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# Glycemic control impact on lipid profile variables in young patients from diyala governorate with type 1 diabetes mellitus

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## BACKGROUND

This study aimed to measure serum lipids in children with type 1 DM and its related to glycemic control .

## OBJECTIVE :

Dyslipidemia increases the frequency and severity of micro and macro-vascular complications of type 1 diabetes (T1DM). Type 1 diabetes mellitus (T1DM) and its related comorbidities are considered an important health issue. Lipoprotein disturbances have been associated with increased cardiovascular disease (CVD) risk in type 1 diabetes mellitus (T1DM). This study aimed to evaluate the impact of glycemic control on lipid profile variables in young patients with T1DM.

## MATERIALS AND METHODS:

This study included 100 children (≤19 years of age) with T1DM who had referred to the outpatient clinics of endocrinology in albatool Hospital in Baqubah , Diyala ,Iraq. Based on American Diabetes Association criteria, patients were divided into two groups including optimal glycemic control (OGC) and poor glycemic control (PGC). Mean lipid level and frequencies of lipid profile abnormalities between the two studied groups were compared.

## RESULTS:

Mean age of the studied population was 10 ± 5.9 years . A total of 70 (70%) and 30 (30%) patients had PGC and OGC, respectively. Hypercholesterolemia was the most common dyslipidemia in both groups (33 [29.1%] of OGC and 63 [39.1%] of PGC patients). The frequency of high low-density lipoprotein (LDL) was significantly higher in patients with PGC than those with OCG ($P = 0.007$). The frequencies of hypercholesterolemia, hypertriglyceridemia, and low levels of high-density lipoprotein were also higher in PGC group, but did not reach the significant threshold.

**CONCLUSION**:

It is suggested that glycemic control is in association with lipid profile abnormality in patients with T1DM. High LDL was significantly more frequent in patients with PGC than those with OGC. It is recommended to investigate the role of glycemic control on other cardiometabolic risk factors of T1DM patients. Our findings could be used for planning preventative strategies for reducing T1DM-related cardiovascular disease.

# Introduction

Type 1 diabetes mellitus (T1DM) is caused by severe insulin deficiency secondary to T-cell-mediated destruction of the insulin-producing β-cells. Data from large epidemiologic studies have demonstrated that the incidence of T1DM is increasing worldwide. Dyslipidemia is very common in patients with T1DM. Dyslipidemia is a significant risk factor for developing cardiovascular disease (CVD) and is associated with higher rates of mortality in patients with T1DM. [1,2,3]

Several studies have shown that poor glycemic control (PGC) and high level of glycated hemoglobin A1c (HbA1c) in patients with T1DM are associated with lipid peroxidation and oxidative stress, both of which contribute to atherosclerosis[4,5]. There are also evidences which demonstrated that intensive insulin therapy could have a significant positive impact on serum lipid levels and consequently on the occurrence of CVD in adulthood. Some previous studies also demonstrated that proper glycemic control could improve the lipid profile of T1DM patients.

Diabetic dyslipidemia is characterized by decreased levels of high-density lipoprotein cholesterol (HDL-C) and increased low-density lipoprotein cholesterol (LDL-C) and triglycerides (TGs).Type 1 diabetes mellitus (T1DM) is associated with an almost threefold higher mortality than the general population.

Glycemic control has been strongly associated with CVD risk. However, even in those individuals with well-controlled T1DM (mean HbA1c < 7%), CVD death is roughly threefold higher compared with their non-diabetic counterparts. Limited data are available on the pattern of lipid profile and its association with glycemic control in Diyala young patients with T1DM.

In this study, we investigated the frequency of dyslipidemia and evaluated its association with glycemic control in a sample of Diyala young patient with T1DM.

## Materials and method

The inclusion criteria were as follows: (1) confirmed diagnosis of T1DM based on the World Health Organization guidelines [6] and (2) being lower than 19 years of age. Exclusion criteria were presence of any underlying liver, kidney, and thyroid disease and the use of medications other than insulin. Patients who were not willing or able to continue the study were also excluded from the study. After enrolling the eligible patients, the objectives and the protocol of the study were completely explained and a written informed consent was obtained from parents/caregivers.

The patients who had other illnesses, hypothyroidism, or taking any other medication were excluded. Diabetes mellitus was diagnosed according to the WHO, International Society for Pediatric and Adolescent Diabetes (ISPAD) criteria

Demographic features and clinical data of the eligible patients were collected which included age, sex, age at T1DM onset, duration of T1DM since diagnosis, weight (kg), height (cm), and body mass index (BMI, $kg/m^2$). After 12 h of overnight fasting, a venous blood sample was collected from each participant for measurement of HbA1c, triglyceride (TG), total cholesterol (TC), low-density lipoprotein (LDL), and high-density lipoprotein (HDL).

