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# Dyslipidemia in type 1 diabetes mellitus: Relation to diabetes duration, glycemic control, body habitus, dietary intake and other epidemiological risk factors

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Type 1 diabetes mellitus;
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Low density lipoprotein-cholesterol (LDL-C);
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**Abstract** *Background:* Diabetes is associated with a high risk of cardiovascular disease (CVD). The classic "diabetic dyslipidemia" is mostly described as hypertriglyceridemia and low levels of HDL-C. Elevated LDL-C is an established risk factor for CVD.
*Objective:* Identify the pattern of dyslipidemia in children and adolescents with type 1 diabetes mellitus regularly following at Diabetes Endocrine and Metabolism Pediatric Unit (DEMPU) at Children's Hospital of Cairo University; and to detect its relation to different risk factors.
*Methods:* Sixty children and adolescents with T1DM, (34 males and 26 females, mean age 12.5 ± 2.4 years and mean duration of diabetes 4.3 ± 2.7 years) were evaluated by full history and clinical examination including 3 day dietetic history for analysis, BMI and waist circumference. Records were revised for mean blood glucose and HbA1c. Fasting lipid profile (total cholesterol, triglycerides, HDL-C and LDL-C) was performed. Thirty-nine healthy age and sex matched children were included as control for lipid profile.
*Results:* Dyslipidemia significantly more frequent among T1DM children and adolescents compared to control subjects (39/60, 65% vs. 11/39, 28.2%, $p < 0.001$); and the dyslipidemic (39/60) compared to normoalbuminuric (21/60) children had significantly higher mean waist circumference. Both groups were comparable regarding age, age at onset and duration of diabetes, family history of diabetes and CVD, degree of glycemic control and dietary analysis.
*Conclusion:* Dyslipidemia is significantly more frequent in children and adolescents with T1DM compared to non-diabetic peers. The most frequent type of dyslipidemia was high LDL-C and low HDL-C in the dyslipidemic group.



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## Introduction

Children diagnosed with type 1 diabetes have a high risk of early subclinical and clinical cardiovascular disease (CVD).[1–3] The American Heart Association categorizes children with type 1 diabetes in the highest tier for cardiovascular risk and recommends both lifestyle and pharmacological treatment for those with elevated LDL cholesterol levels.[4,5]

Global IDF/ISPAD Guideline for Diabetes in Childhood and Adolescence, 2014 recommended screening for fasting blood lipids when diabetes is stabilized in children aged over 10 years. If there is a family history of hypercholesterolaemia, early CVD or if the family history is unknown, screening should start at age 2 years. If normal results are obtained, screening should be repeated every 5 years.[6]

## Objectives

To study the pattern of dyslipidemia in children and adolescents with type 1 diabetes mellitus; and its relation to the duration of diabetes, degree of glycemic control, body habitus, dietary intake and epidemiological risk factors including family history and life-style.

## Materials and methods

### *Study population*

The current study included 60 children and adolescents regularly followed at the Diabetes Endocrine and Metabolism Pediatric Unit (DEMPU), Children's Hospital, Cairo University. Subjects were eligible if they were between 9 and 16 years of age and had type 1 diabetes mellitus (T1DM) for one year or more. Exclusion criteria were the presence of associated hypothyroidism and the use of thyroxin therapy or lipid lowering medications. Thirty-nine healthy age and sex matched children and adolescents were included as control.

### *Procedures*

Detailed history was taken from included patients including the following:

- Detailed medical history including; chronological age, duration and age at onset of diabetes, type and dose of insulin, compliance to diet and insulin therapy, detailed dietetic history in addition to family history of diabetes, hypertension, coronary heart disease and stroke, and history suggestive of diabetic microvascular and macrovascular complications.
- Diet history: each patient was asked for detailed food intake for 3 consecutive days, 3 meals and snacks with emphasis on total caloric intake and fat content (three days recall). A nutritionist had analyzed all components of child's diet and calculated the mean values for total caloric intake (kcal/d), intake of fats, CHO and proteins in grams per day as well as and caloric intake derived from fats (kcal/d).
- Physical activity: type and duration (h/day) of weekly activity was classified as "mild" if regular daily activity, like walking, running, playing football, ascending and descending stairs or bicycling; and "intense" if regular sports are done, like swimming, basketball, karate or gym. Patients having sedentary life were considered "inactive".
- Thorough clinical examination including height, weight, BMI, waist circumference (WC), stage of puberty and blood pressure measurement. The latter was done on 2 separate occasions and after 10 min rests using a sphygmomanometer.
- Assessment of glycemic control by calculating the mean fasting (FBG) and 2 h postprandial blood glucose (PPBG) for one month preceding the study, and the mean glycosylated hemoglobin (HbA1c) over one year prior to the study.

