LIPID PROFILE AMONG CHILDREN AND ADOLESCENTS WITH TYPE 1 DIABETES MELLITUS AT AL-HUSSEIN AND SAYED GALAL UNIVESITY HOSPITALS

By

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ABSTRACT

Background: *Diabetes is a major risk factor for cardiovascular disease (CVD). In patients with type 1 diabetes mellitus (T1DM), atherosclerosis occurs earlier in life, leading to increased morbidity and mortality compared with those in the general population.*

Aim: *This study aimed to describe the frequency and the pattern of dyslipidemia in children and adolescents suffering from T1DM, and its relation to the degree of glycemic control, regular activities, and the duration of diabetes.*

Patients and methods: *This case control study was conducted on 50 children and adolescents with type 1 diabetes mellitus (T1DM) and 25 healthy age and sex matched children and adolescents were recruited from outpatient clinic included in the study as control group from Al-Hussein University Hospital and Sayed Galal Univesity Hospital. All participants were subjected to the following: full history taking, full clinical examination, and investigations including glycosylated hemoglobin , fasting and postprandial blood glucose , lipid profile (TG, LDL-C, HDL-C and TC).*

Results: *There was a high statically significant increase in the frequency of dyslipidemia in diabetic patients (64%). The most common type of dyslipidemia found in the dyslipidemic group was high LDL-C and low HDL-C in 8 patients (25.0%) followed by isolated high LDL-C in 6 patients (18.75%), isolated low HDL-C in 5 patients (15.63%), hypercholesterolemia and high LDL-C in 4 patients (12.50%).*

Conclusion: *This study confirms the hypothesis that LDL-C is the cornerstone for assessment of dyslipidemia.*

INTRODUCTION

Diabetes is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction, and failure of different organs, especially the eyes, kidneys, nerves, heart, and blood vessels **(American Diabetes Association, 2013)**.

Type 1 diabetes mellitus (T1DM) is the most common childhood endocrine disease **(Teles and Fornés, 2012)**.

Diabetes is a major risk factor for cardiovascular disease (CVD). In patients with T1DM, atherosclerosis occurs earlier in life, leading to increased morbidity and mortality compared with those in the general population **(Guy et al., 2009)**.

Coronary artery disease (CAD) is the leading cause of mortality in patients with T1DM **(Wadwa et al., 2005)**.

As a result, the most recent clinical trials on glycemic control for macrovascular risk reduction are woven into concrete clinical practice guidelines in patients with diabetes **(Ali et al., 2010)**.

Dyslipidemia was defined in patients having low density lipoprotein-cholesterol (LDL-C) ≥ 130 mg/dl, high density lipoprotein-cholesterol (HDL-C) < 40 mg/dl, total cholesterol (TC) ≥ 200mg/dl and triglycerides (TG) ≥ 100 mg/dl in age group 0-9 years and ≥ 130 mg/dl in age group 10-19 years **(Kavey REW et al., 2011)** and **(Kwiterovich, 2008)**.

Global International Society for Pediatric and Adolescent Diabetes (IDF/ISPAD) at 2014 recommended screening for fasting blood lipids when diabetes is stabilized in children aged over 10 year **(Wadwa et al., 2014)**.

AIM OF THE WORK

The aim of this work is to evaluate the frequency and pattern of dyslipidemia in children and adolescents with type 1 diabetes mellitus (T1DM).

Ethical Consideration:

- Written Parent consent for the study was obtained before the study.
- Approval of the local ethical committee in the pediatrics department, college and university were obtained before the study.
- The authors declaired no potential conflict of interest

with respect to the research & publication of this article.

- All the data of the patient & results of the study are confidential & the patient has the right to keep it.
- The authors received no financial support for the research & publications of the article.

PATIENT AND METHODS

This case control study was conducted on 50 children and adolescents with type 1 diabetes mellitus (T1DM) a 25 healthy age and sex matched subjects were recruited from outpatient clinic included in the study as control group at Al-Hussein University Hospital and Sayed Galal Univesity Hospitals. They were recruited during the period from the beginning of January 2019 to the end of June 2019 according to inclusion and exclusion criteria below.

Inclusion criteria:

- Type 1 diabetes mellitus (T1DM) children and adolescents.
- Both sexes.
- Age ≥ 9 years.
- Duration of diabetes ≥ 5 years.

