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Serum Sialic Acid in Non-Insulin Dependent Diabetic Mellitus Patients with Microvascular Complications

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ABSTRACT

The purpose of the present study was to test the hypothesis that serum sialic acid, a known powerful risk factor for diabetes mellitus in the general population is elevated in type 2 diabetic patients with micro vascular complications compared with diabetes without any micro vascular complications.

Keywords: Sialic acid, Micro albumin and Creatinine.

INTRODUCTION

Sialic acids are derivatives of a nine carbon acidic sugar, occupies the terminal position at the non-reducing end of N- and O- linked carbohydrate chains. The most abundant number is N- acetyl neuraminic acid [1]. In biological systems, sialic acid has shown to be directly involved in the regulation of many physiological processes. It has several pharmaceutical roles like, preventing gastrointestinal disturbances, neutralizing variety of toxins, clearing throat phlegm and a starting reagent of biochemical derivatives for pharmaceutical use [2]. In human plasma a large quantity of sialic acid is found in orsomucoid, alpha -1-antitrypsin, haptoglobin, fibrinogen, complement proteins and transferring[3]. Some of these sialyted glycoproteins are called acute phase proteins; they rabidly increase in concentration after the onset of an inflammatory reaction [4]. A number of reports have described elevated sialic acid levels in various diseases such as cancer [5], atherosclerosis [6], chronic renal failure [7], chronic glomerulonephritis, and systemic scleroderma [8]. Some non- pathological factors, such as aging, pregnancy, alcohol abuse, and smoking, may cause changes in sialic acid concentration [6]. It has been suggested that such elevation may be due to changes of the biosynthesis and posttranslational glycosylation of the acute- phase glycoproteins in liver [9].

Diabetes mellitus is a group of metabolic disorders characterized by hyperglycemia. It is associated with increased prevalence of microvascular complications [10]. Type 2 diabetes mellitus is the most common form of diabetes is characterized by insulin resistance or abnormal insulin secretion [11]. One of the more depilating aspects of diabetes is the numerous complications that can arise from the disease. These complications include diabetic retinopathy, Kidney nephropathy, peripheral neuropathy [12, 13] and increased prevalence of microvascular complications [10]. The development and severity of these complications are dependent on the duration of the disease and how well it is managed [14] .It has been

shown that elevated total serum Sialic acid (N- acetyl neuraminic acid is a risk factor for cardiovascularmortality in humans [15, 16]. It has been recorded that increased serum sialic acid is associated with microalbumin urea [17, 18].

On the other hand, Crook AM et.al [19] and John et.al [20] pointed out that total serum Sialic acid concentration increased in diabetic patients with microvascular complications. The aim of the present study was to measure serum Sialic acid and their relation with microalbumin urea, serum cholesterol, triglycerides, LDL- cholesterol, HDL, and Creatinine in type 2 diabetic subjects with and without microvascular complications.

MATERIALS AND METHODS

Patients: Three groups of individuals were included in this study:
Group 1: Fourty type 2 diabetic patients without complications.

- Group 2: Fourty three type 2 diabetic patients with retinopathy.
- Group 3: Fourty two type 2 diabetic patients with nephropathy. All patients were admitted for management to Al -Sader Medical City in Najaf. The patients ages ranged between (35- 68) years.

Controls: A healthy subject group of 41 was included in the study as a control group. The age ranged was comparable to that of the enrolled patients. None of these subjects had an obvious systemic diseases.

Blood samples: Venous fasting blood samples (5mL) were collected from both patients and healthy control group in plain tubes containing no anticoagulant. Disposable syringes and needles were used for blood collection. After allowing the blood to clot at room temperature for about 15 min, blood samples were centrifuged at 5000 xg for 15 min. Resulted serum was separated in two aliquots into plain tubes, where stored in -20^{o}C until to be assayed .

Determination of serum sialic acid and lipid profile: Total serum salic acid was measured spectrophotometrically by using method described by Jourdain et.al [21].

Lipid profile (total cholesterol, triglyceride and high density lipoprotein cholesterol) were measured spectrophotometrically by enzymatic reactions using ready for use kits, supplied by Biolabo, France [22] and low density lipoprotein (LDL-C) from Friedewald's formula : LDL- cholesterol = total cholesterol – HDL-C – VLDL-C [23] .

Determination of serum microalbumine and creatinine levels: Serum microalbumin and Creatinine were measured spectrophotometrically by enzymatic reactions using ready for use kits, supplied by Spinreact [24].

RESULTS AND DISCUSSION

Biochemical parameters determined in patient and control groups: The measured parameters of study were tabulated into four groups: diabetic patients without complications, diabetic patients with retinopathy, diabetic patients with nephropathy and control group, each one of these characteristics is presented by (Mean ± SD) , range values and p -values as shown in table 1 . Two sample t-test statistic method was used to calculate the p-values of diabetic patients and control group. The results of the present study showed significantly ($p<0.001$) elevated serum levels of sialic acid in diabetic patients with nephropathy and retinopathy when compared with those of the control group. While, no significant ($p>0.05$) changes in serum levels of sialic acid in diabetic patients without complication when compared with those of the control group.

However, there were significant ($p<0.001$) high serum levels of microalbumin and creatinine in three groups of the patient when compared with those of the control group.

Table 1: Serum sialic acid, microalbumin and creatinine in patients and control group.

