DYSLIPIDAEMIA AMONG FILIPINO CHILDREN WITH INSULIN-DEPENDENT DIABETES MELLITUS: PREVALENCE AND RELATION TO GLYCEMIC CONTROL

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ABSTRACT

Dyslipidaemia is a major risk factor associated with cardiovascular disease among children with insulin-dependent diabetes mellitus (IDDM). Most studies have demonstrated that with increasing poor control of diabetes as reflected by levels of hemoglobin A1c (HbA1c), total cholesterol, total triglyceride and lipoprotein subfractions are likewise increased. This study aims to determine the prevalence of dyslipidaemia among Filipino children with IDDM and further investigate the relationship of dyslipidaemia with glycemic control (HbA1c) and the different variables such as sex, chronologic age, age of onset, dose of insulin, duration of diabetes and blood glucose (FBS). Among 50 IDDM patients studied, 27 females and 23 males, 62% had dyslipidaemia with increased levels of cholesterol, tryglyceride, LDL and decreased HDL. Females were more affected than males ($p<0.02$). The most common combined plasma lipid abnormality was hypercholesterolemia with elevated LDL (25.7%). Among the diabetic patients with dyslipidaemia, 76.9% were not in good glycemic control. Dyslipidaemia was positively correlated with HbA1c at $p<0.043$. Cholesterol ($r=0.45$; $p=0.0010$), triglycerides ($r=0.31$, $p=0.0269$), and LDL ($r=0.56$, $p=0.0001$) were likewise positively correlated with glycemic control. However, no significant relationship was noted with HDL and the other variables such as chronologic age, age of onset, dose of insulin, duration of diabetes and FBS.

In conclusion, this study showed that dyslipidaemia is prevalent among Filipino children with insulin-dependent diabetes mellitus notably among those who were not in good glycemic control. It underscores the need for regular lipid monitoring aside from glucose monitoring in order to initiate early intervention to prevent the dreaded onset of cardiovascular complications.

INTRODUCTION

Insulin-dependent mellitus (IDDM), a common metabolic disorder of children, has been associated with an increased morbidity and mortality from cardiovascular disease (Garcia *et al.* 1974; Kannel *et al.* 1979; Santen *et al.* 1972; Krolewski 1987). Dyslipidaemia is a major risk factor for this condition. The National Cholesterol Education Program (NCEP) in America revealed that elevated cholesterol levels early in life may play a role in the development of adult atherosclerosis (NCEP 1992). The Diabetes Control and Complications Trial (DCCT) showed that younger IDDM patients (ages 13-24) had elevated mean total cholesterol, triglyceride, and LDL cholesterol levels, while HDL was reported to be low (DDCT 1992). Most studies have demonstrated that with an increasing poor control of diabetes as reflected by levels of hemoglobin A1c (HbA1c), total cholesterol, total triglyceride and lipoprotein subfractions are likewise increased (Glasgow *et al.* 1981; Sosenko *et al.* 1980; Semenkovich *et al.* 1989; Asad *et al.* 1994). Glycemic control is significantly correlated with these parameters except for high density lipoprotein Glasgow *et al.* 1981; Sosenko *et al.* 1980; Semenkovich *et al.* 1989; Asad *et al.* 1994).

Thus, a cross-sectoral study was designed (1) to determine the prevalence of dyslipidaemia in Filipino children with IDDM and (2) to further investigate the relationship of dyslipidaemia with each of the different variables such as sex, chronologic age, age of onset of diabetes, dose of insulin (ukg/day), duration of diabetes, blood glucose (FBS) and glycosylated hemoglobin. (HbA1c).

Definition of Terms

Dyslipidaemia – abnormal concentration, composition, or metabolism of lipids and lipoproteins (Gang 1994).

Glycosylated Hemoglobin – the quantity of glucose irreversibly attached to the hemoglobin molecule (Sperling 1990).

SUBJECTS AND METHODS

Study Population

Our study population consisted of diagnosed cases of insulin-dependent diabetes mellitus (IDDM) based on the criteria set by the National Diabetes Data Group (1979). They included diabetic patients who were on a regular follow-up at the Pediatric Endocrine Clinic of the Philippine General Hospital and private patients under the care of Pediatric Endocrinologists. Subjects were informed by mail on the significance of the study, the scheduled investigation and the necessary preparation for the said examination.

The cross-sectional investigation was conducted from November 1995 to March 1996. A total of 50 patients were included in the study after an informed consent. On the scheduled date of examination patients were made to fast 8-10 hours overnight and blood was extracted prior to the morning dose of insulin.

Questionnaires were filled up to supply data on sex, chronologic age, age of onset, duration of diabetes and dose of insulin.

Laboratory Methods

A conventional venipuncture was done to withdraw 10 ml of blood. Three ml of blood was placed in an EDTA tube for glycosylated hemoglobin determination. The remaining 7 ml was placed in a plain tube and allowed to clot at room temperature and centrifuged to separate the serum. Two ml was used for fasting blood glucose which was immediately done and the remaining 5 ml was stored at 4°C for the lipid analysis performed at a specified time.

