

High Risk Factor Values of Cardiovascular Disease and Uric Acid Levels in Sera of Patients with Type 1 Diabetes Mellitus

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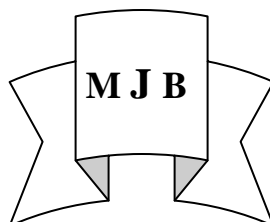
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Abstract

Diabetes mellitus is a chronic illness required ongoing medical care. As a result, laboratory testing has become an essential part of the evaluation and monitoring process in diabetes management. Further tests are required to establish the correlation between hyperglycemia and other disease parameter. Therefore, the correlation between cardiovascular disease risk factor values and uric acid levels in sera of adult patients with type 1 diabetes mellitus (without renal diseases) and healthy controls have been studied.

Total cholesterol, HDL-cholesterol and uric acid in sera of 52 patients (36 males and 16 females) with poor hyperglycemic control type 1 diabetes mellitus and 30 healthy controls (19 males and 11 females) were determined. Results of present study show significantly higher risk factor values ($P < 0.001$), which means increasing in the probability of atherosclerosis incidence. Also hyperglycemia found to be associated with hyperuricemia in type 1 diabetic patients.

الخلاصة

داء السكري مرض مزمن يحتاج إلى عناية طبية متقدمة، نتيجة لذلك، أصبحت الاختبارات المخبرية تشكل جزءاً أساسياً من متابعته. ولتثبيت العلاقة بين ارتفاع نسبة سكر الدم والمتغيرات المستخدمة في تشخيص الأمراض الأخرى يحتاج لأجراء اختبارات إضافية. لذلك تم تقدير العلاقة المترابطة بين عامل الخطورة في الأمراض الوعائية القلبية ومستويات حامض اليوريك في أمصال مرضى بالغين مصابين بداء السكري (النوع الأول) والذين لا يعانون من أمراض كلوية إضافة إلى مجموعة سيطرة.

تم تقدير الكولسترول الكلي و كولسترول البروتين الدهني عالي الكثافة و حامض اليوريك في أمصال مرضى مصابين بداء السكري (النوع الأول) ٥٢ (٣٦ رجل و ١٦ امرأة) إضافة إلى ٣٠ شخصا سليما كمجموعة للسيطرة. أظهرت نتائج الدراسة الحالية ارتفاعا معنويا لعامل الخطورة في الأمراض الوعائية القلبية والتي تعني ازدياد احتمالية حدوث مرض تصلب الشرايين. وجد كذلك بان ارتفاع نسبة سكر الدم يقترن بارتفاع نسبة حامض اليوريك عند المرضى المصابين بداء السكري (النوع الأول).

Introduction

Diabetes mellitus is disease caused by the body's inability to produce or properly use insulin. There are two types of diabetes mellitus; Type 1 diabetes is a disease in which the body does not produce any insulin. This form occurs frequently in children and young adults and accounts for 5%-10% of all diabetes cases. Persons with type1 diabetes must take daily insulin injections to stay alive. Onset is generally abrupt. Type 2 diabetes is a disorder resulting from the body's inability to make enough, or properly use insulin. This is the most common form of diabetes, accounting for 90%-95% of all cases.[1] Onset is often gradual, and symptoms can be difficult to distinguish from other illnesses. People may have had diabetes for 10 years and may have serious complications before actually being diagnosed. [2]

Type 1 Diabetes Mellitus or (insulin dependent diabetes mellitus) is a metabolic disease where the insulin producing β -cell in the pancreatic islets of Lanngerhans are progressively destroyed.[3] Insulin is a hormone, produced by the pancreas, required by the body to convert sugar, starches, and other food into energy.[1] When the insulin production is no longer sufficient to keep the appropriate blood glucose concentration, hyperglycaemia with subsequent glucosuria occurs. The trigger and mechanism of β -cell death are matters of intense debate and research, but it appears to be a combination of genetic predisposition and environmental factors initiating an autoimmune attack. Type 1 diabetic patients require exogenous insulin administration in order to restore a normal metabolic state.[3] For correct dosing of insulin, the patient usually

measures blood glucose several time per day. For long-term evaluation of treatment HbA_{1c}, a glycated form of haemoglobin A, is used to estimate the mean blood glucose level during the two to six weeks preceding sampling.[4]

