The Significance of Lipid Abnormalities in Children with Insulin-Dependant Diabetes Mellitus

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ABSTRACT:

BACKGROUND:

To evaluate serum lipids in children with type 1 diabetes mellitus and its relation to glycemic control, in comparison with sex and age matched non-diabetic children.

METHODS:

Fasting blood glucose, glycosylated haemoglobin (HbA1c) and lipid profile were estimated in 45 children (20 males and 25 females) with type 1 diabetes attending diabetic clinic at Sulaymani children hospital from the period of November 2005 till Jully 2006. Fifty health children (23 males and 27 females) admitted to the same hospital with acute illnesses like respiratory tract infections were randomly selected as controls.

RESULTS:

Mean total cholesterol, triglycerides, LDL-C, VLDL-C, and LDL-C/HDL-C ratio were significantly higher in diabetic children compared to the control. However, there was no significant difference in the levels of HDL-C in both groups .In addition to that, diabetic patients with poor control have a significantly higher levels of blood glucose, total cholesterol, triglycerides, LDL-C and LDL-C/HDL-C ratio as compared to those with good control. A significant correlation between most lipid variables and HbA1c was observed in diabetic patients.

CONCLUSION:

Children with type 1 diabetes should be screened for serum lipids as significant lipid abnormalities are related to glycemic control. Both can be improved with dietary guidelines and insulin therapy.

KEY WORDS: Insulin-dependant diabetes mellitus, Lipids and lipoproteins, Children, Glycemic control.

INTRODUCTION:

Type 1 diabetes is one of the most common chronic disorders in children and adolescents [(1)].Many genetic or metabolic factors seem to play a role in the pathogenesis of diabetes complications, such as retinopathy, neuropathy, nephropathy, and macrovascular disease [(2, 3)]. Good glycemic control reduces the rate of development and progression of diabetes complications in patients with type 1 diabetes, as has been demonstrated by many studies [(4, 5)]. Abnormal lipid metabolism is well documented in children with type1 diabetes[(6)].Both diabetes mellitus and hyperlipidemia are recognized risk factors for atherosclerosis[(7,8)].Several pathology studies have shown that the atherosclerotic process begins in childhood and early adolescence[(8,9,10,11,12)]. Although an increased prevalence of lipid abnormalities in many population with diabetes has been observed, minimal data exist regarding The distribution, correlates, and determinants of lipid levels of children with diabetes[(13)].Therefore, the aim of the study is to evaluate serum lipids in children and adolescent with insulin dependant diabetes mellitus and its relation to glycemic control, in comparison with age-matched non-diabetic control.

PATIENTS AND METHODS:

Patients: The study involved 45 children and adolescents (20males and 25 females) with type1 diabetes attending the diabetic clinic at the Sulaymani children hospital from the period of November 2005 till Jully 2006.Patients had had diabetes for at least 1 year and were well at the time of the sample collection, without ketosis or hypoglycemia. There was no previous selection of the patients based on the control of their diabetes or previous lipid determinations. The mean age was 11.8±3.6 years. The duration of their disease varied from 1-8 years with a mean duration of 3.86 years. All patients received two doses per day of a mixture of intermediate and short action insulin. The mean daily dose of insulin was 0.92 units/kg of body weight.

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None of the patient had a history of other diseases associated with dyslipidemia like hypothyroidism, renal, liver disease, or Down's syndrome. A complete physical examination was carried out for each patient. Informed consent was obtained from one of the parents.

Normal controls:

Fifty healthy children (23 males and 27 females) admitted to the same hospital for acute illnesses like respiratory tract infections were randomly selected as controls. The importance of the procedures was explained to one of the parent and the child where appropriate and informed consent was obtained. Children with chronic illnesses and with family history of diabetes mellitus or cardiovascular diseases were excluded. For each patient and control, height and weight were measured and body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters.

Methods:

Venous blood samples (5ml) were collected after an over night fast in all subjects and before insulin administration in patient with diabetes. Two ml was added to EDTA anticoagulant containing tubes for estimation of glycosylated haemoglobin (HbA1c) and the remainder of the blood samples were allowed to clot at room temperature, then serum was separated and stored at 4^{o}C until analyzed (within two hours) for serum glucose and lipid parameters .Serum concentration of glucose, total cholesterol(TC) , triglycerides (TG)and HDL-cholesterol (after precipitation by phospho - tungstate and $Mgcl_2$) were measure enzymatically in serum using commercial reagents (Teco Diagnostic ,USA) ;all procedures were followed according to instruction of the manufacturer. LDL-cholesterol (LDL-C) value was calculated using the Friedwald equation : LDL-C= TC ─ (HDL-C+TG/5), while VLDL-C was calculated from the formula VLDL-C=TG/5[14] . Glycosylated haemoglubin (HbA1c) levels were determined by using a commercial kit (Stanbio Laboratory;Texas:Cat 0355) based on a colorimetric method [15]; the normal range was 4.2-6.2%.