Parameters	diabetic Patients without complications (n= 40)	diabetic patients with retinopathy (n= 43)	diabetic patients with nephropathy (n= 42)	Control group (n= 41)	P- Value
	Mean ± SD (Range)	Mean ± SD (Range)	Mean ± SD (Range)	Mean ± SD (Range)	
Sialic acid (mg/dl)	50.1 ± 2.7 (39.5 – 52.1)	74.0 ± 2.7 (69.3 – 80.4)	86.0 ± 2.8 (78.4 – 90.3)	45.3 ± 2.0 (45.0 – 47.2)	NS [a] < 0.001 [b] < 0.001 [c]
Microalbumin (mg/dl)	8.0 ± 3.3 (3.5 – 13.1)	101.0 ± 28.0 (68.0 – 132)	133.0 ± 34.3 (82 – 130)	7.5 ± 3.3 (2.8 – 12.3)	< 0.001 [a, b, c]
Creatinine (mg/dl)	2.02 ± 1.58 (1.2 – 4.6)	10.0 ± 2.02 (6.0 – 13.2)	10.01 ± 2.02 (8.5 – 13.8)	1.5 ±1.3 (0.13 – 3.0)	< 0.001 [a, b, c]

SD (Standard Deviation), NS (No significant)
a - Diabetic Patients without complications compared to control group.
b - Diabetic patients with retinopathy compared to control group.
c - Diabetic Patients with nephropathy compared to control group.

Lipid Profile In Patient and Control Groups: The results in table 2 showed that significant increased serum levels of TC ($p<0.001$) in three groups of the patient i.e: diabetic patients without complications, diabetic patients with retinopathy and diabetic patients with nephropathy when compared with those of the control group.

On the other hand, significant ($p<0.05$) elevated serum levels of TG and LDL-C in diabetic patients with nephropathy and retinopathy when compared with those of the control group. While, no significant ($p>0.05$) changes in serum levels of TC and TG in diabetic patients without complication when compared with those of the control group.

However, there was no significant ($p>0.05$) of HDL-C in three groups of the patient when compared with those of the control group.

Table 2: Levels of lipid profile in patients & control group.

Parameters	diabetic Patients without complications (n= 40)	diabetic patients with retinopathy (n= 43)	diabetic patients with nephropathy (n= 42)	Control group (n= 41)	P- Value
	Mean ± SD (Range)	Mean ± SD (Range)	Mean ± SD (Range)	Mean ± SD (Range)	
TC (mg/dl)	147.0 ± 120 (25 – 265)	245.0 ± 129 (119 – 386)	255.0 ±134.0 (115 – 380)	140.0 ± 119 (20 – 260)	<0.001 [a ,b, c]
TG (mg/dl)	121.0 ± 74.1 (45 – 198)	180.0 ± 74.0 (95 – 275)	177.0 ± 79.0 (100 – 280)	121.0 ±77.0 (40 – 195)	N.S [a] < 0.001 [b, c]
HDL-C (mg/dl)	36.0 ± 21.0 (10 – 65)	34.0 ± 19.0 (11 – 60)	38.0 ± 25.0 (10 – 70)	35.0 ±18.0 (12 – 68)	N.S [a ,b, c]

LDL-C (mg/dl)	89.0 ± 75.0 (12 – 170)	160.0 ± 94.0 (55 – 290)	164.0 ± 96.0 (50 – 285)	86.0 ± 75.0 (8 – 162)	NS [a] < 0.05 [b, c]

SD (Standard Deviation), TC (Total cholesterol), TG (Triglyceride), HDL-C (High density lipoproteins cholesterol) , LDL-C (Low density lipoproteins cholesterol), NS (No significant)
a - Diabetic Patients without complications compared to control group.
b - Diabetic patients with retinopathy compared to control group.
c - Diabetic Patients with nephropathy compared to control group.

The serum sialic acid may be used as an inflammatory marker and possible indicator of microvascular complications in type 2 diabetic patients [25]. Studies of incidences of cardiovascular disease or increased diabetes complications among subjects with high fibrinogen and other markers of inflammation [26]. Hyperglycemia and insulin resistance could also promote inflammation, and may be factor linking diabetes to be development of atherosclerosis [27]. Elevated glucose levels could promote inflammation by increased oxidative stress [28]. In type 2 diabetes, the circulating sialic acid concentration is elevated in comparison with non- diabetic subjects [29]. The increased serum sialic acid and microalbumin were strongly related to the presence of microvascular complications like diabetic nephropathy and diabetic retinopathy and caridiovascular risk factors like hypertension in type 2 diabetic patients [29, 30]. Crook M et.al found that serum salic acid was significantly higher in men with diabetic complications than in those without any of the complications [31]. There may be an association between salic acid and complications through the acute phase response. The results of this study, showed serum salic acid concentration increased in diabetic patients with microvascular complications as compared to the diabetic patients without any microvascular complications.

APPLICATIONS

The results of monitoring serum sialic acid in diabetic subject is useful in early predication and presentation of complications.

CONCLUSIONS

1. High serum levels of sialic acid and microalbumin strongly related to the presence of microvascular complications like diabetic nephropathy and diabetic retinopathy in type-2 diabetic patients.
2. Sialic acid is one of the component of vascular membrane, high serum levels suggest extensive damage in diabetic subjects.
3. The increased urinalbumine that association with microvascular complications.
4. The monitoring of serum sialic acid in diabetic subject may help in early predication and present of complications.

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