A major concern in the clinical management of diabetes is the occurrence of severe vascular complications [5] Hyperlipidemia is one of the complications of diabetes mellitus, high triglyceride and cholesterol levels are often associated with type 2 diabetes mellitus[1]. Increased levels of very low density lipoproteins (VLDL) have been reported for type 2 diabetics[2]. High-density lipoproteins (HDL) have been reported to be significantly lower in diabetics than nondiabetics[6,7]. These results are consistent with higher incidence of coronary heart disease in diabetics[8], a poor survival rate of diabetics with myocardial infraction, and the inverse relationship between HDL and the risk of coronary heart disease. In diabetes mellitus type 1 patients with HbA_{1c} >9.5%, W.M. van Waarde et al. found that fasting plasma cholesterol is significantly high, while plasma triglyceride level does not affected. [9]

Several population-based studies [10-12] have shown that subjects with diabetes mellitus have a twofold to fourfold greater risk of all manifestations of atherosclerotic vascular disease compared with nondiabetic subjects. Serum uric acid (UA) has been thought to be in humans a metabolically inert end product of purine metabolism without physiological significance (except gouty diathesis). However, serum uric acid has been associated with insulin resistance [13] as well as, serves as a potent water-soluble antioxidant due to free radical scavenging [14]. Over recent years there has been renewed debate about the nature of association between raised serum uric acid concentration and cardiovascular disease [15].

Therefore the aim of this study is to discuss such association in adult patients with type 1 diabetes mellitus.

Material and Methods

Subjects with type 1 diabetes mellitus [n=52, 36 males with mean age (44.6) and 16 females with mean age (60.9)] admitted to Al Hilla Teaching Hospital, as well as healthy controls [n=30, 19 males with mean age (27.35)

and 11 females with mean age (27.25)] were included in the present study. Venous blood samples were collected from them. Blood samples were centrifuged at (3000 rpm), then the serum obtained was kept at 20° C until the time of analysis, for determination of lipids and uric acid parameters; while blood glucose was determined after one hour of blood drawing. Determination of blood glucose and serum uric acid done

by special kits imported from Randox and Biomaghreb, while total cholesterol and HDL-cholesterol were determined manually using Liebermann-Burchard method. [16]

Results

Blood glucose , Uric acid , total cholesterol ,HDL-C and risk factor of cardiovascular disease are listed in Table 1 in details.

	Male							Female						
	Control			Diabetes Mellitus				Control			Diabetes Mellitus			
	Mean	SD	No	Mean	SD	No	Sig.	Mean	SD	No	Mean	SD	No	Sig.
Blood Glucose (mg/dL)	92.6	7.48	20	272.4	64.81	36	0.00	90	10.7	11	258.03	48.26	16	0.00
Uric acid (mg/dl)	5.26	1.12	20	7.45	1.68	36	0.01	4.87	0.88	11	7.129	1.521	16	0.01
Total cholesterol (mg/dl)	203	24.01	20	205.3	27	36	0.001	186.7	14.2	11	206.1	22.7	16	0.00
HDL-cholesterol (mg/dl)	46	6	20	33.33	4.31	36	0.001	48	7	11	32.7	6.54	16	0.001
Risk index	3.95		20	6.03		36	0.001	3.98		11	6.31		16	0.00

In the present study, blood glucose found to be significantly increase in patients with type 1 diabetes

mellites when compared with healthy controls, as shown in Figure 1.

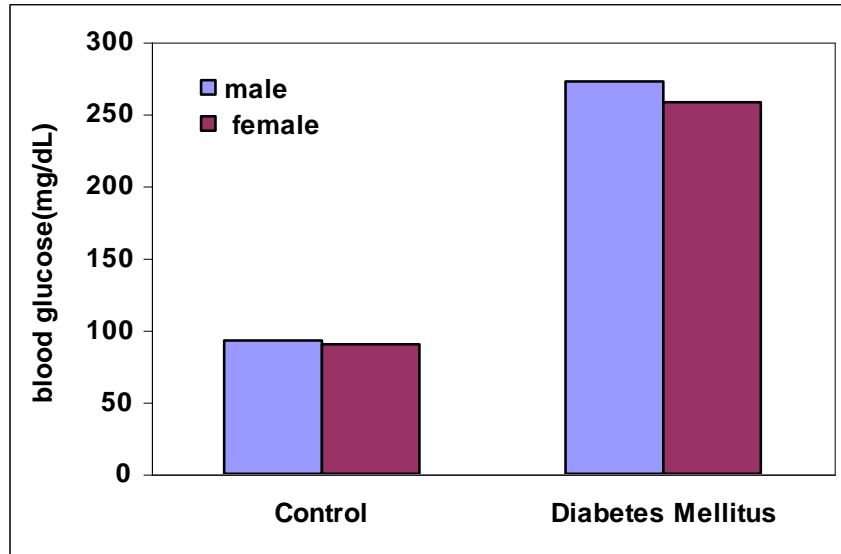


Figure 1 Blood glucose (mg/dL) of patients with diabetes mellitus and healthy controls.

