Cardiovascular Risk Factors in Adolescents with Type 1 Diabetes: Prevalence and Gender Differences

Vuralli D et al. CVD Risk Factors in Adolescents with T1D

Dogus Vuralli¹, Lala Jalilova², Ayfer Alikasifoglu¹, Z. Alev Ozon¹, E. Nazli Gonc¹, Nurgun Kandemir²
¹Division of Pediatric Endocrinology, Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara, Turkey
²Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara, Turkey

What is already known on this topic?
Cardiovascular diseases (CVD) are the most important cause of morbidity and mortality in patients with T1D. Children with T1D had similar or higher prevalence of being overweight or obese compared to their healthy peers.

What this study adds?
Girls with T1D are more likely to be overweight and obese and to have CVD risk than boys. Interventions to reduce the risk of CVD in adults with T1D should begin from childhood and be tailored to compensate for gender variations.

Abstract

Introduction: Cardiovascular diseases (CVD) are the most important cause of morbidity and mortality in patients with T1D. Children with T1D had similar or higher prevalence of being overweight or obese compared to their healthy peers. In this study we aimed to determine prevalence of CVD risk factors in children and adolescents with T1D and the impact of obesity and sex differences on these factors.

Methods: Data of 365 patients (200 girls, 165 boys) who were 10-21 years of age and who had been using intensive insulin therapy with a diagnosis of T1D for at least 3 years were evaluated. Patients were divided into normal weight (NW), overweight (OW) and obese (Ob) groups according to body mass index percentiles. Risk factors for CVD (obesity, dyslipidemia, hypertension) were compared between groups, and impact of gender was also analyzed.

Results: Prevalence of OW/Ob was 25.9% which was significantly higher in girls (30.6% vs 20.1%, p<0.001). Rate of hypertension was highest in OW/Ob girls followed by OW/Ob boys, and similar in NW girls and boys (p<0.001). Mean LDL-c and TG levels were highest in OW/Ob girls, followed by OW/Ob boys, NW girls and NW boys, respectively (p<0.001 and p<0.001, respectively). Mean HDL-c levels were similar among groups. Rates of high LDL-c and TG were similar between OW/Ob girls and boys and higher than NW girls, followed by NW boys (p<0.001 and p<0.001, respectively). Rate of low HDL-c was more common in OW/Ob girls and boys, and higher than NW girls, followed by NW boys (p<0.001). Overall, girls were 1.9 times more likely than boys to have two or more risk factors for CVD. Factors associated with risk for CVD in multiple logistic regression analyses were being a girl, followed by higher daily insulin dose, higher HbA1c, longer diabetes duration (r=0.856; p<0.001).

Discussion: In spite of the increased prevalence for obesity in both sexes, the trend for CVD risk factors has increased more in obese girls, followed by obese boys and girls who are normal weight. Girls with T1D are more likely to be overweight/obese and to have CVD risk than boys, highlighting the need for early intervention and additional studies to elucidate the causes, particularly in girls with T1D.

Keywords: Overweight, obesity, type 1 diabetes, dyslipidemia, hypertension

Dogus Vuralli, Division of Pediatric Endocrinology, Department of Pediatrics, Hacettepe University Faculty of Medicine, Hacettepe District, Altindag Ankara, 06230, Turkey
9+90 312 3051124
dvuralli@hotmail.com
02.03.2023
26.07.2023

Published: 09.08.2023

Introduction
Cardiovascular diseases (CVD) are the most important cause of morbidity and mortality in patients with T1D [1]. CVD is more common, occurs earlier, and has a higher mortality rate in patients with T1D than individuals without diabetes [2]. It has been reported that the pathogenesis of CVD accelerates in the patients with T1D and although CVD rarely presents in childhood, subclinical damage to the cardiovascular system begins in the pediatric age group [3]. Preventing CVD by alleviating cardiovascular risk factors is a crucial treatment goal for patients with T1D.

