	33 ± 20	0.136	0.999	0.148	0.349
AST (UI/L)	27 ± 15	25 ± 9	30 ± 12	0.211	0.599	0.565	0.196
Fasting glucose (mg/dL)	87 ± 6	90 ± 6	90 ± 8	**0.014**	**0.044**	**0.016**	0.985
1-h glucose (mg/dL)	126 ± 17	165 ± 14	173 ± 27	**0.0001**	**0.0001**	**0.0001**	0.263
2-h glucose (mg/dL)	117 ± 14	122 ± 13	161 ± 16	**0.0001**	0.276	**0.0001**	**0.0001**
Fasting insulin (μIU/mL)	20 ± 8	21 ± 9	23 ± 11	0.208	0.858	0.181	0.687
1-h insulin (μIU/mL)	112 ± 50	170 ± 80	150 ± 86	**0.0001**	**0.001**	**0.005**	0.453
2-h insulin (μIU/mL)	98 ± 58	102 ± 60	139 ± 91	**0.003**	0.955	**0.003**	0.068
NAFLD (n)	26 (35 %)	11(38%)	34 (49%)	0.233	0.826	0.340	0.420
Carotid IMT (mm)	0.68 ± 0.15	0.75 ± 0.15	0.75 ± 0.18	**0.025**	**0.043**	**0.014**	0.999

Bold values: p<0.05 is significant.
Data are means ± SD. NGT, normal glucose tolerance; IGT, impaired glucose tolerance; PG, plasma glucose; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein; ALT, Alanine aminotransferase; AST, aspartate aminotransferase; NAFLD, non-alcoholic fatty liver disease; IMT, intima-media thickness.

Table 2
Correlation between carotid IMT and cardio-metabolic variables.

Variables	Pearson's correlation coefficient (r)	*P*
Age (years)	0.146	0.057
Height-SDS	−0.020	0.799
BMI-SDS	0.172	**0.026**
SBP (mmHg)	−0.050	0.548
DBP (mmHg)	0.088	0.289
HbA1c	0.021	0.787
Total cholesterol (mg/dL)	0.026	0.734
HDL-C (mg/dL)	−0.190	**0.013**
LDL-C (mg/dL)	−0.023	0.769
Triglycerides (mg/dL)	0.191	**0.013**
ALT (UI/L)	0.183	**0.017**
AST (UI/L)	0.095	0.217
Fasting glucose (mg/dL)	0.041	0.596
1-h glucose (mg/dL)	0.215	**0.005**
2-h glucose (mg/dL)	0.189	**0.013**
Fasting insulin (μIU/mL)	0.106	0.167
1-h insulin (μIU/mL)	0.136	0.076
2-h insulin (μIU/mL)	0.018	0.816

Bold values: p<0.05 is significant.
Data are means ± SD. BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein; ALT, Alanine aminotransferase; AST, aspartate aminotransferase.

Table 3
Multiple linear regression analyses with carotid IMT as the dependent variable.

Independent variables	β-coefficient	t	*p*
Age (years)	0.129	1.67	0.128
BMI-SDS	0.155	2.07	**0.040**
SBP (mmHg)	−0.101	−1.31	0.180
DBP (mmHg)	0.065	0.81	0.413
Total cholesterol (mg/dL)	0.136	1.76	0.118
HDL-C (mg/dL)	−0.105	−1.34	0.183
LDL-C (mg/dL)	−0.142	−1.81	0.071
Triglycerides (mg/dL)	0.067	0.83	0.410
ALT (UI/L)	0.144	1.82	0.070
AST (UI/L)	−0.091	−1.21	0.207
Fasting glucose (mg/dL)	0.120	1.53	0.138
1-h glucose (mg/dL)	0.151	2.03	**0.044**
2-h glucose (mg/dL)	0.153	2.06	**0.041**
Fasting insulin (μIU/mL)	−0.118	−1.50	0.140
1-h insulin (μIU/mL)	−0.032	−0.41	0.521
2-h insulin (μIU/mL)	−0.040	−0.56	0.507

Bold values: p<0.05 is significant.
IMT, intima-media thickness; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein; ALT, Alanine aminotransferase; AST, aspartate aminotransferase.