Serum total cholesterol, triglycerides increased with worsening control, while serum high density lipoprotein cholesterol concentrations were unaltered. There were also positive correlations between glycated haemoglobin and total cholesterol, triglycerides in diabetic children. Thus, abnormalities in circulating lipids are common in young subjects with IDDM but largely disappear if blood glucose concentrations are reasonably controlled.

Lipid values were analyzed and classified according to the American Academy of Pediatrics Guidelines and National Cholesterol Education Program III (NCEP III) guidelines. As part of the routine protocol used in the Diabetes Unit, physical exercise was strongly encouraged at least twice a week during school activities. All patients were regularly seen by the same dietitian, and a low-fat diet was recommended. During the study, it was suggested that no changes be made in diet or physical activity. An informed consent form was signed by the patients or by a parent of those younger than 18 years.

Dyslipidemia was define based on american diabetic associated criteria [7] as having at least one of the following : TC >170 mg/dL, HDL <40 mg/dL in men, HDL <50 mg/dL in women, LDL >100 mg/dL, and TG >150 mg/dL. Optimal glycemic control (OGC) was defined as per criteria laid by ADA guidelines [7] as follows: (1) 7.5%< HbA1c <8.5% for patients lower than 6 years of age; (2) HbA1c <8% for patients with 6–12 years of age; and (3) HbA1c <7.5% for patients with 13–19 years of age. Based on these criteria, the patients were divided into two groups including OGC and PGC. We compared the frequencies of lipid profile abnormalities in these two groups of patients.

# Results

Of 100 eligible cases, 60 (60%) were boys and 40 (40%) were girls. The mean age was 10 ± 5.9 years (range: 4–18 years), and the mean BMI was 18.7 ± 7.8 kg/$m^2$. The mean age at onset of T1DM was 8 ± 6 years (range 2–14 years), and the mean duration of T1DM since diagnosis was 5 ± 3 years (range 1.0–11.0 years). Details of demographic and clinical characteristics of the study population are presented in Table 1. mean level of lipid profiles and Hb A1C were not significantly different between diabetic girls and boys. Table 2 presents the laboratory characteristics of the studied patients. Overall, 75 (75%) cases had dyslipidemia which included 42 (42.0%) patients with hypercholesterolemia, 15 (15%) patients with high levels of LDL, 13 (13%) patients with low levels of HDL, and 5 (5 %) patients with hypertriglyceridemia.

**Table 1**

Demographic characteristics and mean level of lipids in type 1 diabetic patients

| Men level of lipids | Boys | Girls | *P* |
|---|---|---|---|
| Age (years) | 12.8±4.2 | 13.3±7.1 | NS |
| HbA1c | 8.1±1.7 | 8.3±1.9 | NS |
| Cholesterol (mg/dl) | 80±37.4 | 83.2±31.9 | NS |
| Triglyceride (mg/dl) | 163.8±30.4 | 159.8±30.3 | NS |
| HDL-cholesterol (mg/dl) | 52.4±13.7 | 54.3±17.8 | NS |
| LDL-cholesterol (mg/dl) | 88.2±25.5 | 91.6±22.4 | NS |

HbA1c=Glycated hemoglobin, HDL=High-density lipoprotein, LDL=Low-density lipoprotein

## Table 2

Lipid profile (mean±standard deviation) of type 1 diabetic patients with optimal glycemic control and poor glycemic control

| Lipids | Patient with OGC | Patient with PGC |
|---|---|---|
| HDL cholesterol (mg/dl) | 54.53±18.59 | 54.32±14.68 |
| LDL cholesterol (mg/dl) | 86.27±21.73 | 91.92±25.77 |
| Cholesterol (mg/dl) | 156.36±25.99 | 165.41±33.12 |
| Triglyceride (mg/dl) | 75.14±28.67 | 88.13±38.82 |

According to the cutoffs of HbA1c recommended by the AAD, 65 (65%) patients had PGC, whereas the remaining 35(35%) had OGC.

Hypercholesterolemia was the most common dyslipidemia in both groups, which was seen in 33 (29.1%) and 63 (39.1%) of patients with OGC and PGC, respectively. The frequency of high LDL was significantly higher in patients with PGC ($P$ = 0.007). The frequencies of hypercholesterolemia, hypertriglyceridemia, and low levels of HDL were also higher in PGC group, but they did not reach the significant threshold.