Obesity in the childhood period is considered to be an important risk factor for CVD in adulthood [4]. Being overweight and having abdominal adiposity have been associated with atherosclerosis and dyslipidemia [5]. Children with T1D had the similar or higher prevalence of being overweight or obese compared to their healthy peers, with rates reaching 25–35% [6–11]. The risk of CVD is already high in T1D, and this risk may increase with obesity. It is observed that obesity-related comorbidities increasingly affect individuals with T1D. Obese individuals with T1D have lower insulin sensitivity than non-obese with T1D, and it has been recently shown that CVD risk factors are increased in children with T1D who are overweight or obese [12]. A report of the Exchange study showed a higher prevalence of hypertension and dyslipidemia in obese patients with T1D than in non-obese patients [13]. A recent study involving children and young adults with T1D showed a higher rate of MS in overweight and obese individuals [14]. Unhealthy behavioral habits contribute to increased cardiovascular risk. Smoking and a sedentary lifestyle are associated with major CVD morbidity and mortality in individuals with T1D [15]. In this study we aimed to determine the prevalence of CVD risk factors in children and adolescents with type 1 diabetes and the impact of obesity and sex differences on these factors (how are they related to obesity and sex).
Methods

The data of 365 patients (200 girls, 165 boys) who were 10-21 years of age and who had been using intensive insulin therapy (89% multiple-dose insulin therapy, 11% insulin pump) with a diagnosis of T1D for at least 3 years were evaluated in this descriptive, cross-sectional study. The diagnosis of T1D was confirmed by the presence of anti-GAD, anti-islet, or anti-insulin antibodies. The body weight was measured as kilograms using a digital weighing scale (SECA, 769) with a sensitivity of 0.1 kg. The height was measured in meters with the patients in the standing position using a stadiometer (Harpenden, Holtain Ltd., Crymych, Dyfed, UK) with a sensitivity of 0.1 cm. All the measurements were made by a nurse trained in auxology. BMI was calculated as weight in kilograms divided by height in meters squared and converted to BMI percentiles for age and sex using the Centers for Disease Control and Prevention (CDC) growth charts from 2000 (Centers for Disease Control and Prevention: BMI for children and teens, https://www.cdc.gov/nci/epidemiology/bmi/child-for-age.htm). Those with a BMI <10 percentile were considered as underweight (UW), BMI ≥10 and BMI <85 percentile normal weight (NW), BMI≥ 85 and BMI<95 percentile overweight (OW), and BMI≥ 95 percentile obese (Ob).

There was only two patients who were UW and we did not include the underweight group in further analysis in the study, since the number was very small and as we aimed to compare normal weight versus overweight and obese cases. Since the number of patients in the obese group was low, when comparing in terms of CVD risk factors regarding genders, the OW and Ob groups were combined and the cases were divided into two groups as NW and OW/Ob. At the time of evaluation, the chronological age, body weight, height, body mass index (BMI), blood pressure, hemoglobin A1c (HbA1c), lipid profile, and daily insulin dose per body weight (IU/kg/day) were noted. The age at diagnosis and duration of diabetes were also recorded. All cases had HbA1c values checked every 3 months and as the HbA1c value in the study, the average of the four HbA1c values examined in the last year before the evaluation was taken. Insulin dose was defined as the total daily units of insulin divided by the body weight in kilograms and total daily insulin dosage was obtained by randomly selecting three days from the patient records.

Blood pressure was measured with a standardized automatic sphygmomanometer in the right arm with an appropriately sized cuff in the sitting position after 10 minutes of rest, and the average of three measurements was recorded for analysis. For the definition of high blood pressure, the definitions determined by the NHBPEP study group for children and adolescents were used [16]. A mean systolic or diastolic blood pressure above the 95th percentile defined by age, sex, and height was considered high.

Lipid profiles ([triglyceride (TG), total cholesterol (TC), high-density lipoprotein-cholesterol (HDLC), and low-density lipoprotein-cholesterol (LDL-c)] were determined by the fasting blood samples. Serum lipid levels were measured by autoanalyzer (Roche Diagnostics). Lipid values were evaluated according to the recommendations of the American Diabetes Association (ADA) and the International Diabetes Federation (IDF) [17, 18]. LDL-c ≥ 100 mg/dl, total cholesterol ≥ 200 mg/dl, triglyceride ≥ 150 mg/dl were defined as high. HDL-c < 40 mg/dl for 10-16 years old and <40 mg/dl for boys >16 years old and <50 mg/dl for girls >16 years old was considered low. Dyslipidemia was considered to be an elevation of one or more lipid or lipoprotein levels or for HDL-c reduced levels. The presence of at least two risk factors for CVD such as the presence of obesity (BMI≥85 percentile), high triglyceride levels, low HDL-c levels, and hypertension were considered as increased cardiovascular risk.

