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DYSLIPIDAEMIA IN RECENTLY DIAGNOSED YOUNG SUBJECTS OF TYPE 1 DIABETES MELLITUS WITH NORMAL/FAVOURABLE BMI: A RISK FACTOR OF MACROVASCULAR DISEASE

AQEELA HAMAD AND H. JAVAID QURESHI
Department of Physiology & Cell Biology, University of Health Sciences, Lahore - Pakistan

ABSTRACT
The aim of the study was to evaluate the lipid profile of recently diagnosed uncomplicated young type 1 diabetic children. This cross- sectional prospective study based on total of 79 subjects between the ages of 9-16 years, it includes 39 diabetic children (both male and females) & 40 sex and age matched normal healthy children as controls. The study subjects underwent detailed medical history and examination. Individuals with a history of type 2 diabetes mellitus, Cushing's syndrome, thyrotoxicosis, obesity, hypertension or any major illness and those on medications known to affect body composition excluded from the study. Fasting blood samples were drawn from the participants for biochemical assays. Anthropometric and blood pressures both systolic and diastolic were measured by standard methods. The characteristics of study sample & mean lipid levels are shown in table 1, 2 & 3. Type 1 diabetic children have elevated levels of lipids despite short duration of disease and normal BMI as compared to healthy age and sex matched control children. Type 1 diabetic male children had more dyslipidaemia as compared to female type 1 diabetic patients. The results indicate dyslipidaemia in type 1 diabetic children despite short duration of diabetes. High lipid profile along with poor metabolic control is an important risk factor for chronic complications of diabetes mellitus like micro vascular and macro vascular diseases. There is intense need of early screening and interventions, to prevent cardiovascular disease in high risk diabetic patients.

INTRODUCTION

Type 1 diabetes, also known as juvenile diabetes, is widely thought to be an organ specific autoimmune disease. Type 1 diabetes is characterized by an inadequate secretion of insulin by the β-cells of **pancreas**[1] and usually has a sudden and dramatic onset, ketoacidosis, and insulin dependency at a relatively early age. The incidence of type 1 diabetes has increased globally over the past decades. It has been estimated that on an annual basis some 65,000 children aged less than 15 years develop type 1 diabetes mellitus.[2] Increased blood sugar levels also result in significant disturbance in lipid metabolism including both qualitative and quantitative change in the lipids.[3]

There are several studies that have evaluated dyslipidaemia in type II diabetic patients,[4-8] but dyslipidaemia in type 1 diabetic patients and specially young children with short duration of diabetes remains largely undiagnosed and undertreated. It has been shown that the quantity of plasma lipids gives an adequate information about the risk of complications.[9]

Dyslipidaemia is a preventable major risk factor for cardiovascular disease (CVD). The intensity of dyslipidaemia predicts macrovascular complication such as a coronary artery disease in patients with type 1 diabetes mellitus. Diabetic children and adolescents revealed significant disorder in lipid metabolism including both qualitative and quantitative abnormalities of lipids. For the patients in the group of 9-16 years ATPIII guide line values were considered and existence of dyslipidaemia was defined as LDL > 130 mg/dl, HDL < 40 mg/dl (males) & <50 mg/dl (females), total cholesterol 200mg/dl and triglycerides 150 mg/dl.[10]

In spite of an increased risk of CVD in type 1 diabetes, little is known in relation to responsiveness and adequacy of dyslipidaemia management in this population. Thus the object of this study was to investigate, lipid profile in recently diagnosed uncomplicated type 1 diabetic children with normal BMI, for primary prevention and early diagnosis of high risk Type 1 diabetic patients.

MATERIAL AND METHODS

The present study was based on 39 type 1 diabetic patients (19 males and 20 female subjects) and 40 non-diabetic controls between the ages of 9-16 years. The duration of diabetes was more than one year and was undergoing periodic follow-up examinations at the Diabetic Clinic of Children Hospital Lahore. Written informed consent to partici-

pate in the study was obtained from each subject and/ his or her parents.

Inclusion criteria
The study subjects, who underwent a detailed medical examination, was diagnosed type I diabetes mellitus for more than one year and no signs of acute or chronic illness.

Exclusion criteria
Subjects with history of type II diabetes mellitus (DM), taking medications known to affect body growth or lipid metabolism, with endocrinopathies (e.g. Cushing's syndrome, Down syndrome, acromegally, thyrotoxicosis, etc.) or any major illness since birth, were excluded from the study. None of the subjects had any clinical evidence of hypertension, infection, connective tissue disease, liver dysfunction, or angiopathy. None of the subjects were taking antihypertensive, antiplatelet, or lipid –lowering medications at the time of the study.

Study Design
This is a cross-sectional prospective study. The subjects were divided into the following 2 age-matched groups:
Group I Children with Type 1 DM (n=39).
Group II healthy Children without Type 1 DM (n= 40).

Physical Measurements and Blood collection
Body weight (BW) and height were recorded for all patients. Body mass index (BMI) was calculated according to the equation: BMI = BW (kg)/height (m).[2]

Blood pressure (BP) was measured from the right arm in a sitting position using an appropriate cuff size. The first and fifth Krotokoff sounds were recorded as systolic and diastolic BP, respectively.

Six ml of venous blood was drawn from the cubital vein. In all cases blood was withdrawn between 09.00-10.00 h. The blood samples were centrifuged immediately and glucose levels were measured the same day. The remaining serum sample was aliquoted and stored at -80°C until used.

Analytical determinations
All biochemical parameters were determined in duplicate using standard procedures.