Exclusion criteria:

- Type 2 diabetes mellitus (T2DM) patients.
- Age > 9 years.
- Patients on lipid lowering medications.
- Patients with congenital anomalies.

Study groups:

1- Patient group: 50 children with type 1 diabetes.

2- Control group: 25 healthy age and sex matched children.

METHODS:

All patients and subjects will be evaluated by:

History taking:

Full history was taken and records review, laying stress on:

- Demographic data: name, chronological age, sex and residence.
- Age at the onset of diabetes.
- Diabetes duration.
- Insulin therapy during the last year; including:
  - The daily total dose of insulin (calculated as IU/kg/day).
  - The type of insulin (Regular &Isophane or Glargine).
  - The number of daily injections.
- Family history of diabetes, hypertension, dyslipidemia.

- Diet history: each patient was asked for detailed food intake for 3 consecutive days, 3 meals and snacks.
- Physical activity: type and duration (hrs/day).
- Acute complications e.g. hyperglycemia and hypoglycemia.
- Chronic complications e.g. nephropathy, retinopathy and neuropathy.

Clinical examination:

1-General examination:

Complete general examination was done foreach patient as follows:

- Anthropometric measurements, including:
  1. Body weight in (kg) was measured on digital electronic scale.
  2. Height in (cm).
  3. Body Mass Index (BMI) calculated as weight (kg) / height (m2).
  4. Waist Circumference (WC) in (cm).
- Skin manifestations of hyperlipidemia e.g. xanthomas.
- Examination of the insulin injection sites e.g. lipohypertrophy and local allergic reactions (erythema, pruritus & induration).
- Signs suggesting chronic diabetes complications.

2-Systemic examination:

Complete systemic examination was done for each patient including cardiovascular, chest, abdominal and neurological systems.

Laboratory investigations:

1- Fasting and 2hrs postprandial blood sugar.

2- Glycosylated hemoglobin (HbA1c).

3- Fasting lipid profile: was measured for each patient in the study, after 12-hr overnight fast, including: serum Total cholesterol (TC), Triglycerides (TG), High density lipoprotein-cholesterol (HDL-C) and Low density lipoprotein-cholesterol (LDL-C).

Criteria for the diagnosis of diabetes:

Glycosylated hemoglobin (HbA1C) ≥ 6.5%. OR Fasting blood glucose (FBG) ≥ 126 mg/dl (7.0 mmol/l). Fasting is defined as no caloric intake for at least 8h. OR Postprandial blood glucose (PPBG) ≥ 200mg/dl (11.1mmol/l). OR In a patient with classic symptoms of hyperglycemia or

hyperglycemic crisis, a random blood glucose (RBG) ≥ 200 mg/dl (11.1 mmol/l). **(American Diabetes Association, 2017)**.

Dyslipidemia was defined in patients having low density lipoprotein-cholesterol (LDL-C) ≥ 130 mg/dl, high density lipoprotein-cholesterol (HDL-C) < 40 mg/dl, total cholesterol (TC) ≥ 200mg/dl and triglycerides (TG) ≥ 100 mg/dl in age group 0-9 years and ≥ 130 mg/dl in age group 10-19 years **(Kwiterovich, 2008)**.

RESULTS

Table (1): Comparison between patients and control regarding Age and Sex

		Patients	Control	p-value
Age (Years)	**Mean±SD**	13.40±2.5	12.50±2.25	**0.175**
	Range	9.00-19.00	9.00-19.00	
Sex	**Male**	26 (52%)	15 (56%)	0.720
	Female	24 (48%)	10 (44%)	

There were no statistically significant difference as regards age and sex between the case and control (p = 0.175, 0.720 respectively).

Table (2): comparison between patients and control according to dyslipidemia

Dyslipidemia	Patients	control	P – value
Yes	32 (64%)	7 (28%)	**0.002**
No	18 (36%)	18 (72%)	
Total	50 (100%)	25 (100%)	

Dyslipidemia in the form of LDL-C ≥ 130 mg/dl, HDL-C < 40 mg/dl, TC ≥ 200mg/dl and TG ≥ 100 mg/dl in age group 0-9 years and ≥ 130 mg/dl in age group 10-19 years.

There was high a statistically significant in the frequency of dyslipidemia group in children and adolescents with (T1DM) 32 (64.0%) compared to 7 (28%) of the healthy control group ($p<0.002$).

