Dyslipidemia in Egyptian Children and Adolescents with Type 1 Diabetes Mellitus

Thesis
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ABSTRACT

Background: Dyslipidemia is a significant CVD risk factor in persons with diabetes. CVD is the leading cause of death in people with T1DM. **Objective:** To evaluate the frequency, pattern and relations of dyslipidemia in children and adolescents with T1DM in DEMPU. **Method:** In this cross-sectional study, fasting lipid profile of 60 patients aged ≥ 9 years with T1DM was measured and compared with that of 39 healthy age and sex matched children. **Results:** Dyslipidemia was found in 65.0% of patients compared with 28.2% of the control group with a statistically significant difference ($p < 0.001$). Fifty percent of the patients had elevated LDL-C levels with a mean of 102.0 ± 34.4 mg/dl and a positive significant correlation with BMI. There were positive significant correlations between the dyslipidemia and female sex and activity. The most frequent type of dyslipidemia was high LDL-C and low HDL-C. Dyslipidemia was found regardless the family history, degree of glycemic control, BMI SDS, diabetes duration and dietary habits. **Conclusion:** Dyslipidemia in children and adolescents with T1DM was significantly more frequent than in healthy control subjects. So, screening and management may be considered especially in diabetic females. LDL-C is the 'cornerstone' for assessment of lipoprotein-related CVD risk. Activity is important for prevention of dyslipidemia.

Key Words: Type 1 diabetes mellitus, dyslipidemia, low density lipoprotein-cholesterol, high density lipoprotein-cholesterol, cardiovascular disease risk, activity, body mass index, children and adolescents.

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LIST OF ABBREVIATIONS

ACEI	Angiotensin converting enzyme inhibitors
ADA	American Diabetes Association
AIP	Atherogenic Index of Plasma
Apo A	Apoprotein A
Apo B	Apoprotein B
Apo C	Apoprotein C
Apo E	Apoprotein E
BG	Blood glucose
BMI	Body mass index
BP	Blood pressure
CAD	Coronary artery disease
CETP	Cholesterol ester transfer protein
CM	Chylomicrons
CSII	Continuous Subcutaneous Insulin Infusion
CVD	Cardiovascular disease
DBP	Diastolic blood pressure
DCCT	Diabetes Control and Complications Trial
DEMPU	Diabetes Endocrine and Metabolism Pediatric Unit
DKA	Diabetic ketoacidosis
DM	Diabetes mellitus
FBG	Fasting blood glucose
FER_{HDL}	Fractional esterification rate of cholesterol
FFA	Free fatty acid
GAD	Glutamic acid decarboxylase
HbA1c	Glycosylated hemoglobin
HDL-C	High density lipoprotein-Cholesterol
HHS	Hyperglycemic hyperosmolar state
HLA	Human leukocyte antigen
HMG-CoA	Hydroxy methylglutaryl- Coenzyme A
HTGL	Hepatic triglyceride lipase
IA2	Tyrosine phosphatase autoantibodies
IAA	Insulin autoantibodies
ICA	Islet cell autoantibodies
IDF	International Diabetes Federation
IDL	Intermediate density lipoprotein
INS	Insulin gene
ISPAD	International Society for Pediatric and Adolescent Diabetes
LCAT	Lecithin cholesterol acyl transferase

LDL-C	Low density lipoprotein-Cholesterol
Lp (a)	Lipoprotein (a)
LPL	Lipoprotein lipase
MDI	Multiple Daily Injections
MS	Metabolic syndrome
PAD	Peripheral artery disease
PPBG	Postprandial blood glucose
SAT	Subcutaneous abdominal adipose tissue
SBP	Systolic blood pressure
SD	Standard deviation
SDS	Standard deviation score
SMBG	Self-monitoring of blood glucose
T1DM	Type 1 diabetes mellitus
T2DM	Type 2 diabetes mellitus
TC	Total cholesterol
TDEI	Total daily energy intake
TG	Triglycerides
TLC	Therapeutic Lifestyle Changes
VAT	Visceral adipose tissue
VLDL	Very low density lipoprotein
VNTR	Variable number of tandem repeats
WC	Waist circumference

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INTRODUCTION

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INTRODUCTION

Type 1 diabetes mellitus (T1DM) is the most common childhood endocrine disease **(Teles and Fornés, 2012)**. The suggestion that there will be an epidemic of diabetes by 2025 and that we can therefore expect a massive increase in macrovascular disease has focused attention on the mechanisms by which diabetes promotes atherosclerosis to such an extent **(Tomkin, 2008)**.

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)**. Cardio-metabolic risk factor management has evolved considerably with the continued emergence of new and thought-provoking evidence. 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 is a preventable major risk factor for CVD. There are several studies that have evaluated dyslipidemia in patients with type 2 diabetes mellitus (T2DM), but dyslipidemia in patients with T1DM and especially young children with short duration of diabetes remains largely undiagnosed and undertreated **(Wadwa et al., 2005)** and **(Hamad and Qureshi, 2008)**. It has been shown that the quantity of plasma lipids gives adequate information about the risk of complications. The intensity of dyslipidemia predicts macrovascular complication such as a CAD in patients with T1DM. Diabetic children and adolescents revealed significant disorder in lipid metabolism including both

qualitative and quantitative abnormalities of lipids **(Hamad and Qureshi, 2008)**.

Dyslipidemia was defined by American Diabetes Association (ADA) as having low density lipoprotein-cholesterol (LDL-C) ≥ 100 mg/dl, high density lipoprotein-cholesterol (HDL-C) < 40 mg/dl (males) & < 50 mg/dl (females), total cholesterol (TC) ≥ 200mg/dl and triglycerides (TG) ≥ 150 mg/dl **(Wysham et al., 2012)**. Dyslipidemia is present if one or more of these lipid or lipoprotein levels are abnormal **(Kwiterovich, 2008)**.

LDL-C is a well-recognized risk factor for atherosclerosis-related diseases, in particular CAD. This is well illustrated in the multiple risk factor intervention trial by **Stamler et al. (1993)** where CAD death was positively correlated to plasma cholesterol level. Oxidized LDL-C may also stimulate secretion of cytokines and growth factors by endothelial cells, smooth muscle cells and macrophages. This results in complex changes in the arterial wall involving further attraction of macrophages, proliferation of smooth muscle cells and laying down of extracellular matrix, altogether completing the process of atherosclerosis. So, primary emphasis should be placed on LDL-C lowering, while interventions to lower the TG levels and raise HDL-C levels may also be very useful **(Chowdhury and Pandit, 2012)**.

In addition, chronic hyperglycemia promotes the glycation of LDL-C, and both glycation and oxidation are believed to increase the atherogenicity of LDL-C. Both of these processes may impair function and/or enhance atherogenicity even in those with T1DM with a normal lipid profile **(John Mancini et al., 2013)**. For these reasons, improvement in diabetic control leads to improvement in cardiovascular outcome in diabetes **(Tomkin, 2008)**.

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) following at the Diabetes Endocrine and Metabolism Pediatric Unit (DEMPU), Children's Hospital, Cairo University; and to study the relation of dyslipidemia to their age, age at onset and duration of diabetes, degree of glycemic control, insulin dose, body mass index (BMI), waist circumference (WC) and epidemiological risk factors including family history, diet and life-style.

REVIEW OF LITERATURE