The study was approved by the Institutional Ethics Committee (Local Ethics Committee, Approval number: 16969557-2202).

Statistical methods:

Data analyses were performed by using SPSS for Windows, version 22.0 (SPSS Inc., Chicago, IL, United States). The normality of the continuous variables was tested by Kolmogorov-Smirnov test. Countable data were described as mean ± standard deviation (SD) and categorical data were described as the number of cases (%). Statistical analysis differences between two independent groups were compared by Student’s t-test. The differences among more than two independent groups were analyzed by one-way ANOVA. When the p-value from one-way ANOVA was statistically significant, posthoc Bonferroni corrections were used with either a p-value of 0.0167 or 0.0125 to know which group differ from others.

Clinical and laboratory parameters affecting having two or more risk factors for CVD were first evaluated using univariate analysis. The factors that were significant in the univariate analysis were then evaluated with multivariable logistic regression analysis. Independent variables used in the regression analysis were as follows: gender, age, evaluation, HbA1c levels, daily insulin dose, duration of diabetes, presence of type 2 diabetes in the family. A p-value of less than 0.05 was considered statistically significant.

Results

Three hundred sixty-five patients (200 girls, 165 boys) who were followed for at least 3 years with the diagnosis of T1D were included in the study. The mean age of the patients at the time of evaluation was 16.4 ± 3.7 years (range 10-21 years), mean age at diagnosis was 9.6 ± 3.6 years (range 5-17 years), and mean diabetes duration was 7.0±3.1 years (range 3-14 years). 89% of the cases were using multiple-dose insulin therapy and 11% were using an insulin pump therapy. Mean HbA1c was 8.8 ± 2.6 %, and mean total daily insulin dose was 1.0 ± 0.3 IU/kg. There was no difference between boys and girls in terms of age at evaluation, HbA1c level, duration of diabetes and daily dose of insulin.

The prevalence of OW and Ob was 19.3% and 6.6% in the study population (22.6%, and 8% in girls and 15.2%, and 4.9% in boys). The rate of overweight and obesity was higher in girls than boys (p<0.001). Three groups (NW, OW and Ob) were at similar ages and HbA1c levels at the time of evaluation. BMI-SDS was positively correlated to the duration of diabetes (r: 0.768, p<0.001). Daily dose of insulin per body weight was the highest in the Ob group followed by the OW and NW group (1.7±0.3 IU/kg/d, 1.3±0.3 IU/kg/d, and 0.9±0.2 IU/kg/d, respectively, p<0.001). The Ob group had the highest rate of hypertension followed by the OW and NW groups (p<0.001). Ob group had the highest mean LDL-c, TG and total cholesterol levels and the lowest HDL-c levels followed by the OW and NW groups (p<0.001, p<0.001, respectively, p<0.001 and p<0.001, respectively) (Table 1).

Overall hypertension prevalence was 9.4% in the whole population. Rate of hypertension was highest in OW/Ob girls followed by OW/Ob boys, and similar in NW girls and boys (p=0.003) (Table 2). Mean LDL-c and TG levels were highest in OW/Ob girls, followed by OW/Ob boys, NW girls and NW boys, respectively (p<0.001 and p<0.001 respectively) (Figure 1, Panel 1 and supplementary table 1). The mean HDL-c levels were similar among groups (Figure 1, Panel 1 and supplementary table 1). Rates of high LDL-c and TG were similar between OW/Ob girls and boys and higher than NW girls, followed by NW boys (p<0.001 and p<0.001, respectively) (Table 2). Rate of low HDL-c was similar in OW/Ob girls and boys, and higher than NW girls, followed by NW boys (p<0.001) (Table 2). Rate of having at least two risk factors was highest for CVD in OW/Ob girls, followed by OW/Ob boys, NW girls, and NW boys (p<0.001) (Table 2). Overall, girls were 1.9 times more likely than boys to have two or more risk factors for CVD (37/199 vs 16/164).

The patients with two or more risk factors for CVD were older, had higher HbA1c levels, were using a higher dose of daily insulin per kg of body weight, and had longer duration of diabetes in comparison to those with low risk for CVD; which sustained in gender specific analyses (Table 3).