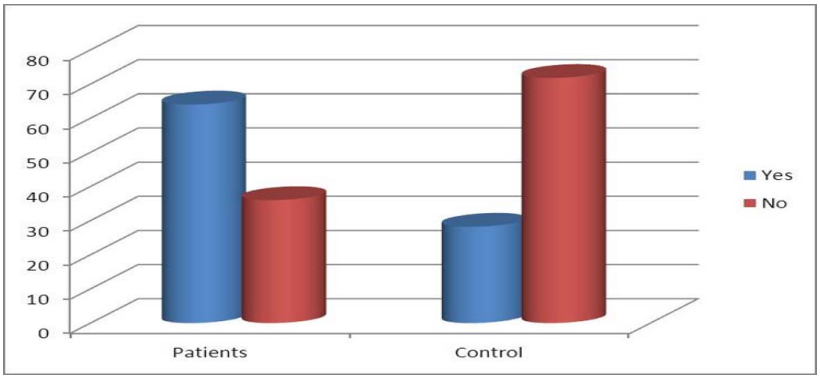

Figure (1): Comparison between patients and control regarding dyslipidemia.

Table (3): Comparison between patients and control as regards fasting lipid profile

Lipid Profile	Patients (N = 50)	Control (N = 25)	t-test	p-value
TC (mg/dl)				
Mean±SD	164.88±39.54	152.22±30.55	1.457	0.232
Range	104.0-279.0	99.0-243.0		
TG (mg/dl)				
Mean±SD	85.85±49.50	82.50±42.22	0.193	0.662
Range	24.0-247.0	30.00-253.00		
HDL-C (mg/dl)				
Mean±SD	49.78±17.98	47.28±11.33	0.575	0.450
Range	16.0-141.0	14.00-80.00		
LDL-C (mg/dl)				
Mean±SD	98.60±35.80	91.55±26.70	1.426	0.237
Range	37.00-189.00	18.00-178.00		

TC <200 mg/dl, TG <150 mg/dl, HDL-C ≥ 40 mg/dl in males, ≥ 50 mg/dl in females, LDL-C <100 mg/dl
TC: Total cholesterol. TG: Triglycerides. HDL-C: High density lipoprotein-Cholesterol. LDL-C: Low density lipoprotein-Cholesterol. SD: Standard deviation.

There were no statistically significant difference as regards the values of the fasting lipid profile between the case and control.

Table (4): Comparison between patients and control as regards abnormal lipid concentrations

	Cases (n=50)		Controls (n=25)	
Lipids	**Frequency**	**Percent**	**Frequency**	**Percent**
↑TC (mg/dl)	9	18%	3	12%
↑TG (mg/dl)	4	8%	1	4%
↓HDL-C (mg/dl)	19	38%	5	25%
↑LDL-C (mg/dl)	25	50%	4	16%

Dyslipidemia cutoff points: TC ≥200 mg/dl, TG ≥150 mg/dl, HDL-C < 40 mg/dl in males, < 50 mg/dl in females, LDL-C ≥ 100 mg/dl.

Regarding the abnormal lipid profile concentrations in the study our study groups showed:

25 patients (50.0%) of the patients had elevated LDL-C levels (≥ 100mg/dl), 19 patients (38.0%) had low HDL-C levels (< 40 mg/dl in males & < 50 mg/dl in females), 9 patients (18.0%) had elevated TC levels (≥ 200mg/dl) And 4 (8.0%) had elevated TG concentrations (≥ 150 mg/dl). Compared with 4 patients (16%), 5 patients (25%), 3 patients (12%) and 1 patient (4%) of the control children respectively.

Table (5): Age, age at onset of diabetes, diabetes duration and insulindose in and normolipidemic groups:

Anthropometry	Dyslipidemic (n=32)	Normolipidemic (n=18)	p - value
	Mean ± SD	Mean ± SD	
Age (yr)	13.40 ± 2.36	12.50 ± 2.05	0.118
Female Sex	19 (59.38%)	5 (27.78%)	0.047*
Age at onset of DM (yr)	8.61 ± 2.96	8.01 ± 2.01	0.451
Duration of DM (yr)	5.7± 3.1	5.5± 2.60	0.455
Insulin dose (IU/kg/day)	1.10 ± 0.27	1.17 ± 0.49	0.508

The most common type of dyslipidemia found in the dyslipidemic group was high LDL-C and low HDL-C in 8 patients (25.0%) followed by isolated high LDL-C in 6 patients (18.75%), isolated low HDL-C in 5 patients (15.63%), hypercholesterolemia and high LDL-C in 4 patients (12.50%).