Diabetic children were classified as good (HbA1c up to 8.5%), fair (HbA1c 8.6-10%), and poor control (HbA1c >10%)[16].

Statistical analysis:

Results were expressed as mean ± SD.Differences between diabetic and control groups were assessed using the student's t - test .Differences between variables in the three groups that were classified according to their glycemic control were assessed using one way analysis variance (ANOVA).Correlation between variables were assessed by calculating Pearson's correlation coefficients. Differences in the number of subjects with hyperlipidemia among diabetic and control groups were analysed using Fisher´s exact test. P values<0.05 were considered as significant.

RESULTS:

A total of 95 children and adolescent were included in the study, 45 of them were with type1 diabetes mellitus. Table1 summarizes the characteristics of the study groups. This table shows that there was no significant statistical difference in the mean age and BMI between diabetic patients and controls(P>.05).The mean fasting blood glucose and glycosylated haemoglobin (HbA1c) were significantly higher in diabetic patients as compared to the control, which is an expected finding. Mean total cholesterol, triglyceride, LDL-C, VLDL-C and LDL-C/HDL-C ratio were significantly higher in diabetic children compared to control group. However, there were no significant differences in the level of HDL-C in both groups. Table 2 presents the mean blood glucose levels and lipid variables in relation to glycemic control. Diabetic patients with poor control have a significantly higher levels of blood glucose, TC,TG,LDL-C and LDL-C/HDL-C ratio as compared to those having good control. No significant difference was found in the level of HDL-C and VLDL-C among the three groups.

A significant correlation between most lipid variables and HbA1c levels was observed among the diabetic patients (table3). It seems that these associations occurs at continuous level in the diabetic group rather than at a specific level of HbA1c as intermediate values were seen in patients with fair glycemic control. No such correlations were found in the control group. There was no relationship between HDL-C or VLDL-C levels and HbA1c in any of investigated groups. The pattern of hyperlipidemia in children with diabetes and control is shown in table 4 .Out of 45 diabetic patients, 15 patients (33%) had hypercholesterolemia (TC level>200mg/dl), while 4 patients (8.8%) had aborderline cholesterol level (170-200mg/dl). In comparison with the control group, 3 (6%) had a borderline cholesterol level and none had a total cholesterol>200 mg/dl (P< 0, 000003).Hypertriglycerdemia (TG>150mg/dl) was present in 16 patients (35.5%) compared to 5 subject (10%) in the control group (P 0.003). Hypertriglyerdemia alone was present in 6 patients, while the rest had also hypercholesterolemia.

Elevated LDL-C>130 mg/dl was present in 15(33%)in diabetic patient only ,where as border level of LDL-C(110-130 mg/dl)was found in 18 (40%) diabetic patients as compared to 3(6%) in the controls(P<0.0001). All of the 15 patients with elevated LDL-C had hypercholesterolemia and this was associated with hypertriglycerdemia in 7 out the 15 diabetic patients. This indicated that a combination of more than one lipid abnormalities was observed in our diabetic patients.

In addition to that the LDL-C/HDL-C ratio (atherogenic index>3.5) was significantly higher in patients with insulin dependant diabetes mellitus as compared to the control group (P<0.01) .

Table 1: Characteristic of the studied groups

	Diabetes	Controls	P.value
Number	45	50	
Age	11.8± 3.6	11.5±3.7	NS
BMI	17.6±3.8	17.7± 3.3	NS
Glucose mg/dl	232±92	80 ±12	<0.001
HbA1c %	9.8±4.2	4 ±0.8	<0.001
Cholesterol mg/dl	178±56	128± 30	<0.001
Triglyceride mg/dl	146±95	102 ±30	<0.001
HDL-C mg/dl	47±12	44 ±11	NS
LDL-C mg/dl	105±48	63 ±26	<0.001
VLDL-C mg/dl	30±16	23 ±6	<0.05
LDL-C/HDL-C	2.4±1.2	1.58 ±0.8	<0.001

NS= Not significant

Table2: Blood lipids and glucose in relation to glycemic control

	Good control	Fair control	Poor control	P. Value
Number	19	13	13	
Age	12± 3.2	10.7± 3.3	12.6 ±4.6	NS
BMI	18.4± 4.5	15.8 ±1.6	17.8± 4.4	NS
Glucose mg/kg	200 ±19	195± 49	318 ±72	<0.01
Cholesterol mg/dl	148 ±33	180 ±51	230± 43	<0.001
Triglyceride mg/dl	116 ±36	150± 110	197 ±72	<0.05
HDL-C mg/dl	43 ±17	44± 11	46± 30	NS
LDL-C mg/dl	78 ±24	102 ±46	138 ±38	<0.001
VLDL-C mg/dl	26± 16	33± 21	32 ±16	NS
LDL-C/HDL-C	1.6 ±0.6	2.5 ±1.4	3 ±1.4	<0.05

Table 3 : Relationship between lipid variables and HbA1c concentration.

