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EDITORIAL

Association Between Lipid Profile and Glyceamic Control in Sudanese Children with Type 1 Diabetes Mellitus at Gezira State, Sudan

Mohammed A Hamza[1], Khalid E. Khalid[1], Osman K Saeed [2]and Huda M Haroun [3]

1. Department of Biochemistry and nutrition, Faculty of Medicine, University of Gezira
2. Department of Medicine, Faculty of Medicine, University of Gezira.
3. Department of Pediatric, Faculty of Medicine, University of Gezira.

Corresponding author: Mohammed A Hamza. Department of Biochemistry and nutrition, Faculty of Medicine, University of Gezira. P.O.box:20 Wad - Medani,Sudan.Tel: +249511854279 - Fax: +249511843415 - E.mail: faggad94@yahoo.com

Abstract:

Introduction: Diabetes mellitus describes a metabolic disorder of multiple aetiology characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both.

Objectives This study aimed to assess the metabolic control of type 1 diabetes mellitus (T1DM) in Sudanese children.

Methods: One hundred and seventy four children with type 1 diabetes mellitus were enrolled in this study; 56 healthy non-diabetic children served as a control group. Glycosylated hemoglobin (HbA1c), total cholesterol (TC), triacylglycerol (TG), low density lipoprotein-cholesterol (LDL-C), high density lipoprotein-cholesterol (HDL-C) were measured, very low density lipoprotein-cholesterol (VLDL), and LDL-C/HDL-C ratio were calculated.

Results: HbA1c,TC, LDL-C LDL-C/HDL-C ratio and TG were significantly higher among diabetic group compared to non-diabetic group ($P<0.001$ and $P<0.05$ for TG).In the diabetic group, there was a positive significant correlation of: HbA1c with TC, TG, HDL- C, LDL-C, VLDL and LDL/HDL ratio; TC with TG, HDL- C, LDL-C, VLDL and LDL/HDL; TG with LDL- C, VLDL and LDL/HDL ratio; HDL-C with LDL-C;LDL-C with VLDL and LDL/ HDL;VLDL-C with LDL/HDL ratio. A significant negative correlation was observed between HDL- C and LDL/HDL ratio. Diabetic group with poor metabolic control (HbA1c level >8).had significantly higher levels of TC and LDL-C ($P<0.001$),TG and VLDL ($P<0.01$), HDL-C and LDL-C/ HDL-C ratio ($P<0.05$) compared with diabetic group with good metabolic control (HbA1c <8%).

Conclusion: 85.63% of diabetic patients were found to have poor metabolic control (HbA1c level >8).

الملخص:

يوصف مرض السكري بأنه من المسببات المرضية المتعددة التي تتميز بفرط سكر الدم المزمن واضطراب في التمثيل الغذائي (اضطرابات من الكربوهيدرات والدهون واستقلاب البروتين) الناتج عن نقص في إفراز الأنسولين، عمل