DISCUSSION

In this case control study, fasting lipid profile, including serum total cholesterol (TC), serum triglycerides (TG), HDL-C and LDL-C, were measured in 50 children and adolescents with (T1DM at Pediatric department of Al-Hussain and Sayed Galal university hospitals.

In our study (as shown in **table 1**), the mean age cases were of 13.40±2.5 years (range 9.0-19.0 years) and a mean duration of diabetes was (4.78± 2.56years) (range 1.2-11.2years) and control had a mean age of (12.50±2.25 years) (range 9.0-19.0 years).

In our study (as shown in **table 2** and **figure 1**), there was high statistically significant in the frequency of dyslipidemia group in children and adolescents with (T1DM) 32 (64.0%) compared to 7 (28%) of the healthy control group ($p<0.002$).

This result 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 with statistically significant difference except for HDL-C.

Wiltshire et al (2003) confirmed that hyperlipidemia remains common in children and adolescents with (T1DM) compared with control subjects (35.4% vs. 14.7).

In our study (as shown in **table 3**), the mean TC and LDL-C were higher among the cases than controls but difference didn't reach statistical significance. Regarding mean TC was (164.88±39.54 mg/dl vs. 152.22±30.55 mg/dl, p=0.232), mean LDL-C was (98.60±35.80mg/dl vs. 91.55±26.70 mg/dl, p= 0.237), while the means TG and HDL-C were found to be similar in cases and control with insignificant difference (85.85±49.50 mg/dl vs. 82.50±42.22 mg/dl, p= 0.662) and (49.78±17.98 mg/dl vs. 47.38±11.33 mg/dl, p= 0.450) respectively.

These results agree with **Gunczler et al (2006)** who found that TG and HDL-C levels as well as the concentrations of TC, and LDL-C were similar in adolescents with (T1DM) and control subjects with no statistically significant difference.

In our study (as shown in **table 4**) regarding the pattern of dyslipidemia, 50% of the diabetics had elevated LDL-C levels followed by 38% had low HDL-C levels, 18% had elevated TC levels (as a part of mixed hyperlipidemia; not isolated hypercholesterolemia) and 8.0% had elevated TG concentrations compared with 15.4%, 25.6%, 4.0% and 2.0% of the healthy control subjects respectively.

This finding is in agreement with **Gunczler et al (2006)** who found that TC, LDL-C and TG levels were elevated in 34.4%, 25.0% and 15.6% of the adolescents with (T1DM) respectively compared with 20.0%, 13.3% and 6.7% of the control subjects.

In our study (as shown in **table 4**), the most frequent type of dyslipidemia was high LDL-C and low HDL-C in 25.0% of the children and adolescents with (T1DM) and dyslipidemia, while high LDL-C and hypercholesterolemia with and without hypertriglyceridemia were found to be the most common types in (31.0%) of the children with (T1DM) in **Al-Naama et al (2002)** study or (33.0%)of the children with (T1DM) in **Rahma et al (2006)** study.

In our study (as shown in **table 5**), most of dyslipidemic group were female with statistically significantly difference in the dyslipidemic group than the normolipidemic group (59.38%vs. 27.78%, p= 0.047).

This finding is in agreement with **Krantz et al (2004)** and **Schwab et al (2006)** who found that lipid levels were significantly higher in female subjects compared with male subjects with (T1DM), However, no statistically significant difference of HDL-C was found between female and male subjects in **Schwab et al (2006)**.

In the present work (as shown in **table 5**), the mean duration of diabetes showed no statistically significant difference between the dyslipidemic group and the normolipidemic group (5.7± 3.1 yrs and 5.5± 2.60 yrs respectively); there were patients with less than 5 years diabetes duration and having dyslipidemia.

This finding is in agreement with **Maahs et al (2007)** who found that there was no relationship between the lipid abnormalities in pediatric (T1DM) and the duration of diabetes.

In the present work (as shown in **table 5**), mean insulin dose was higher in the normolipidemic group than in dyslipidemic group but difference didn't reach statisticaly significance (1.17 ± 0.49IU/kg/day vs. 1.10 ± 0.27IU/kg/day, p= 0.508).