Variables	Diabetic patients	controls
Total cholesterol	0.72©	o.12
Triglyceride	0.64©	0.20
HDL-C	0.01	0.09
LDL-C	0.70©	0.08
VLDL-C	0.15	0.21
LDL-C/HDL-C	0.52©	0.05

Values are Pearson's Correlation Coefficients
© P<0.01

Table 4 : Hyperlipidemia in children with diabetes and controls.

Parameter	Diabetes (n=45) No.	(%)	Control (n=50) No.	(%)	P. value
Total cholesterol mg/dl					
170-200	4	(8.8)	3	(6)	NS
>200	15	(33)	0	0	0.000003
Triglyceride>150 mg/dl	16	(35.5)	5	(10)	0.003
HDL-C >35 mg/dl	9	(20)	12	(24)	NS
LDL-C mg/dl					
110-130	18	(40)	3	(6)	0.0001
>130	15	(33)	0	0	0.000003
LDL-C/HDL-C>3.5 (Atherogenic index)	10	(22)	2	(4)	0.01

DISCUSSION:

Extremely precise measurements of lipids and lipoproteins obtained on national samples of United states children by the lipid research clinics in 1970s established the most widely quoted ´normal´ lipid levels for children[11,17].These data were used to establish the currently used cut points for classification and intervention . Most previous studies of lipids and lipoproteins in insulin dependant diabetics have been performed in children and adolescents and the abnormalities found are somewhat contradictory. Tamborlane et al[18],in a group of non-obese ketosis-prone diabetics of both sexes found a significant decrease of total cholesterol and triglycerides after treatment with insulin. Mann et al[19] found similar results in children. They observed either hypercholesterolemia or hypertriglyceridemia or both in poorly controlled children of both sexes. Neither of the above authors measured lipoproteins. In contrast, Chase and Glasgow[20] reported in diabetic children, considered to be in good control, a significant increase of total cholesterol, triglycerides and LDL and decrease levels of HDL. In this study, the mean total cholesterol level was significantly higher in diabetic children as compared to the control group and hypercholesterolemia (TC>200mg/dl) was present in a significantly higher number of diabetic patients as compared to the control group. These results are in agreement with similar studies [6,16,21,22,23,24],although others did not observed such correlation[25,26].Possible explanation for variation between reports include; the diet of the general population , the duration and severity of diabetes and different laboratory methods. Furthermore, there was a significant difference in the mean total cholesterol level among diabetic patients in relation to glycemic control, where poorly controlled patients have significantly higher total cholesterol level in comparison to those with good control. Comparable results were obtained in other studies[16,21,27]. The present study showed that diabetic patients have a significantly higher serum triglyceride level compared to the control group and 35.5% of diabetic patients have hypertriglyceridemia (TG>150md/dl) in comparison to only 10% in the control group (P<0.003). In addition to that there was a significant correlation between triglyceride level and glycemic control. These results are consistent with the findings of other studies ([16, 24]. It has been shown that HDL-C level is inversely correlated with the magnitude of risk for coronary heart disease caused by atherosclerosis. Although most studies of lipid in children with type1 diabetes have shown increase cholesterol and triglycerides, particularly with poor metabolic control, results for HDL-C have been conflicting. Some investigators have found normal or lower HDL-C in type1 diabetes [16,28,29] , whereas others have found higher HDL-C in children[21,30] .In this study, no significant difference in HDL-C levels between diabetics and controls were found. Similar to others[16,20] we found no correlation between HDL-C level and the degree of glycemic control, whereas a negative correlation was observed by others[31].Difference in diet, physical activity and treatment might perhaps explain some of the wide variation of HDL-C reported in Juvenile diabetes[32] . It has been well established that high LDL-C level is closely related to the progression of atherosclerosis. LDL-C levels less than 110 mg/dl are considered acceptable, and levels greater than 130 mg/dl are considered elevated. LDL-C levels of 110-130 mg/dl are considered borderline and necessitate repeat measurement in 1 year [11].

Our study showed that diabetic children, particularly with poor glycemic control were associated with significant correlation with LDL-C levels.

A borderline LDL-C level was found in 40% of diabetic subjects and 6% of the control group, whereas an elevated LDL-C level was found in diabetic children only. As LDL-C level was increase and HDL-C unchanged, the percentage of atherogenic index (LDL-C/HDL-C>3.5) was higher in diabetic patients than in the control group.

This study demonstrated as others have[6,16,22,28,33], that the LDL-C and LDL-C/HDL-C ratio, both generally accepted risk indicators of atherosclerosis, were found to correlate significantly with metabolic control in diabetic children.

CONCLUSION:

Our findings support the hypothesis that poor control of blood glucose is associated with atherogenic lipid profiles. The prevalence of hyperlipidemia is impressively high in our diabetic population and indicates that all IDDM patients should have a serum lipid and lipoprotein analysis done annually; blood glucose control and dietary guidelines should be improved in these cases.

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