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Research Article

ASSOCIATION OF SERUM SIALIC ACID AND SERUM URIC ACID LEVELS WITH FASTING BLOOD GLUCOSE LEVELS IN TYPE-2 DIABETES MELLITUS PATIENTS

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ABSTRACT

Objectives: The objective of the study was to estimate the serum sialic acid and serum uric acid levels in patients with type-2 diabetes mellitus and non-diabetic individuals and determining the association of serum sialic acid and serum uric acid levels with fasting blood glucose levels in patients with type-2 diabetes mellitus and also in non-diabetic individuals.

Methods: The study was a cross-sectional analysis where 70 individuals in the age group of 30–70 years participated during 6 months period. This included two groups, one for type-2 diabetes patients as cases and other non-diabetics as controls. In each group, 35 individuals participated. There were 15 males and 20 females in type-2 diabetic group and 16 males and 19 females in non-diabetic group. Fasting blood glucose, serum sialic acid, and serum uric acid were estimated in both the groups.

Results: In this study, the serum sialic acid levels of type-2 diabetes mellitus were shown to be increased (76.60 ± 7.89) when compared to non-diabetics (39.66 ± 9.55) with a statistically significant, $p < 0.001$. The serum uric acid concentrations were also found to be slightly elevated in type-2 diabetes mellitus (4.48 ± 0.79) when compared to non-diabetics (4.28 ± 0.89) with a statistically non-significant, $p = 0.323$.

Conclusion: Based on this study, it is concluded that serum sialic acid and serum uric acid levels have been found to be positively associated with type-2 diabetes mellitus in both men and women, indicating the risk of developing microvascular complications in those patients. Therefore, estimating the sialic acid and uric acid levels can aid in the early diagnosis and prevention of microvascular complications caused by type-2 diabetes mellitus.

Keywords: Sialic acid, Uric acid, Type-2 Diabetes Mellitus, Microvascular complication.

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INTRODUCTION

Diabetes mellitus is one of the chronic metabolic syndromes characterized by increased levels of blood glucose that affect carbohydrate metabolism due to insulin deficiency or because of the factors that hinder insulin action [1] and it is related to long-term damage to multiple organs [2]. It is one of the chronic diseases most widely experienced in the world and has more than doubled the number of adults with diabetes over the past three decades [3]. Type-2 diabetes mellitus accounts for 90–95% of all cases of diabetes that is characterized by chronic hyperglycemia, leading to multiple organ systems failure, which, in turn, increases morbidity and mortality [4]. Due to persistent hyperglycemia and inadequate diabetes regulation, some risks occur. These include microvascular disorders such as retinopathy, nephropathy, and neuropathy [5]. A correlation has been suggested in many of the prospective studies between specific inflammatory markers and type-2 diabetes mellitus, and it is also believed that inflammation contributes to the progression of type-2 diabetes mellitus [6].

Sialic acid is among the markers for inflammation of the acute-phase response [7]. It is a family of derivatives of acetylated neuraminic acid which make up an important component of glycoproteins and glycolipids [8]. Many of these glycoproteins have sialic acid as the end sugar in their chain of oligosaccharide [9]. It functions as a cofactor of many cell receptors and is correlated positively with most acute-phase reactants [8]. Serum sialic acid concentration in type-2 diabetes mellitus is often found to be significantly increased and it is associated with microvascular complications as reported in some prospective studies [10,11].

The final product of purine metabolism is uric acid. Hypoxanthine and xanthine are oxidized to uric acid through xanthine oxidase. As its by-product, it generates O_2 and H_2O_2. Hyperuricemia may be strongly linked to an insulin resistance syndrome which is a type-2 diabetes risk factor [12]. Recent studies have also found the serum uric acid to be type-2 diabetes risk factor [13]. A positive correlation between high serum uric acid and diabetes mellitus has been documented in some studies [14-19] while there was no association [20] or inverse relationship in some other studies [21,22]. Hence, the relationship between the levels of serum uric acid and diabetes mellitus has not yet been clear.

Our research, therefore, aimed to examine the association of serum sialic acid and serum uric acid with fasting blood glucose levels in diabetics and non-diabetics individuals.