Factors associated with risk for CVD in multiple logistic regression analyses were being a girl, followed by higher daily insulin dose, higher HbA1c, longer diabetes duration (Table 4) (p=0.856; p<0.001).

Discussion

The prevalence of obesity in children and adolescents with T1D is increasing parallel to the general population [6, 19, 20]. One in four T1D patients in this study had BMIs over the 85th percentile, which is greater than that of healthy Turkish children [21-23]. Although there are no nationwide statistics on the frequency of obesity in children and adolescents with T1D, a few regional studies also found a similar prevalence [24, 25]. Previous researches from various regions of the world revealed that 25–38.5% of children with T1D had overweight and obesity [6,
In the current study, overall prevalence of hypertension was similar to the previous studies. However, we showed that hypertension was more common in obese girls with T1D in contrast to obese non-diabetic populations. The prevalence of blood pressure is greater in boys than in girls [36, 37]. However, it should be noted that this difference [36, 38] was less remarkable than the difference between normal weight vs obese diabetic population (%6-5 vs 4%-3.5%, p<0.001). It’s interesting to note that earlier research with T1D patients showed a comparable rise in the prevalence of hypertension in both boys and girls.

Dyslipidemia is recognized as one of the most important CVD risk factor in patients with diabetes [38]. Hypertriglyceridemia causes a disease, which is characterized by increased LDL-c and TG levels and low HDL-c levels [39, 40]. The EDIC study showed that elevated LDL-c and low HDL-c lasting more than 10 years are associated with a higher CVD risk in the T1D population [41]. Diabetes is a disease that causes accelerated atherosclerosis and therefore requires regular lipid monitoring and early intervention [42]. Most studies showed that 26-58% of children with T1D have lipid levels above these defined values [43-45]. Adolescent girls with T1D were reported to have higher mean TG, LDL-c, and ApoB levels than boys, although HbA1c levels were different from boys, suggesting that girls with T1D are at risk for CVD starting from younger ages [45]. In the current study, mean LDL and TG were greater in obese girls than in obese boys, however the prevalence of increased LDL and triglyceride as CVD risk factors was similar in both obese boys and girls with T1D.

It was also thought that the higher prevalence of overweight/obesity and CVD risk in subjects with T1D compared to non-diabetic populations is associated with more progressive early atherosclerotic lesions [50, 51]. However, this predilection does not seem to be preserved in patients with T1D [47, 48]. The prevalence of at least two risk factors for CVD such as the presence of obesity (BMI≥85 percentile), high triglyceride levels, low HDL-c levels, and hypertension were considered as increased cardiovascular risk in the current study. These findings suggest that obesity plays a significant role in the development of CVD. However, it is not clear if female sex may also be a second risk factor.

A recent study showed that the rate of MS was higher in overweight (28%) and obese (53.5%) cases than normal weight (4.9%) in a population of children, adolescents and young adults with T1D [13]. These rates were higher than those in the non-diabetic population where it is reported to have a median prevalence of 11.9% (range 2.9-33.7%) and 22.2% (range 10-66%) in overweight and obese children respectively [46]. The prevalence of MS (0-1%) is even less in normal weight non-diabetic children population [46]. In children and adolescents, a limited number of studies report a gender predilection for MS, which is mostly in favor of boys [36]. However, this predilection does not seem to be preserved in patients with T1D [47, 48].

The presence of at least two risk factors for CVD such as the presence of obesity (BMI≥85 percentile), high triglyceride levels, low HDL-c levels, and hypertension were considered as increased cardiovascular risk in the current study. These findings suggest that obesity plays a significant role in the development of CVD. However, it is not clear if female sex may also be a second risk factor.

A recent study showed that the rate of MS was higher in overweight (28%) and obese (53.5%) cases than normal weight (4.9%) in a population of children, adolescents and young adults with T1D [13]. These rates were higher than those in the non-diabetic population where it is reported to have a median prevalence of 11.9% (range 2.9-33.7%) and 22.2% (range 10-66%) in overweight and obese children respectively [46]. The prevalence of MS (0-1%) is even less in normal weight non-diabetic children population [46]. In children and adolescents, a limited number of studies report a gender predilection for MS, which is mostly in favor of boys [36]. However, this predilection does not seem to be preserved in patients with T1D [47, 48].