Cholesterol was analyzed by enzymatic colorimetric determination using cholesterol oxidase with a reference value of 200 mg/dl (5.18 mmol/L) as set by the National Cholesterol Education Program for Adolescence (NCEP). Triglyceride was measured by lipase-glycerol kinase method with reference value for males at 60-165 mg/dl (0.68-1.88 mmol/L) and for females at 40-140 mg/dl (0.46-1.60 mmol/L). High density lipoprotein (HDL) is the supernatant after precipitating the serum with phosphotungstic acid-magnesium ions with reference values for males at 35-55 mg/dl (0.90-1.40 mmol/L) and for females 45-65 mg/dl (1.20-1.70 mmol/L). Low density lipoprotein (LDL) was calculated using the Friedewald formula with reference value set by NCEP at 130 mg/dl (3.37 mmol/L).

LDL=Total cholesterol-HDL-Trigylceride/5

Glycosylated hemoglobin (HbA1c) was measured by the Eagle Diagnostic Glycohemoglobin (Ghb) procedure which employs a weakly binding cation-exchange resin in a zwitterionic buffer for a rapid separation of Ghb from non-glycosylated hemoglobin. The glycohemoglobin-containing supernatant was poured into a cuvet for measurement of absorbance by spectrophotometer at 415 nm.

Glycemic control using HbA1c was determined as follows:

Good Control	7.5-9.0%
Fair Control	9.0-10.0%
Poor Control	>10%

Blood glucose concentration (FBS) was measured by an enzymatic colorimetric determination using glucose-peroxidase reaction with a reference value of 70-110 mg/dl. (3.9-6.1 mmol/L)

Statistical Method

There were eleven variables considered in this study namely sex, age in years, age of onset, duration of diabetes, dose of insulin, cholesterol, triglyceride, high density lipoprotein (HDL), low density lipoprotein (LDL), blood glucose (FBS) and glycosylated hemoglobin (HbA1c). Using the Pearson's Correlation Coefficient, relationship among the different variables was determined. Because the expected frequencies were small, the Fisher's Exact Test was used to correlate the

different variables between patients with dyslipidaemia and those without dyslipidaemia.

Results

A total of 50 patients with insulin-dependent diabetes mellitus (IDDM), 27 females and 23 males, were included in the study. As shown in Table 1, the patients had a mean age of 14.42 years, with age of onset ranging from 1-19 years (mean=10.70). The mean duration of diabetes was 3.54 years with patients receiving an average daily insulin of 0.98 units/kg body weight. However majority of diabetics were not in good glycemic control with a mean HbA1c of 10.08% and FBS of 223.4 mg/dl. (12.40 mmol/L).

Among 50 patients studied, 31 had dyslipidaemia with a prevalence of 62% as shown in Figure 1. Cholesterol, triglyceride, LDL levels were increased in contrast to HDL which was decreased (Fig. 2).