Uric acid of patients with with type 1 diabetes mellites found to be significantly increase when compared with healthy controls, as shown in Figure2.

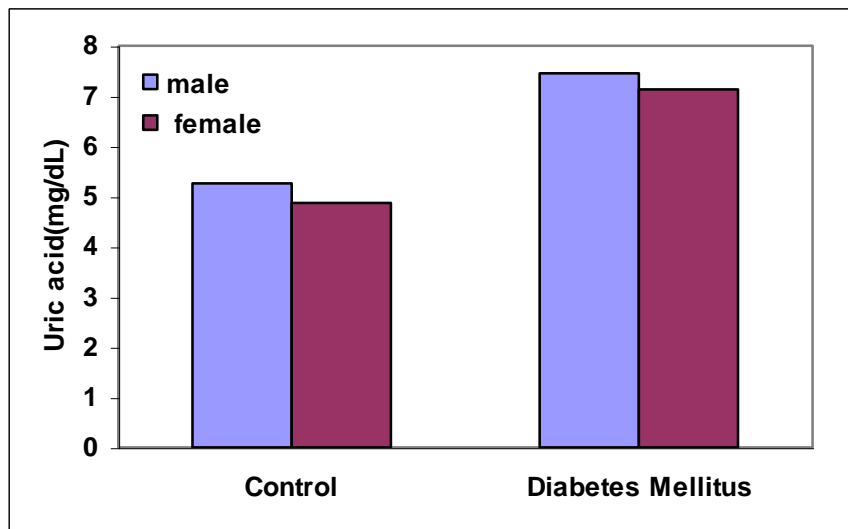


Figure 2 Uric acid (mg/dL) of patients with diabetes mellitus and healthy controls.

Also, total cholesterol was compared with healthy controls, as significantly increase in patients with shown in Figure 3. with type 1 diabetes mellites when

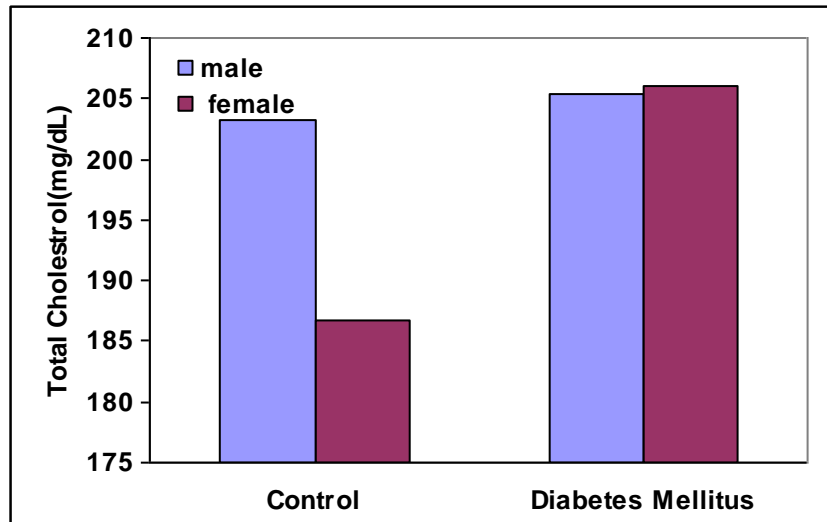


Figure 3 Total cholestrol (mg/dL)of patients with diabetes mellitus and healthy controls.

Whereas, HDL-C found to be compared with healthy controls, as shown in significantly decrease in patients with Figure 4. type 1 diabetes mellites when

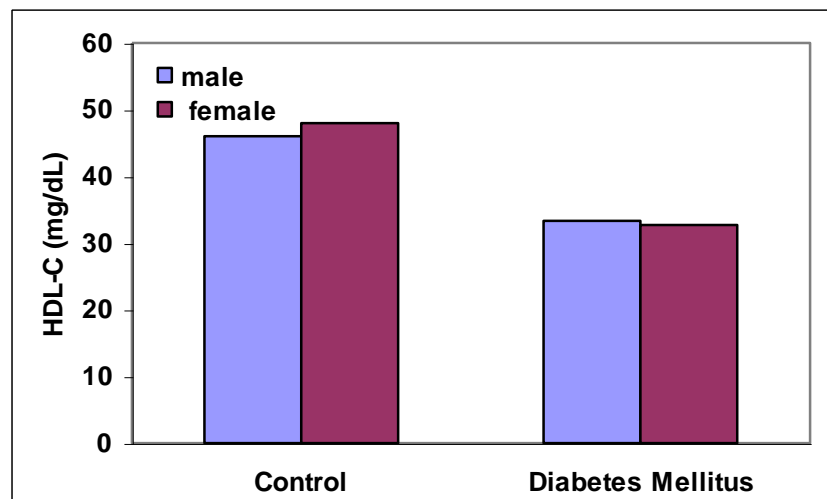


Figure 4 HDL-C (mg/dL)of patients with diabetes mellitus and healthy controls.