Discussion

In this cross-sectional study, we found that NGT children with obesity, whose 1-h post-load PG is ≥155 mg/dL, have an increased carotid IMT as compared with NGT subjects with 1-h post-load PG <155 mg/dL, which is a finding consistent with the study of Succurro et al. that was performed in adult patients [17]. In addition, it is observed that NGT patients with 1-h post-load PG ≥155 mg/dL have a similar cardiometabolic risk profile, including 1-h post-load PG levels, with IGT individuals, who are considered at high risk for both T2DM and CVD. In particular, when we compared the three glucose homoeostasis parameters, a stronger correlation was observed with 1-h post-load PG and carotid IMT as compared with FPG and 2-h post-load PG. The mechanism by which elevated 1-h PG is associated with increased carotid IMT, surrogate marker for atherosclerosis, has not been elucidated yet. A higher degree of insulin resistance could be one possible explanation as demonstrated by Succurro et al. [17]. In their study they found that NGT subjects with 1-h post-load PG ≥155 mg/dL have lower insulin sensitivity as compared with NGT individuals with 1-h post-load PG <155 mg/dL. In our study we have shown that 1-h post-load insulin levels are significantly higher (170 ± 80 μIU/mL vs.112 ± 50 μIU/mL) in patients with NGT with ≥155 mg/dL than in patients with NGT with <155 mg/dL. It was even higher than in patients with IGT. However, insulin levels were not correlated with carotid IMT in our study, this might suggests that post

prandial hyperglycemia rather than hyperinsulinemia plays role in progression of atherosclerosis. There is a wide evidence from many studies demonstrating that significant fluctuations in plasma glucose levels have more deleterious effect on cardiovascular system than continuous glucose elevations. Marfella et al. reported that maintaining plasma glucose at 15 mmol/L for 2 h resulted in increased mean heart rate, systolic and diastolic pressure and plasma catecholamine levels [23]. Endothelial function measured by flow-mediated endothelium-dependent vasodilation of brachial artery and myocardial perfusion were also negatively affected by post-prandial hyperglycemia in two different studies [24,25]. Besides these clinical studies, many in vitro and animal studies demonstrated the hazardous effect of post-prandial hyperglycemia on the endothelial cells. At the cellular level, acute hyperglycemia creates oxidative stress through overproduction of free radicals in the mitochondria which in turn mediates the apoptotic effects [26]. Monocyte adhesion to endothelial cells which is an early finding in atherosclerosis increases in response to acute glucose elevations and it is even higher in diabetic rats fed to create postprandial glucose spikes than rats fed at libitum despite a higher HbA1c in the latter group [27].

The pathophysiology of NAFLD is associated with lipotoxicity, inflammatory cytokines, apoptosis, and insülin resistance [28]. Also, oxidative stress is well known as one of the most important factor for inflammation and progression of hepatic fibrosis in NAFLD patients [29]. It is suggested that hyperinsulinemia and hyperglycemia, especially glycemic variability, are important predictive factors in glucose impairment for the progression of hepatic fibrosis in NAFLD [30]. Variability of blood glucose might also induce monocyte adhesion to endothelial cells, activate inflammatory cytokines and inflammation, and increase oxidative stress in the liver of patients with NAFLD [30]. The relationship between NAFLD and dysglycemia including T2DM, IFG and IGT has been demonstrated in both adults and children. According to Bedogni et al. approximately 40% of the children with obesity had NAFLD [31]. IGT or T2DM was present in 25% of the children with NAFLD versus 8% of those without NAFLD [31]. Early post-load hyperglycemia at 1-h has also been shown to be associated with increased NAFLD risk in adults with NGT [18]. It was surprising that we could not detect an increased risk of having NAFLD in children with 1-h post-load PG $\geq$155 mg/dL. The risk was increased but not statistically significant in our cohort with IGT. This finding might be related to the relatively low number of cases with 1-h post-load PG $\geq$155 mg/dL in our study population besides limited sensitivity of USG to detect early cases of NAFLD since ALT levels were positively correlated with carotid IMT. Liver biopsy rather than USG would be able to demonstrate a significant association between NAFLD and 1-h post-load PG $\geq$155 mg/dL. Although we could not identify an association between NAFLD and 1-h post-load PG we could demonstrate an increased carotid IMT in patients with NAFLD. This was expected because pathophysiological mechanisms in dysglycemia that lead to cardiovascular and hepatic changes are basically similar.

In conclusion, 1-h post-load PG $\geq$155 mg/dL in children with obesity is as important as IGT with respect to cardiovascular risks. It may even capture NGT children with obesity who are at risk for developing cardiovascular problems. Long-term follow-up studies with large cohorts could also demonstrate its value for predicting future risk of metabolic syndrome and T2DM. Revision of ADA criteria for identifying prediabetic conditions and adding 1-h post-load PG $\geq$155 mg/dL to these criteria should be considered.

Declaration of interest

None.

Funding source

No funds were provided for this study.

Author contributions

S. Kılınç and Z. Atay designed and directed the project. S.Kılınç and Z. Atay took the lead in preparing the draft manuscript with medical writing assistance. All other authors contributed to data collection, participated in data analysis and interpretation, and critically reviewed the draft manuscript.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.orcp.2020.02.001.

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