## Table 3

Frequency (percentage) of different patterns of dyslipidemia in type 1 diabetic patients with optimal glycemic control and poor glycemic control

| **Dyslipidemia** | patient with OGC % | Patient with PGC % |
|---|---|---|
| Hypertriglyceridemia | 2.7 | 8.4 |
| Hypercholesterolemia | 29.1 | 39.1 |
| High LDL cholesterolemia | 13.8 | 12.3 |
| Low HDL cholesterolemia | 12.8 | 26.6 |

OGC=Optimal glycemic control, PGC=Poor glycemic control, HDL=High-density lipoprotein, LDL=Low-density lipoprotein

## Discussion

Based on our findings, dyslipidemia was present in as high as 75 % of diyala children with T1DM. The most common lipid profile abnormality in our study was hypercholesterolemia (35%), which was followed by high LDL (20 %). Furthermore, patients with PGC had a significantly higher frequency of high LDL in comparison with patients with OGC. These findings are clinically significant, as they call attention to the importance of glycemic control as a potential modifiable risk factor for dyslipidemia in T1DM.

The reported pattern of lipid profile abnormalities in T1DM varies in different studies. In line with the results of our study, Schwab *et al.* [8] reported that hypercholesterolemia was the most common lipid abnormality in 27,358 German and Austrian children with T1DM. Similarly, in a study on Korean children, Kim *et al.* demonstrated that hypercholesterolemia and high LDL were the most frequent types of dyslipidemia in T1DM. Similar findings were also found in studies by al-Naama *et al.*[9] and Rahma *et al.*[10]in Iraqi children. A recent study in Bangladesh also reported a 66% rate of hypercholesterolemia and a 75% rate of high LDL for T1DM patients. [11] It should be noted that the diabetic children in the index studies included patients with PGC as they had mean fasting blood glucose of 232.0 mg/dl and HbA1c of 9.8%. In a study on Egyptian children with T1DM, Herman *et al.* [12]and Kantoosh *et al.* [13]demonstrated that hypertriglyceridemia was the most common type of dyslipidemia. These differences across the studies are probably related to different glycemic controls across the studied populations.

Our study showed that patients with higher HbA1c level had higher frequency of high LDL. In the literature, large bodies of evidence have shown a strong association between high levels of HbA1c and an adverse lipid profile in T1DM; however, there is uncertainty about the thresholds of HbA1c beyond which lipid levels begin to change.

Maahs *et al.* [1] reported a positive association between HbA1c and both TC and non-HDL. In another engaging report from the SEARCH for Diabetes in Youth (SEARCH) study on American children with T1DM, Guy *et al.* [14] demonstrated that diabetic patients with HbA1c <7.5% had lower frequency of dyslipidemia, which was similar to the healthy controls.

On the other hand, patients with HbA1c ≥7.5% had a significantly higher frequency of hypercholesterolemia and high LDL in comparison with healthy controls.

Finally, in the study of Herman *et al.* [12] on Egyptian children, high levels of HbA1c in the untreated newly diagnosed patients were associated with significantly higher serum TG level in comparison with treated patients with good glycemic control. The findings of the mentioned studies along with the results obtained from the present study highlight the important role of glycemic control in decreasing the frequency of dyslipidemia in patients with T1DM.

Approperate glycemic control reduces the risk of CVD and mortality in patients with T1DM. It has been shown that appropriate glycemic control over a mean of 6.5 years reduced CVD complications by 57% in T1DM[15]. Moreover, OGC is associated with fewer diabetic complications and better metabolic control[16]. At the present time, several guidelines for glycemic control exist in the literature. The ADA treatment goals for glycemic control recommend HbA1c values of lower than 7.0%. The International Diabetes Federation and the American Association of Clinical Endocrinologists recommend an HbA1c value of lower than 6.5%.However, only a few proportions of the patients can attain the optimal glycemic targets. As an example, only 44% of American diabetic patients have been able to maintain an HbA1c value of OGC[17]. Therefore, glycemic control remains a serious challenge for health-care systems worldwide. [18] Given the benefits of OGC, strong efforts should be taken by public health authorities and the medical community to improve glycemic control among patients with diabetes.

findings of this study must be interpreted in view of its limitations; most importantly, the relatively small sample size. Future studies with larger sample size are warranted to further explore the pattern of dyslipidemia in different populations of Iraqi children with T1DM.

It is suggested that the pattern of dyslipidemia in relation to glycemic control is varied in different populations which could be due to the genetic and ethnic lifestyle background of the populations.

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