Serum glucose levels were determined by the glucose oxidase method using a commercial reagent kit (HUMAN Gesellschaft fur Biochemica und Diagnostica GmbH, GERMANY). Fasting lipid profile for each subject was obtained by measuring serum TAG by GPO-PAP method (HUMAN), HDL-and LDL-cholesterol by a direct quantitative method (Roche Diagnostics GmbH, Mannheim, Germany). The estimations were made with a Humalyzer 3000 chemistry analyzer (Human, Weisbaden, Germany). HbA1-c was estimated by affinity liquid chromatography with a D-SI Glycomat (Provalis Diagnostics, Deeside, UK).

Statistical analysis
Mean and standard deviations were determined for quantitative data. The significance of differences among the two groups was analyzed by student's t-test. P value < 0.05 was considered statistically significant. Calculations were carried out with the SPSS version 14 (SPSS, inc, Chicago, IL, USA).

RESULTS

The anthropometric, BMI, BP characteristics of the subjects in the control and type 1 diabetic children. The proportion of male and female in both the groups was similar. Both groups had similar ages and BMI (Table 1).

Table 1: *Anthropometric characteristics of type 1 diabetes subjects.*

Variable	Controls	Diabetic Type 1 Patients
Number of subjects(n)	40	39
Age(years)	09±16	09±16
Gender		
Male	20	19
female	20	20
Duration of diabetes	Nil	≥ 1 year
BMI (Kg/m^2)	16.4	17.96
Systolic blood pressure(mm Hg)	100.75	99.74
Diastolic blood pressure(mm Hg)	63.13	62.82

The mean ± SEM values and p- values of biochemical parameters were performed in the control and diabetic groups (Table 2 and 3). Mean total cholesterol, LDL-cholesterol were significantly higher in diabetic children than control group whereas no statistically significant difference was observed in serum TG levels in male diabetic children but its value was higher in female children. Serum LDL-cholesterol levels were also statistically significant. Serum HDL-Cholesterol levels were statistically significant.

DISCUSSION

In our study population, despite the absence of other risk factors like obesity and hypertension there was evidence of dyslipidaemia. A recent study showed, presence of dyslipidaemia and hypertension in overweight type 1 diabetic patients and and they also admitted that such metabolic distur-

Table 2: *Biochemical parameters of male subjects.*

Variables	Diabetic Type 1 Males	Control Males	P-Value
Plasma glucose level (mg/dl)	320.1 ± 23.22	97.00 ± 1.35	0.05
HbA1C %	10.3 ± 0.55	5.21 ± 0.08	<0.001
HDL (mg/dl)	38.4 ± 1.13	50.50 ± 2.64	<0.001
Triglycerides (mg/dl)	195.9 ± 15.81	163.64 ± 15.97	<0.001
Cholesterol (mg/dl)	234.4 ± 9.26	122.81 ± 5.17	<0.001
LDL (mg/dl)	327.8 ± 18.98	88.03 ± 4.37	<0.001

p-value <0.05

Table 3: *Biochemical parameters of female subjects.*

Variables	Diabetic Type 1 Females	Control Females	P-Value
Blood glucose level (mg/dl)	309.22 ± 9.33	96.41 ± 1.30	(0.00)
HbA1C %	9.60 ± 0.58	5.29 ± 0.10	<0.001
Cholesterol (mg/dl)	215.8 ± 6.19	134.8 ± 4.80	<0.001
Triglycerides (mg/dl)	280.4 ± 33.62	137.5 ± 7.71	<0.001
HDL (mg/dl)	41.3 ± 1.47	53.7 ± 3.02	(0.002)
LDL (mg/dl)	304.6 ± 28.23	93.8 ± 1.72	<0.001

p-value <0.05

bances may begin to develop even in type 1 diabetic patients with normal BMI.[11]

Coronary heart disease is the leading cause of mortality in patients with type 1 diabetes. As in persons with type 2 diabetes and the general population, dyslipidaemia is a considerable dangerous factor for Coronary heart disease (CHD) in type 1 diabetic patients.[12] Many studies indicate that 55% of the U.S. general population and 51% of adults aged 20-59 years with diabetes have hypercholesterolaemia.[13-14] European data indicates a similar prevalence of 51% of type 1 diabetic adults with dyslipidaemia in the Eurodiab study.[15] Although lipid profiles in type 1 diabetic patients tended to be better than the patients with type 2 diabetes, recent studies[16-17] suggest a need for more insistent lipid lowering in type 1 diabetic patients to diminish CHD risk. While some patients do good to non pharmacological interventions, including development of glycaemic control, exercise, and weight loss, others may require medication to recover lipid levels. However, the available literature suggests that dyslipidaemia is undertreated in this high-risk population.[18]

Coronary artery disease (CAD) rates are high for persons having a diabetes of duration 20-30 years duration, (and thus aged in their early 30s at the time of the event), having a 1.5% annual risk of a major CAD event. Despite supervision of complications, major excess mortality still exists in the type 1 diabetes population compared to the non-diabetic populations.[20]

Several studies suggest failure to show a major decline in CAD may reveal a weaker association to glycaemia than is seen for other complications.[21-23] Recent data from Diabetes Control and Complications trial / Epidemiology of Diabetes Interventions and Complications study follow up show a strong advantage of intensive therapy on cardiovascular disease outcomes.[24] For coronary artery disease, that shows the least favourable alteration over time, these results suggest the need for a focus on its other risk factors e.g., blood pressure and lipids, which are poorly controlled.[25]

It is **concluded** that Lipid profile assessed in 9 to 16 years old young diabetic children predicts high risk patients independently of contemporaneous risk factors, because in this study the patients showed statistically significant elevation of plasma lipids despite normal BMI, short duration of diabetes and normal blood pressure. These findings suggest that there is intense need for early interventions to prevent complications in future.

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