According to the results of total cholesterol and HDL-C of present study, risk factor of cardiovascular disease

revel significant increase when compared with healthy controls, as shown in Figure 5.

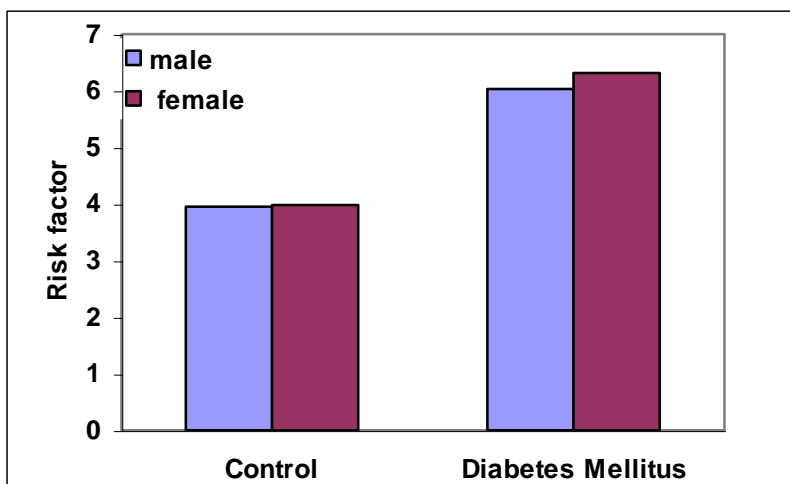


Figure 5 Risk factor of patients with diabetes mellitus and healthy controls.

Discussion

Results in the table 1 show that the diabetic patients are poor glycemc control and also show increase in the level of uric acid in the patients compared with the healthy control group, this can be attributed to either the increase in uric acid production or decrease in its excretion.[17] However there are physiological and pathological factors that influence serum uric acid level such as renal diseases.

In the study of Grous et al (1987) [18] hyperuricemia was more frequently in those with abnormal angiograms, and uric acid levels were related to

lipoproteins abnormalities. Moreover, studies performed with carotid ultrasound or angiography [19,20] have suggested that there is linear relationship between carotid atherosclerosis and hyperuricemia.

Uric acid is one of the major endogenous water-soluble antioxidants of the body. There is accumulating evidence that increased oxidative stress is closely related to diabetes and its vascular complications Thus, high circulating uric acid levels may be an indicator that the body is trying to protect itself from the deleterious effects of free radicals by increasing the products of endogenous antioxidants, eg,

uric acid. There is also some evidence that uric acid may have a direct role in the atherosclerotic process, because human atherosclerotic plaque contains more uric acid than do control arteries. Inflammation is one of the features of atherosclerosis, and uric acid crystals may induce inflammatory responses that are reduced by lipoproteins, which have an ability to bind uric acid crystals. [17]

Table 1 shows that the results of total cholesterol in the patients are significantly higher than control. This can attributed to increase fatty acid degradation due to high concentration in the liver and the end product is acetyl coA, which is the main product. The acetyl coA is used for the synthesis of cholesterol and ketone bodies which released in the blood could lead to hypercholesterolemia[21]) . While the results show reducing in the levels of HDL-cholesterol which could be explained by the loss of apo-c2 which is essential for increasing the activity of lipoprotein lipase (LPL) which result increase triglyceride level and low HDL-cholesterol [22,23]. According to above results it has been decided to estimate risk factor in diabetic patients, this reflect the increase in the total

cholesterol and reduction of HDL-cholesterol, and it was calculated from the following relationship as indicated in table [24].

Total cholesterol

Risk factor = _____

HDL- cholesterol

The results show difference between male and female in cholesterol levels this could be attributed to the hormonal changes associated with sex deference [25].

Results of present study show higher risk factor values, which means increasing in the probability of atherosclerosis incidence. Also hyperglycemia found to be associated with hyperuricemia in type 1 diabetic patients.

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