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الانسولين أو كليهما.هدفت هذه الدراسة لاستخدام التقييم الكيموحيوي لمعرفة مدي التحكم لضبط السكر عند مرضي السكري النوع الاول. إشتملت هذه الدراسه علي 174طفل مصابين مرض السكري و56 أصحاء من نفس العمر.تضمنت هذه الدراسة القياسات الكيموحيويه الأتيه: خضاب الدم المسكر، الكوليستيرول ، ثلاثي أسيل الجليسرول و الكوليستيرول المرتبط بالبروتينات الشحميه منخفضة وعاليه الكثافة والبروتينات الشحميه المنخفضة جدا ونسبة البروتينات الشحميه منخفضة الكثافة الي البروتينات الشحميه عالية الكثافة. وجد أن تركيز كل من خضاب الدم المسكر، الكوليستيرول ، الكوليستيرول المرتبط بالبروتينات الشحميه منخفضة الكثافة ونسبة البروتينات الشحميه منخفضة الكثافة الي البروتينات الشحميه عالية الكثافة وثلاثي أسيل الجليسرول يرتفع إرتفاعا ذا معني عند مجموعة مرضي السكري.مستوي خضاب الدم المسكر يرتبط إرتباطا موجبا ذا معني مع كل من الكوليستيرول ، ثلاثي أسيل الجليسرول والبروتينات الشحميه عالية ومنخفضة الكثافة والبروتينات الشحميه المنخفضة جدا ونسبة البروتينات الشحميه منخفضة الكثافة الي البروتينات الشحميه عالية الكثافة، الكوليستيرول مع كل من ثلاثي أسيل الجليسرول والبروتينات الشحميه عالية و منخفضة الكثافة والبروتينات الشحميه المنخفضة جدا ونسبة البروتينات الشحميه منخفضة الكثافة الي البروتينات الشحميه عالية الكثافة ، يرتبط ثلاثي أسيل الجليسرول مع كل من البروتينات الشحميه منخفضة الكثافة والبروتينات الشحميه المنخفضة جدا ونسبة البروتينات الشحميه منخفضة الكثافة الي البروتينات الشحميه عالية الكثافة . كما أن مستوي البروتينات الشحميه عالية الكثافة يرتبط إرتباطا ذا معني مع نسبة البروتينات الشحميه منخفضة الكثافة الي البروتينات الشحميه عالية الكثافة.طبقا لتقسيم مجموعة الدارسين لمرض السكري العالميه الأمريكيه أظهرت هذه الدراسه أن نسبة (85.63) من المرضي يبلغ معدل خضاب الدم المسكر عندهم أكثر من 8% (ضبط غير مقبول) بينما (14.37%) يبلغ معدل خضاب الدم المسكر عندهم أقل من 8% (ضبط مقبول). وجدت هذه الدراسة ان مرضي السكري والذين لديهم ضبط غير مقبول لخضاب الدم المسكر ترتفع عندهم مستويات الكوليستيرول ، ثلاثي أسيل الجليسرول و الكوليستيرول المرتبط بالبروتينات الشحميه منخفضة وعاليه الكثافة والبروتينات الشحميه المنخفضة جدا ونسبة البروتينات الشحميه منخفضة الكثافة الي البروتينات الشحميه عالية الكثافة ارتفاعا ذا معني مقارنة مرضي السكري والذين لديهم ضبط مقبول لخضاب الدم المسكر.

Introduction:

Diabetes mellitus is a group of metabolic diseases characterized by chronic hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The abnormalities in carbohydrate, fat, and protein metabolism that are found in diabetes are due to deficient action of insulin on target tissues. [1]. Diabetes is major health problem that affects increasing numbers of persons in the developed world with a worldwide prevalence of 346 million people in 2004 [2].

Type 1 Diabetes Mellitus, accounting for only 5–10 % of diabetes cases worldwide. [3].

However, in Sudan TIDM is not rare and it is a disease with high morbidity rate and complications. Prevalence of TIDM was estimated at 0.1 % among school children 7-14 years of age [4]. Glycosylated hemoglobin (HbA1c) concentration reflects the integrated blood glucose control over the lifespan of erythrocytes (120 days). HbA1c is most sensitive to changes in glycemic control occurring in the month before measurement [5]

Concentration of serum lipids is another important index of overall metabolic control in diabetic patients and should be monitored regularly, as diabetes mellitus is known as an independent risk factor in atherosclerosis [6]. Many longitudinal studies have shown a large excess of cardiovascular mortality in TIDM patients as compared to nondiabetic controls. Although diabetes appears to be an independent cardiovascular risk factor, increase in total

and low density lipoprotein – cholesterol (LDL-C) together with a decrease of high density lipoprotein – cholesterol (HDL-C) are more pronounced in diabetes with cardiovascular disease [7].