No significant correlation were found between serum TG of the diabetics and insulin dose in contrast to **Wiltshire et al (2003)** and **Ladeia et al (2006)** who found that serum TG correlate positively with insulin dose in children and adolescents with (T1DM).

CONCLUSION

1- This study showed that dyslipidemia in children and adolescents with type 1 diabetes mellitus (T1DM) was significantly more frequent than in control subjects especially among diabetic females.

2- The most frequent type of dyslipidemia in children and adolescents with T1DM was high LDL-C and low high density lipoprotein-cholesterol (HDL-C), while the classic diabetic dyslipidemia in the form of hypertriglyceridemia was much less frequent.

RECOMMENDATION

According to results achieved in our study the following recommendations are highlighted:

1- All children and adolescents with type 1 diabetes mellitus (T1DM) aged 9 years or older should be screened for dyslipidemia by measuring (TG, TC, LDL-C, HDL-C & VLDL) regardless their family

history, body mass index (BMI), life-style, dietary habits, diabetes duration or glycemic control.

2- Therapeutic Lifestyle Changes (TLC) focusing on weight control and increased physical activity to improve the lipid profile in children and adolescents with diabetes.

3- Further studies on the frequency and pattern of dyslipidemia in other age groups of infants and children with T1DM following up at outpatient clinic or pediatric department.

4- Further studies on the effect of lifestyle changes, weight control, and glycemic control on the improvement of dyslipidemia in children and adolescents with T1DM are needed; and to identify the need, efficiency and safety of pharmacologic treatment.

5- Further studies on larger number of children and adolescents with T1DM are needed to assess the power of lipoprotein ratios or "atherogenic indices" in CVD prediction.

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نسبة الدهون بالدم في الأطفال والبالغين المصابين بمرض السكري من النوع الأول في مستشفى الحسين و سيد جلال الجامعي

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***قسم طب الأطفال** قسم الباثولوجيا الاكلينيكية ـ كلية الطب – جامعة الأزهر**

يرتبط مرض السكري بارتفاع مخاطر الاصابة بأمراض الأوعية الدموية بنحو ٢ – ٤ أضعاف من الأفراد غير المصابين بمرض السكري وتعتبرأمراض القلب والأوعية الدموية هي السبب الرئيسي للوفاة بين الأشخاص المصابين بداء السكرى من النوع الأول والثانى. لذلك ، فمن الضروري أن تتم المعالجة المكثفة لكل العوامل المؤدية للاصابة بأمراض القلب والأوعية الدموية في الأشخاص الذين يعانون من مرض السكري، بما في ذلك اختلال نسبة الدهون فى الدم.

يرتبط اختلال نسبة الدهون فى الدم في داء السكري من النوع الأول ارتباطاً وثيقاً بدرجة السيطرة على مستويات الجلوكوز , ففي حالة سوء التحكم بنسبة السكر في الدم ترتفع نسبة الدهون الثلاثية كصفة مميزة فى الأشخاص المصابين بداء السكرى من النوع الأول , ويمكن تفسير ذلك بشكل جيد أنه بسبب نقص الأنسولين وكما هو متوقع تعود نسبة الدهون الثلاثية للمستوى الطبيعى مع العلاج بالأنسولين الكافي. البروتين الدهني منخفض الكثافة والكولستيرول هما "حجر

الزاوية " لتقييم مخاطر الاصابة بأمراض القلب والأوعية الدموية المتصمة بالبروتين الدهني.

أظهرت نتائج الدراسة أن انتشار اختلال نسبة الدهون فى الدم في الأطفال والمراهقين المصابين بداء السكري من النوع الأول أعلى بكثير مما كانت عليه في الضابطة ٦٤٪ مقابل ٢٨٪ ، القيمة الاحتمالية <٠,٠٢ لم يكن هناك فرق كبير بين المرضى والضوابط بخصوص متوسط مستويات كل من الكولستيرول الكمي، الدهون الثلاثية و البروتين الدهني عالي الكثافة - و بين الكوليسترول و البروتين الدهني منخفض الكثافة –(الكوليسترول مشترك بين المجموعتين).

النوع الأكثر شيوعا هو ارتفاع البروتين الدهني منخفض الكثافة – الكوليسترول وانخفاض البروتين الدهني عالي الكثافة - الكوليسترول بنسبة ٢٥٪ فى المجموعة المختلة الدهون.