The presence of at least two risk factors for CVD such as the presence of obesity (BMI≥85 percentile), high triglyceride levels, low HDL-c levels, and hypertension were considered as increased cardiovascular risk in the current study. These findings suggest that obesity plays a significant role in the development of CVD. However, it is not clear if female sex may also be a second risk factor.
emerge in the early course of T1D, beginning with adolescence. In particular, adolescent girls with T1D have higher CVD risk factors than boys. Therefore, early diagnosis and gender-specific intervention will allow to reduce the risk of CVD morbidity and mortality later in life in women with T1D.

**Study Limitations**

One of the strengths of this study was the considerably large sample size of children and adolescents with a long follow-up period from a single center. Participants in the study were exposed to comparable management strategies which is an important strong suit. This study also has some limitations. First, since data were gathered retrospectively, measurements such as waist circumference were absent, despite the fact that it is optimal to evaluate obesity using waist circumference in children and adolescents. Second, some potential confounders of obesity and CVD risk (i.e. physical activity, dietary practices, and socioeconomic status) were not accounted for. Last but not the least this was not a longitudinal study. In addition, this is not a population-based study and the prevalence rates are not applicable to the entire population of children and adolescents with T1D. Also, we did not compare our patients to a control group of non-diabetic children.

**Conclusion**

In conclusion, this study showed that more than one-fourth of children and adolescents with T1D were overweight or obese. In spite of the increased prevalence for obesity in both sexes, the trend for CVD risk factors has increased more in obese girls, followed by obese boys and girls who are normal weight.

Girls with T1D are more likely to be overweight and obese and to have CVD risk than boys, highlighting the need for early intervention and additional studies to elucidate the causes, particularly in girls with T1D. Interventions to reduce the risk of CVD in adults with T1D should begin from childhood and be tailored to compensate for gender variations. Individuals with T1D may experience less CVD morbidity and mortality as a result of early identification of CVD risk factors and possible gender-specific treatments, which may ultimately lead to better long-term outcomes.

**Statement of Ethics**

This study protocol was reviewed and approved Hacettepe University Ethics Committee, approval number 16/09/57-2202.

**Conflicts of Interests**

The authors have no conflicts of interest to declare.

**Funding Sources**

The authors have no funding sources to declare.

**Author Contributions**

D.V. contributed to conception, design, acquisition, analysis, interpretation, writing, review, and final approval of the version to be published. L.J. contributed to acquisition, analysis, interpretation, and final approval of the version to be published. A.A., Z.A.O., and E.N.G. contributed equally to acquisition, interpretation, writing, review, and final approval of the version to be published. N.K. contributed to conception, design, interpretation, writing, review, and final approval of the version to be published; the order in which each author is listed was decided collectively and unanimously approved by all their co-authors.

**References**


42. Glaser NS, Geller DI, Hmo H, Gittelman S, Malloy M, Lawson Wilkins Pediatric Endocrine Society Committee on Drugs and Therapeutics. Detecting and treating hyperlipidemia in children with type 1 diabetes mellitus: are standard guidelines applicable to this special population? Pediatr Diabetes. 2015; 16(2 Pt 2):442-459.


Table 1. Clinical and laboratory characteristics of the patients with T1D according to the BMI percentiles

<table>
<thead>
<tr>
<th>Gender</th>
<th>A Normal Weight</th>
<th>B Overweight</th>
<th>C Obese</th>
<th>Overall p</th>
<th>A vs B p</th>
<th>A vs C p</th>
<th>B vs C p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Girl</td>
<td>138 (38.0%)</td>
<td>45 (12.4%)</td>
<td>16 (4.4%)</td>
<td>&lt;0.001</td>
<td>&lt;0.001*</td>
<td>&lt;0.001*</td>
<td>0.04*</td>
</tr>
<tr>
<td>Boy</td>
<td>131 (36.1%)</td>
<td>25 (6.9%)</td>
<td>8 (2.2%)</td>
<td>&lt;0.001</td>
<td>&lt;0.001*</td>
<td>&lt;0.001*</td>
<td>0.006*</td>
</tr>
<tr>
<td>Age at evaluation (years)</td>
<td>16.3±3.6</td>
<td>16.7±3.4</td>
<td>16.7±2.9</td>
<td>0.415</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>8.8±2.5</td>
<td>8.7±1.4</td>
<td>8.5±1.0</td>
<td>0.025</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin dose (IU/kg/day)</td>
<td>0.9±0.2</td>
<td>1.0±0.3</td>
<td>1.0±0.3</td>
<td>&lt;0.001*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of diabetes (years)</td>
<td>6.4±2.8</td>
<td>7.9±2.5</td>
<td>10.9±1.8</td>
<td>&lt;0.001*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td>168.7±33.4</td>
<td>182.5±29.5</td>
<td>225.0±13.0</td>
<td>&lt;0.001*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td>61.7±13.2</td>
<td>56.1±8.5</td>
<td>47.0±2.9</td>
<td>&lt;0.001*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDL (mg/dl)</td>
<td>99.4±28.4</td>
<td>124.5±13.0</td>
<td>143.2±8.8</td>
<td>&lt;0.001*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TG (mg/dl)</td>
<td>89.6±46.5</td>
<td>112.3±30.6</td>
<td>136±12.4</td>
<td>&lt;0.001*</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Significant after adjusting for multiple comparisons (Bonferroni’s correction; p value for significance 0.0167)