### *Biochemical analysis*

- Laboratory assessment for lipid profile was done, after a 12-h overnight fast, including: serum total cholesterol (TC) by cholesterol oxidase–peroxidase method, serum triglycerides (TG) by glycerokinase-peroxidase method, high density lipoprotein-cholesterol (HDL-C) by Stanbio HDL-C Procedure No. 0599 and low density lipoprotein-cholesterol (LDL-C) = TC-(HDL-C)-(TG/5).

Dyslipidemia was defined by the American Diabetes Association (ADA)[7] as having low density lipoprotein-cholesterol (LDL-C) $\geqslant$100 mg/dl, high density lipoprotein-cholesterol (HDL-C) $<$40 mg/dl (males) and $<$50 mg/dl (females), total cholesterol (TC) $\geqslant$200 mg/dl and triglycerides (TG) $\geqslant$150 mg/dl; and dyslipidemia was considered present if one or more of these lipid or lipoprotein levels are abnormal.[8]

### *Statistical analysis*

Data were statistically described in terms of mean (standard deviation ($\pm$SD), median and range, or frequencies (number of cases) and percentages when appropriate. Comparison of numerical variables between the study groups was done using Mann Whitney U test for independent samples. For comparing categorical data, Chi square ($\chi^2$) test was performed. Exact test was used instead when the expected frequency is less than 5. $P$ values less than 0.05 were considered statistically significant. All statistical calculations were done using computer programs SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 15 for Microsoft Windows.

## Results

The sixty cases of children and adolescents with T1DM included 34 males and the thirty-nine non-diabetic control subjects included 18 males. The mean age was 12.5 (range 9.0–19.5) years in cases and 12.0 $\pm$ 2.2 (range 9.0–16.0) years in controls, $p > 0.05$.

The mean age at onset of diabetes in the studied group was 8.2 $\pm$ 2.6 (range 2.5–14.5) years, and the mean duration of diabetes was 4.3 $\pm$ 2.7 (range 1.0–12.0) years and the mean insulin dose was 1.1 $\pm$ 0.4 (range 0.5–2.7) IU/kg/day.

The frequency of dyslipidemia in the diabetic group was 65% (39/60) compared to 28.2% (11/39) in the control group with highly significant difference ($p < 0.001$).

Within the diabetic group, comparison of the fasting serum lipid profile (mean $\pm$ SD, and median) between those with

**Table 1** Fasting serum lipid profile of dyslipidemic and normolipidemic patients with diabetes.

| Serum lipids | Dyslipidemic group ($n$ = 39) | | Normolipidemic group ($n$ = 21) | | $P$-value |
|---|---|---|---|---|---|
| | Mean ± SD | Median | Mean ± SD | Median | |
| TC (mg/dl) | 175.3 ± 38.7 | 173.0 | 148.2 ± 32.9 | 153.0 | 0.007* |
| TG (mg/dl) | 92.1 ± 43.7 | 84.0 | 64.3 ± 36.4 | 49.0 | 0.002* |
| HDL-C (mg/dl) | 47 ± 18.6 | 44.1 | 53.1 ± 12.6 | 52.0 | 0.023* |
| LDL-C (mg/dl) | 112.5 ± 34.2 | 113.0 | 82.4 ± 25.7 | 79.6 | 0.001* |

TC, total cholesterol; TG, triglycerides; HDL-C, high density lipoprotein-cholesterol; LDL-C, low density lipoprotein-cholesterol.
* Significant $<0.05$.