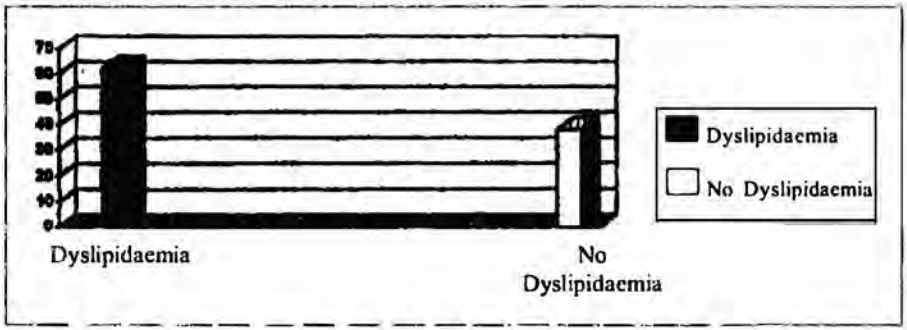

Figure 1. Prevalence of Dyslipidaemia in IDDM Patients

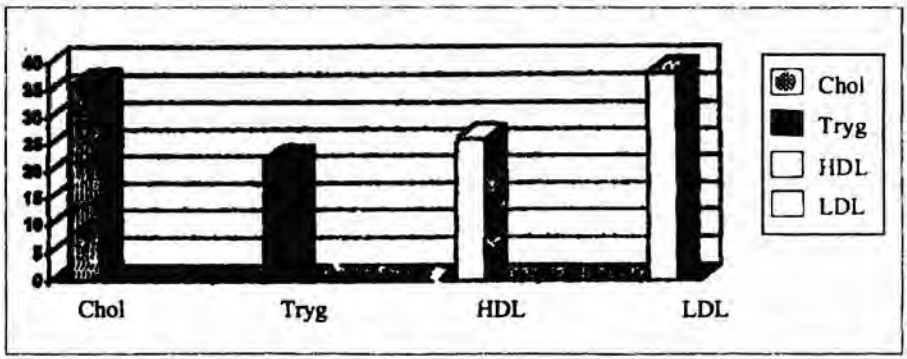

Figure 2. Frequency of Abnormal Lipids and Lipoproteins in IDDM Patients

Table 2 demonstrates the most common combined forms of dyslipidaemia. These were hypercholesterolemia with elevated LDL (25.7%) and hypercholesterolemia, hypertriglyceridemia with elevated LDL (16.0%). Comparing diabetics with dyslipidaemia and those without dyslipidaemia, the Fischer's Exact Test showed a positive correlation $p<0.043$ between dyslipidaemia and HbA1c. Significantly less number of patients (22.4%) were observed to have dyslipidaemia in the group with good glycemic control than in the fair and poor glycemic control (76.9%)

Likewise significantly more females were noted to be affected than males ($p<0.02$) Twenty-one diabetic females (42%) were with dyslipidaemia as compared with only 10 (19.6%) diabetic males. Cholesterol was also positively correlated with HbA1c ($p<0.017$). Although the chronologic age, age of onset, duration of diabetes, dose of insulin and FBS were relatively higher in patients with dyslipidaemia when compared with patients without dyslipidaemia, these were not statistically significant.

The Pearson's Correlation Coefficient Test revealed a significant correlation between HbA1c and cholesterol, as well as with triglyceride and LDL. However, there was no correlation seen with HDL and HbA1c.

Table 1. Clinical and Biochemical Characteristics of Study Population (N=50)

Characteristics	*Mean*	*Standard Deviation*
Chronologic age	14.42	5.86
Agent of onset	10.70	4.73
Duration of diabetes	3.54	3.86
Dose of insulin	0.98	0.43
Blood glucose (FBS)	223.4	107.1
Glycosylated Hemoglobin (HbA1c)	10.08	2.38
Cholesterol	198.7	60.57
Triglyceride	94.12	62.91
High Density Lipoprotein (HDL)	54.16	22.1
Low Density Lipoprotein (LDL)	125.4	51.46

Table 2. Lipid Profile and HbA1c of IDDM Patients with Dyslipidaemia

Variables	*Glycemic Control (HbA1c)*			
	Good (%)	*(Fair %)*	*Poor (%)*	*Total (%)*
Cholesterol (Chol)	–	3.2	3.2	6.4
Triglyceride (Tryg)	3.2	3.2	–	6.4
HDL	6.4	3.2	9.6	19.2
LDL	–	–	3.2	3.2
Chol + LDL	3.2	3.2	19.3	25.7*
Chol + HDL + LDL	–	–	3.2	3.2
Chol + Tryg + LDL	3.2	3.2	9.6	16.0*
Chol + Tryg +HDL	–	–	3.2	3.2
Chol + Tryg + HDL + LDL	–	–	3.2	3.2
Tryg + HDL	–	3.2	–	3.2
Trgy + HDL + LDL	–	–	3.2	3.2
HDL + LDL	6.4	–	–	6.4
	22.4%		76.9%	

DISCUSSION

Failure to achieve good glycemic control is highly associated with dyslipidaemia in IDDM.

As reported in the DCCT (1992), elevated total cholesterol, LDL cholesterol, triglyceride, and decreased HDL cholesterol, appear to occur predominantly in younger female diabetic patients (ages 13-24) with relatively higher HbA1c levels. In our study, 76.9% of the 62% IDDM patients with dyslipidaemia were not in good glycemic control especially among females. Several studies have confirmed these findings, showing the importance of diabetic control on serum lipids and lipoproteins in IDDM.

Glasgow *et al* (1981) reported a positive correlation between control and serum cholesterol, triglyceride and low density lipoprotein. High density lipoprotein was not significantly correlated with control. Sosenko et al (1980) demonstrated that with increasingly poor control of diabetes, there was an associated statistically significant increase in total cholesterol, triglyceride and lipoprotein subfractions except for HDL cholesterol.

Similarly, Semenkovich *et al.* (1989) revealed that HbA1c was positively correlated with the levels of the total plasma cholesterol, triglyceride, low density lipoprotein and negatively correlated with the level of high density lipoprotein

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LDL	–	–	3.2	3.2
Chol + LDL	3.2	3.2	19.3	25.7*
Chol + HDL + LDL	–	–	3.2	3.2
Chol + Tryg + LDL	3.2	3.2	9.6	16.0*
Chol + Tryg +HDL	–	–	3.2	3.2
Chol + Tryg + HDL + LDL	–	–	3.2	3.2
Tryg + HDL	–	3.2	–	3.2
Trgy + HDL + LDL	–	–	3.2	3.2
HDL + LDL	6.4	–	–	6.4
	22.4%		76.9%	

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