Table 2. Clinical and laboratory characteristics of the patients with T1D according to the BMI percentiles and genders

<table>
<thead>
<tr>
<th>Gender</th>
<th>A NW Girls (n=138)</th>
<th>B OW/Ob Girls (n=61)</th>
<th>C NW Boys (n=131)</th>
<th>D OW/Ob Boys (n=33)</th>
<th>Overall p</th>
<th>A vs B p</th>
<th>A vs C p</th>
<th>A vs D p</th>
<th>B vs C p</th>
<th>B vs D p</th>
<th>C vs D p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at evaluation (yrs)</td>
<td>16.2±2.7</td>
<td>16.6±3.8</td>
<td>16.4±3.7</td>
<td>16.9±3.5</td>
<td>0.498</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>8.7±1.6</td>
<td>8.5±1.0</td>
<td>8.9±3.1</td>
<td>8.6±1.8</td>
<td>0.649</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyper tension</td>
<td>4.7% (20/138)</td>
<td>21.3% (13/61)</td>
<td>6.1% (8/131)</td>
<td>15.2% (5/33)</td>
<td>0.003</td>
<td>&lt;0.001*</td>
<td>0.716</td>
<td>&lt;0.001*</td>
<td>&lt;0.001*</td>
<td>0.008*</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>TG ≥150 mg/dl</td>
<td>14.5% (20/138)</td>
<td>34.4% (21/61)</td>
<td>6.1% (8/131)</td>
<td>27.3% (9/33)</td>
<td>&lt;0.001</td>
<td>&lt;0.001*</td>
<td>&lt;0.001*</td>
<td>&lt;0.001*</td>
<td>&lt;0.001*</td>
<td>0.020</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>HDL &lt;40 mg/dl (Girls &gt;16 years of age)</td>
<td>11.6% (16/138)</td>
<td>21.3% (13/61)</td>
<td>6.1% (8/131)</td>
<td>18.2% (6/33)</td>
<td>&lt;0.001</td>
<td>&lt;0.001*</td>
<td>0.003*</td>
<td>0.005*</td>
<td>&lt;0.001*</td>
<td>0.678</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LDL &gt;100 mg/dl</td>
<td>36.2% (50/138)</td>
<td>62.3% (38/61)</td>
<td>22.9% (30/131)</td>
<td>54.6% (18/33)</td>
<td>&lt;0.001</td>
<td>&lt;0.001*</td>
<td>0.006*</td>
<td>0.002*</td>
<td>&lt;0.001*</td>
<td>0.392</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>36.2% (50/138)</td>
<td>62.3% (38/61)</td>
<td>22.9% (30/131)</td>
<td>54.6% (18/33)</td>
<td>&lt;0.001</td>
<td>&lt;0.001*</td>
<td>0.006*</td>
<td>0.002*</td>
<td>&lt;0.001*</td>
<td>0.392</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>At least two criterias positivity for MS (Obesity and/or TG ≥150 mg/dl and/or HDL &lt;40 mg/dl (Girls &gt;16 years of age) and/or Hypertension)</td>
<td>11.6% (16/138)</td>
<td>34.4% (21/61)</td>
<td>5.3% (7/131)</td>
<td>27.3% (9/33)</td>
<td>&lt;0.001</td>
<td>&lt;0.001*</td>
<td>0.002*</td>
<td>&lt;0.001*</td>
<td>&lt;0.001*</td>
<td>0.009*</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>