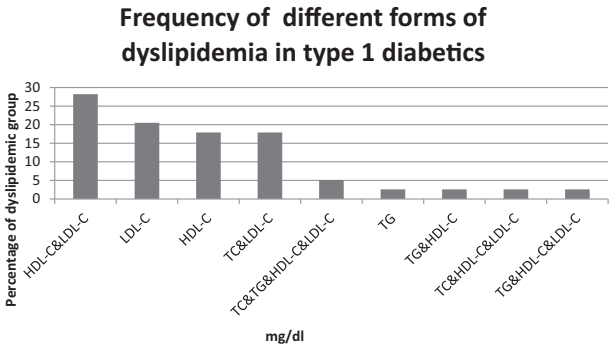


**Figure 1** Percentage of different forms of dyslipidemia in type 1 diabetics showing that the most frequent form is high LDL-C with low HDL-C.

dyslipidemia and those with normolipidemia revealed significantly higher values of TC, TG and LDL-C, and significantly lower values of HDL-C in the former (Table 1).

The most frequent form of dyslipidemia found in the dyslipidemic group was high LDL-C with low HDL-C in 28.20%, followed by isolated high LDL-C in 20.51%. Abnormality in all parameters of lipid profile was found in 5.12% (Fig. 1).

Within the dyslipidemic group, more than 75% had high LDL, either isolated or in association with other lipid abnormalities; and more than 55% had abnormally low HDL either isolated or in association with other lipid abnormalities; while the classic diabetic dyslipidemia in the form of hypertriglyceridemia was much less frequent (2.6%).

Comparison between the dyslipidemic and normolipidemic groups with T1DM regarding their demographic, clinical and laboratory data revealed significantly higher percentage of female sex ($p$ = 0.025), but comparable mean values of chronological age, age at onset and duration of diabetes, and insulin dose (Table 2).

There was no significant difference between the two groups regarding the frequency of family history of diabetes and cardiovascular risk.

The mean values of BMI, BMI SDS and WC were compared and showed statistically significant differences between dyslipidemic and normolipidemic groups as regards BMI and WC, $p$ = 0.024 and 0.018, respectively (Table 3).

According to the mean BMI SDS, 6 patients (15.4%) were obese ($>+2$ SD) in the dyslipidemic group [mean BMI SDS = 0.9 ± 1.2], while in the normolipidemic group, one patient (4.8%) was obese [mean BMI SDS = 0.4 ± 1.3] with no significant difference ($p$ = 0.270).

Glycemic control of the two groups was compared regarding the mean HbA1c over one year prior to the study, the mean fasting and postprandial blood glucose. (FBG) and (PPBG), over one month prior to the study, with no statistically significant difference (Table 4).

Comparison of degree of activity in both groups revealed significant difference, $p$ = 0.033 (Table 5).

Comparison of dietary analysis of the two groups showed no statistically significant difference between the dyslipidemic and normolipidemic diabetics (Table 6).

## Discussion

In the present study, dyslipidemia was found in a significantly higher percentage of children and adolescents with type 1 diabetes (65%) compared to that of the non-diabetic control group (28.2%). This agrees with Rahma et al. (2006) who found that 66% of the children with T1DM were dyslipidemic compared to 34% of the non-diabetic control group.[9] Also this agrees with the findings of Wiltshire et al. and Patiakas et al.[10,11]

In the current study, the most frequent type of dyslipidemia was high LDL-C and low HDL-C in 28.2% of the children and adolescents with T1DM and dyslipidemia, while high LDL-C and hypercholesterolemia with and without

**Table 2** Mean chronological age, age at onset and duration of diabetes, and insulin dose in dyslipidemic and normolipidemic groups.

| | Dyslipidemic group ($n$ = 39) | | Normolipidemic group ($n$ = 21) | | $P$-value |
|---|---|---|---|---|---|
| | Mean ± SD | Median | Mean ± SD | Median | |
| Age (year) | 12.8 ± 2.6 | 12.4 | 12.1 ± 2 | 12.0 | 0.471 |
| Age at onset of DM (year) | 8.6 ± 2.8 | 8.7 | 7.5 ± 2 | 7.3 | 0.104 |
| Duration of DM (year) | 4.1 ± 2.7 | 3.0 | 4.6 ± 2.6 | 4.0 | 0.291 |
| Insulin dosage (IU/kg/day) | 1 ± 0.3 | 1.0 | 1.2 ± 0.5 | 1.1 | 0.512 |

DM, diabetes mellitus.