Dyslipidaemia is a major risk factor for cardiovascular disease in patients with type 2 diabetes. In contrast, many patients with well-controlled type 1 diabetes may have lipid blood levels that do not significantly differ from those without diabetes. It has even been suggested that well-controlled type 1 diabetes may sometimes be associated with more favourable total cholesterol, low density lipoprotein-cholesterol (LDL-c) and high density lipoprotein-cholesterol (HDL-c) levels than found in many non-diabetic individuals [8].

Previous studies in type 1 diabetes consistently reported a correlation between HbA1c and more atherogenic lipid profile [9]. The Diabetes Control and Complications Trial reported that total cholesterol, LDL cholesterol and triglycerides increased with elevated HbA1c, but HDL cholesterol was not correlated [10].

Study Objectives: to assess lipid profile in Sudanese Children with T1DM and its relation to glycemic control by measuring glycosylated hemoglobin (HbA1c),to calculate atherogenic indices (LDL-C/ HDL-C) ans to correlate between glycemic control and the concentration of lipid profile.

Methods:

This is a cross-sectional study carried out in Wad Medani Paediatric Hospital. One hundred and seventy four (174) Sudanese children with type 1 diabetes mellitus were enrolled in this study (diabetic group) with age up to 16 years, and 56 healthy children with no history of DM, or other autoimmune diseases serving as age-matched (control group).

Children who had TIDM according to the WHO criteria (WHO, 1980) were enrolled based on the following:

- Age up to 16 years.
- One year or more duration of the disease.
- Taking insulin therapy since the diagnosis of the disease.

Exclusion Criteria

- Age >16 years.
- Patients with renal disease, liver disease, Downs's syndrome, hypothyroidism and Rickets.
- Patients receiving medical regimen of corticosteroids.

A questionnaire was designed to obtain data including: demographic data and laboratory investigations.

Fasting blood (5ml) was collected from diabetic patients and the control and divided into two sterile containers: 2 ml in a tube containing the anti coagulant (EDTA), used for estimation of glycosylated haemoglobin and the rest of the blood sample (= 3ml) was added in a plain container followed by centrifugation and serum was used for estimation of total cholesterol (TC), triacylglycerides (TG), high density lipoprotein–cholesterol (HDL-C).

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Low density lipoprotein–cholesterol (LDL-C) value was calculated using the Friedewald equation: LDL-C = TC - (HDL-C + TG/ 5), while VLDL- C was calculated using the formula: VLDL-C = TG / 5 [11]. HbA1c,TC,TG and HDL-C were done by enzymatic colorimetric methods.

The data was analyzed using the SPSS computer program (version 21). Results were expressed as mean± SD. Differences between diabetic and control groups were assessed using the t test. The differences were considered significant if the *P*-value was less than 0.05.

Results:

Biochemical Parameters: presented in table (1)

Glycosylated haemoglobin (HbA1c), Total cholesterol (TC) , LDL-C and LDL-C/ HDL-C)

The diabetic group showed significantly higher levels in the mean value compared with control group (P<0.001).

Triglycerides (TG)

The diabetic group had significantly higher levels in the mean value of TG compared with control group (P<0.05).

HDL-C and VLDL

No significant differences were observed in the mean values of any one of these parameters between the two study groups.

Table (1): Biochemical parameters in diabetic and non diabetic groups.

Variables	Diabetics (N=174)	Non Diabetics (N=56)	*p*- value
HbA1c %	10.72±2.18	6.05±1.34	p<0.001
TC (mg/dl)	124.43±27.76	98.71±22.10	p<0.001
TG (mg/dl)	99.05±47.71	85.18 ±39.47	p<0.05
LDL-C (mg/dl)	62. 81±18.97	36.73±12.00	p<0.001
HDL-C (mg/dl)	41.68±9.55	44.93±14.81	NS
VLDL	19.87±9.56	17.39±7.79	NS
LDL-C/ HDL-C	1.55±0.53	0.86±0.27	p<0.001

NS**:** No significant

Correlation between the biochemical parameters in the diabetic and control group

Correlation Coefficient in the diabetic and control group is presented in Table 2. A significant positive correlation was observed between GHb and TC, TG, HDL- C, LDL- C,

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VLDL and LDL/HDL (r = 0.587, P<0.001; r = 0.361, P<0.001 ; r = 0.215, P<0.01; r = 0.365, P<0.001; r = 0.374, P<0.001 ; r = 0.374, P<0.001) respectively, while in the control group a significant positive correlation was observed between HbA1c, TC and LDL-C (r = 0.329, P<0.05; r = 0.351, P<0.01) respectively.