*Significant after adjusting for multiple comparisons (Bonferroni’s correction; p value for significance 0.0125)
Table 3. Comparison of patients according to the presence of increased cardiovascular risk

<table>
<thead>
<tr>
<th></th>
<th>All patients</th>
<th>p value</th>
<th>Girls</th>
<th>P value</th>
<th>Boys</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CVD risk (+)</td>
<td></td>
<td></td>
<td>CVD risk (+)</td>
<td></td>
<td>CVD risk (+)</td>
</tr>
<tr>
<td>Age at evaluation (yrs)</td>
<td>18.2 ±2.5</td>
<td>&lt;0.001</td>
<td>16.1 ±2.7</td>
<td>15.9 ±2.3</td>
<td>&lt;0.001</td>
<td>18.6 ±2.5</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Girls</td>
<td>37 (69.8%)</td>
<td>162(52.3%)</td>
<td>16 (39.2%)</td>
<td>148(47.7%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Boys</td>
<td>18.1 ±2.5</td>
<td>&lt;0.001</td>
<td>18.1 ±2.5</td>
<td>18.6 ±2.5</td>
<td>16.3 ±3.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>9.7±1.4</td>
<td>&lt;0.001</td>
<td>9.5±1.0</td>
<td>10.3±1.9</td>
<td>8.7±2.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Insulin dose (IU/kg/day)</td>
<td>1.4±0.3</td>
<td>&lt;0.001</td>
<td>1.5±0.3</td>
<td>1.3±0.2</td>
<td>0.9±0.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes duration (yrs)</td>
<td>9.7±1.5</td>
<td>&lt;0.001</td>
<td>9.9±1.9</td>
<td>6.6±2.3</td>
<td></td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Table 4. Factors affecting having two or more risk factors for CVD based on multivariate regression analysis

<table>
<thead>
<tr>
<th>Variables</th>
<th>Standardized Beta coefficient</th>
<th>Odds ratio</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Being a girl</td>
<td>5.605</td>
<td>11.483</td>
<td>6.480</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Longer diabetes duration</td>
<td>0.832</td>
<td>1.137</td>
<td>1.033</td>
<td>0.04</td>
</tr>
<tr>
<td>Higher HbA1c</td>
<td>0.980</td>
<td>2.635</td>
<td>1.179</td>
<td>0.03</td>
</tr>
<tr>
<td>Higher daily insulin dose</td>
<td>1.036</td>
<td>3.409</td>
<td>1.695</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Supplementary Table 1. Mean lipid levels of patients with T1D according to the BMI percentiles and genders

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>TC (mg/dl)</td>
<td>176.7±43.2</td>
<td>205.6±49.0</td>
<td>160.3±35.6</td>
<td>194.2±36.7</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>0.002</td>
<td>&lt;0.001</td>
<td>0.005</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td>61.4±14.0</td>
<td>57.7±8.7</td>
<td>62.0±12.6</td>
<td>54.0±11.1</td>
<td>0.630</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDL (mg/dl)</td>
<td>112.4±30.9</td>
<td>153.6±29.6</td>
<td>89.3±21.2</td>
<td>127.9±22.9</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>0.006</td>
<td>&lt;0.001</td>
<td>0.004</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>TG (mg/dl)</td>
<td>105.4±53.4</td>
<td>132.5±51.4</td>
<td>77.1±34.6</td>
<td>121.4±36.8</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>0.003</td>
<td>&lt;0.001</td>
<td>0.004</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Significant after adjusting for multiple comparisons (Bonferroni’s correction; p value for significance 0.0125)

Figure 1. Lipid levels of patients with T1D according to gender and weight status

Panel 1. HDL-c levels
Panel 2: LDL-c levels
Panel 3: Total cholesterol levels
Panel 4: TG levels
Panel 3

Total Cholesterol levels (mg/dl)

Groups

- NW Girls
- OW/Ob Girls
- NW Boys
- OW/Ob Boys

P<0.001

Panel 4

Triglyceride levels (mg/dl)

Groups

- NW Girls
- OW/Ob Girls
- NW Boys
- OW/Ob Boys

P<0.001