**Table 3** Mean values of anthropometric measures of dyslipidemic and normolipidemic groups.

| Anthropometry | Dyslipidemic group ($n$ = 39) | | Normolipidemic group ($n$ = 21) | | $P$-value |
|---|---|---|---|---|---|
| | Mean ± SD | Median | Mean ± SD | Median | |
| BMI (kg/m$^2$) | 21.5 ± 5 | 21.1 | 19 ± 4.5 | 18.0 | 0.024* |
| BMI SDS | 0.9 ± 1.2 | 0.8 | 0.4 ± 1.3 | 0.6 | 0.136 |
| WC (cm) | 80.3 ± 12 | 80.0 | 73.5 ± 12.7 | 70.0 | 0.018* |

BMI SDS, body mass index standard deviation score; WC, waist circumference.
* Significant $<0.05$.

**Table 4** Mean HbA1c, FBG and PPBG in dyslipidemic and normolipidemic groups.

| Glycemic control | Dyslipidemic group ($n$ = 39) | | Normolipidemic group ($n$ = 21) | | $P$-value |
|---|---|---|---|---|---|
| | Frequency | Percent (%) | Frequency | Percent (%) | |
| *Mean HbA1c (%)* | | | | | |
| Good (<7.5) | 15 | 38.5 | 11 | 52.4 | 0.412 |
| Fair (7.5–9.0) | 18 | 46.2 | 6 | 28.6 | |
| Poor (>9.0) | 6 | 15.4 | 4 | 19.0 | |
| *Mean FBG* (mg/dl)* | | | | | |
| Good (90–145) | 4 | 10.3 | 3 | 14.3 | 0.452 |
| Fair (>145) | 6 | 15.4 | 1 | 4.8 | |
| Poor (>162) | 29 | 74.4 | 17 | 81.0 | |
| *Mean 2 h PPBG* (mg/dl)* | | | | | |
| Good (90–180) | 15 | 38.5 | 8 | 38.1 | 0.672 |
| Fair (180–250) | 13 | 33.3 | 9 | 42.9 | |
| Poor (>250) | 11 | 28.2 | 4 | 19.0 | |

HbA1c, glycosylated hemoglobin; BG, blood glucose; FBG, fasting blood glucose; PPBG, postprandial blood glucose.
* BG (FBG and PPBG) is the mean of glucometer readings.

**Table 5** Comparison of frequency of physical activity in dyslipidemic and normolipidemic groups.

| Activity | Dyslipidemic group ($n$ = 39) | | Normolipidemic group ($n$ = 21) | | $P$-value |
|---|---|---|---|---|---|
| | Frequency | Percent (%) | Frequency | Percent (%) | |
| Inactive (sedentary life) | 9 | 23.1 | 0 | 0.0 | 0.033* |
| Mild (regular activities) | 24 | 61.5 | 19 | 90.5 | |
| Intense (regular sports) | 6 | 15.4 | 2 | 9.5 | |

* Significant $<0.05$.

hypertriglyceridemia were found to be the most common types in Al-Naama et al. and Rahma et al.[9,12] The diabetic children in these two studies showed high risk glycemic control according to the mean fasting blood glucose (FBG) (232.0 ± 92.0 mg/dl) and HbA1c (9.8 ± 4.2%).

Herman et al. (1998) and Kantoosh et al. (2002) reported that in Egyptian diabetic children, hypertriglyceridemia was the predominant type and reported significantly higher serum TG and HbA1c levels in the untreated freshly diagnosed children with T1DM than that in the treated diabetics with good glycemic control1.[13,14] Patiakas et al. (2007) found that hypercholesterolemia was the most frequent type and hypertriglyceridemia is the least frequent type in diabetic patients[11] in contrast to Alrabaty et al. (2009) who stated that hypertriglyceridemia is the most common pattern of dyslipidemia in children and adolescents with T1DM.[15] These differences are probably related to different glycemic controls across the studies.