A significant positive correlation was observed in the diabetic group between TC and TG, HDL- C , LDL- C, VLDL and LDL/HDL (r = 0.564, P<0.001; r = 0.544, P<0.001; r = 0.877, P<0.001; r = 0.560, P<0.001; r = 0.419, P<0.001) respectively , while in the control group a significant positive correlation was observed between TC, HDL-C and LDL-C (r = 0.772, P<0.001; r = 0.749, P<0.001) respectively.

A significant positive correlation in the diabetic group was observed between TG and LDL-C, VLDL and LDL/HDL (r = 0.272, P<0.001; r = 0.998, P<0.001; r = 0.160, P<0.05) respectively, while in the control group a significant positive correlation was observed between TG and VLDL (r = 0.940, P<0.001).

A significant positive correlation in the diabetic group was observed between HDL- C and LDL-C (r = 0.264, P<0.001) and a significant negative correlation was observed between HDL- C and LDL/HDL (r = - 0.435, P<0.001), while in the control group a significant positive correlation was observed between HDL-C and LDL-C (r = 0.321, P<0.05), and a significant negative correlation was observed between HDL-C and LDL/HDL (r = - 0.571, P<0.001).

A significant positive correlation in the diabetic group was observed between LDL-C,VLDL and LDL/ HDL (r = 0.270, P<0.001; r = 0.279, P<0.001) respectively, while in the control group a significant positive correlation was observed between LDL-C and LDL/HDL (r = 0.521, P<0.001).

A significant positive correlation in the diabetic group was observed between VLDL-C and LDL/HDL (r = 0.161, P<0.05).

Table (2):. Correlation between the biochemical parameters in the diabetic and control group

Variable	HbAc	TC	TG	HDL-C	LDL-C	VLDL
HbAc						
TC (diabetic) **TC (control)**	.587*** .329*					
TG (diabetic) **TC (control)**	.361*** .237	.564*** .192				
HDL-C (diabetic) **HDL-C (control)**	.215** .092	.544*** 772***	.082 -.224			
LDL-C (diabetic) **LDL-C (control)**	.573*** .351**	.877*** .749***	.272*** -.011	.264*** .321*		

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VLDL (diabetic)	.365***	.560***	.998***	.078	.270***	
VLDL (control)	.259	.173	.940***	-.236	.006	
LDL/ HDL (diabetic)	.374***	.419***	.160*	-.435***	.279***	.161*
LDL/ HDL (control)	.200	-0.063	.140	-.571***	.521***	.161

* P< 0.05 ** P< 0.01 *** P< 0.001

Assessment of Metabolic Control of Diabetic Patients

Degree of metabolic Control in Diabetic Patients Using HbA1c Concentration

Metabolic control was assessed using the HbA1c levels, according to the national diabetes study group classification [12] and graded as:-

I) Excellent and acceptable control (HbA1c <8%)

II) Poor control (HbA1c >8%)

The majority 149 (85.63%) of diabetic group were classified in poor metabolic control.

Comparison of means of the lipid profile parameters grouped according to metabolic control

Table 3 shows the comparison of means of the lipid profile parameters in diabetic group according to metabolic control

The diabetic group with HbA1c >8% had significantly higher levels of TC and LDL-C (P<0.001), TG and VLDL (P<0.01), HDL-C and LDL-C/ HDL-C ratio (P<0.05) compared with diabetic group with HbA1c <8%.