In this study, the female sex was significantly higher in the dyslipidemic group than the normolipidemic group (53.8% vs. 23.8%, $p = 0.025$), this finding is in agreement with Krantz et al. and Schwab et al.[16,17] This finding is in contrast to the results reported by Alrabaty et al. (2009) and Patiakas et al. (2007) who found that there was no relationship between the lipid abnormalities in children and adolescents with T1DM and the gender.[11,15]

In the present work, mean duration of diabetes showed no significant difference between the dyslipidemic group and the normolipidemic group (4.1 ± 2.7 and 4.6 ± 2.6 years respectively); there were patients with less than 2 years diabetes duration and having dyslipidemia. This finding is in agreement with Kanagalakshmi and Sultana (2012) and Guy et al. (2009) who found that the dyslipidemia in children and adolescents with T1DM is present despite short duration of diabetes.[18,19] This is in contrast to the results reported by Moayeri and Oloomi (2006) who found that lipid concentrations correlate positively with the duration of diabetes.[20]

In the present study, mean waist circumference (WC) was significantly higher in the dyslipidemic group than in the normolipidemic group (80.3 ± 12.0 cm compared to

**Table 6** Comparison of dietary analysis in dyslipidemic and normolipidemic groups.

| Diet | Dyslipidemic group ($n$ = 39) | | Normolipidemic group ($n$ = 21) | | $P$-value |
|---|---|---|---|---|---|
| | Mean ± SD | Median | Mean ± SD | Median | |
| Fat in diet (gm/day) | 51.8 ± 19.5 | 47.6 | 45.3 ± 18.4 | 40.3 | 0.180 |
| CHO in diet (gm/day) | 296.7 ± 100.8 | 286.8 | 283.8 ± 81.9 | 289.7 | 0.762 |
| Protein in diet (gm/day) | 66.4 ± 19.9 | 66.0 | 58.2 ± 27.5 | 57.0 | 0.143 |
| Total calories (kcal/day) | 1875.4 ± 561.8 | 1750.7 | 1721.0 ± 468 | 1763.7 | 0.434 |
| Calories from fat (kcal/day) | 466.1 ± 175.5 | 428.0 | 407.9 ± 165.7 | 363.0 | 0.180 |

CHO, carbohydrates.

73.5 ± 12.7 cm, $p$ = 0.018). This result is in concordance with Teles and Fornés (2012) and Kanagalakshmi and Sultana (2012) who found higher WC in the dyslipidemic group than the normolipidemic group of pediatric and youth populations with T1DM.[18,21]

In this study, the majority of the dyslipidemic group (46.2%) had suboptimal glycemic control [mean HbA1c = 7.9 ± 1.0%], while in the normolipidemic group, most of them (52.4%) had optimal control [mean HbA1c = 8.0 ± 1.6%] with no significant difference between both groups regarding mean HbA1c. This result is in concordance with Muchacka-Bianga et al. (2006) and Kantoosh et al. (2002) who found that lipid disorders in children with T1DM may be present regardless of their metabolic control.[14,22] On the contrary, Teles and Fornés (2012) and Guy et al. (2009) found that poorer (inadequate) glycemic control is related to higher serum lipids levels..[19,21] Ladeia et al. (2006) and Krantz et al. (2004) found significant correlations between glycemic control and lipids.[16,23]

In the current study, there was a significant difference between the dyslipidemic group and the normolipidemic group as regards the degree of activity, $p$ = 0.033. This agrees with Schwab et al. (2006) and Muchacka-Bianga et al. (2006) who stated that physical inactivity and dyslipidemia are potentially atherogenic risk factors in children and adolescents with T1DM.[17,22]

In the present work, mean daily caloric intake from dietary fats was higher in the dyslipidemic group than in the normolipidemic group but difference did not reach statistical significance (466.1 ± 175.5 kcal/day compared to 407.9 ± 165.7 kcal/day, p = 0.180). Similarly, Wiltshire et al. (2003) who found that dietary fats do not contribute to hyperlipidemia in children and adolescents with T1DM and that hyperlipidemia relates primarily to metabolic control, with limited impact from dietary factors. They suggested that treatment of hyperlipidemia should primarily be directed at improving metabolic control.[10]

## Conclusion

Dyslipidemia in children and adolescents with type 1 diabetes mellitus (T1DM) was significantly more frequent than in non-diabetic peers. Dyslipidemia was significantly more frequent among females with higher mean waist circumference (WC) and physically inactive. The most frequent type of dyslipidemia was high LDL-C and low HDL-C in 28.2%.

## Conflict of interest

None declared.

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