Table (3): comparison of means of the lipid profile parameters in diabetic group according to metabolic control.

Variables	Diabetic patients with HbA1c <8%	Diabetic patients with HbA1c >8%	p value
TC (mg/dl)	101.20 ±16.47	128.33± 27.40	< 0.001
TG (mg/dl)	76.52 ±30.12	102.83 ±49.13	0.010
LDL-C (mg/dl)	48. 08 ±10.82	65.28 ±18.95	< 0.001
HDL-C (mg/dl)	37.54 ±7.76	42.37 ± 9.67	0.019
VLDL (mg/dl)	15.32 ±5.98	20.64 ±9.84	0.010
LDL-C/ HDL-C	1.33±0.38	1.59 ±0.54	0.021

Discussion:

In this study the T1DM group had significantly higher levels of HbA1c compared with non diabetic subjects. These results are in agreement with [13] the mean glycosylated

hemoglobin values were significantly higher in diabetic patients as compared to the control group.

There is evidence that atherosclerosis begins in early life and that hypercholesterolemia plays an important role in its evolution [14]. In children group, normal total cholesterol level should be less than 170 mg/dl. Total serum cholesterol of 170-199 mg/dl is border line, while that above 200 mg/dl is considered to be elevated; i.e. hypercholesterolemic [15].

The current study showed that the mean total cholesterol level was significantly higher in diabetic children as compared to the control group. This finding is in agreement with previous studies [16]. This finding is in disagreement with previous studies [17], a possible explanation for this may be due to differences in; duration of diabetes, severity of diabetes, degree of glycemic control, diet, and different laboratory methods. Furthermore, there was a significant difference in mean total cholesterol level among diabetic patients group according to glycemic control, where the group with poor glycemic control has significantly higher TC levels compared to those with good glycemic control.

The mean serum triglyceride level was elevated in the diabetic patients compared to the control group and the diabetic patients had hypertriglyceridemia in comparison to the control group. In addition to that, there was a significant correlation between TG level and HbA1c. These results are similar to earlier reports [18]. It has been shown that individuals with T1DM, who are untreated or inadequately treated, have elevations in both fasting and postprandial TG levels in association with reduced activity of lipoprotein lipase [19].

High density lipoproteins (HDL-C) are inversely associated with atherosclerosis and atherosclerotic diseases. The current data showed no significant difference in HDL-C level between diabetics and control in line with other studies [20], while in contrast with studies that reported markedly elevated HDL-C in T1DM [21] and showed no correlation between HDL-C level and the degree of glycemic control.

LDL-C and atherogenic index (LDL-C/HDL-C) in this study are significantly higher in the diabetic patients compared with the control group. In the present study, LDL-C and the LDL-C/HDL-C ratio, both generally accepted risk indicators of atherosclerosis, were found associated significantly with glycemic control in diabetic children. This is in agreement with previous studies [20]. [22] which suggested that poor glycemic control further deteriorates lipid and lipoprotein abnormalities. TC and LDL-C levels are often elevated in poor glycemic control, and the compositional changes in LDL particle may further increase the risk of coronary heart diseases.

A significant positive correlation between TG, LDL-C, VLDL cholesterol and LDL/ HDL ratio in diabetic children and glycemic control were observed. This finding is in agreement with previous report that showed a positive correlation with total cholesterol, [17].

Conclusions:

The Sudanese diabetic children were found to have significant changes in lipid profiles when compared to Sudanese normal children control group. There was a significantly

increased LDL-C accompanied by a decreased HDL-C level in diabetics. Rising LDL-C acts as a risk factor of developing cardiovascular disease.

Most of the patients are considered to have unacceptable glycaemic control state (85.63%).

We recommend that testing of Glycosylated Haemoglobin and lipid profiles as part of routine investigations. This may help in developing early preventive or therapeutic measures for cardiovascular diseases and diabetes complications.

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