METHODS

Seventy individuals in the age group of 30–70 years during the 6 months period participated in this study. This included two groups, one for type-2 diabetes patients as cases and other non-diabetics as controls. In each group, 35 individuals participated. There were 15 males and 20 females in type-2 diabetic group and 16 males and 19 females in non-diabetic group.

Inclusion criteria

This study has recruited all newly diagnosed or already diagnosed type-2 diabetes mellitus patients taking oral hypoglycemic medication. A fasting blood glucose level of 126 mg/dl or higher was taken, based on the diagnostic criteria of the American Diabetes Association [23].

Exclusion criteria

Excluded criteria from this study were cases of type-2 diabetes mellitus that was associated with acute and chronic inflammatory disorders, obesity, pregnancy, pre-existing kidney diseases, gout, medications influencing uric acid levels, HIV/AIDS medicines. and thyroid disorders.

Blood collection, separation, storage, and analysis of sample

After overnight fasting, 2 ml of venous blood sample was collected using all aseptic precaution in plain Vacutainer for the assessment of serum sialic acid and serum uric acid and 1 ml blood sample was collected in fluoride Vacutainer for the estimation of fasting blood glucose. The plain Vacutainer was centrifuged at 3000 r.p.m for 15 min to separate the serum and the serum was stored at −20°C till estimation of sialic acid and uric acid. Both the fasting blood glucose (Glucose oxidase-Peroxidase method) and serum uric acid (modified Trinder method) levels were estimated using VITROS 5600 (fully automated biochemistry analyzer). Serum sialic acid was measured using Ehrlich's reagent in spectrophotometer.

Ehrlich's method of measuring serum sialic acid was based on the method stated by Sydow *et al*. (1988) [24]. A 400 µl of serum was mixed with 1.2 ml of 5% perchloric acid for 5–10 min at 100°C and centrifuged at 2000 rpm for 5 min. The supernatant (400 µl) was mixed with 400 µl of Ehrlich reagent (5 g of p-dimethylaminobenzaldehyde/50 ml of HCl/50 ml of distilled water). After incubation at 100°C for 15 min, a spectrophotometer was used to read the optical density at 525 nm.

Ethics approval

The research was carried out after obtaining written consent from the patient and ethical approval from the Institutional Ethical Committee.

Statistically analysis

Independent sample *t*-test was used to see the mean difference between the two groups for measurement scale data. $p < 0.05$ is considered as statistically significant at 95% confidence level. $p < 0.001$ is regarded as highly significant. The statistical software SPSS version 24.0 was used in the analysis.

RESULTS

The results of various investigations conducted on two study groups are shown in Tables 1 and 2. The results are compared between case and control groups.

Fasting blood glucose

The mean values of fasting blood glucose of the control group and the case group are shown in Table 1. Highly significant difference is found in the case group when compared to the control group with higher values found in the case group. There is 92.39% increase in the case group when compared to the control group.

Serum sialic acid

The mean values of serum sialic acid of the control group and the case group are shown in Table 1 and Fig. 1. Highly significant difference is found in the case group when compared to the control group with higher values found in the case group. There is 93.14% increase in the case group when compared to the control group.

Serum uric acid

The mean values of serum uric acid of the control group and the case group are shown in Table 1 and Fig. 2. There is no significant difference found in the case group when compared to the control group with slightly higher values found in the case group, which is non-significant with $p = 0.323$.

Correlation of fasting blood glucose, serum sialic acid, and serum uric acid in the case group

The correlation between fasting blood glucose, serum sialic acid, and serum uric acid in the case group is shown in Table 2.

DISCUSSION

Much attention has been paid in recent years to the relationship between inflammation and diabetes mellitus. The serum sialic acid was found to be one of the acute-phase markers associated with diabetes mellitus. Blood glucose elevation encourages inflammation by increasing the oxidative stress. Resistance to insulin and hyperglycemia can promote inflammation, which may be a related factor in diabetes development and atherosclerosis [25]. The vascular permeability is regulated by the moiety of sialic acid. The vascular endothelium carries a high amount of sialic acid, so sialic acid is released into circulation when vascular damage occurs [26]. The present research was, therefore, carried out

Table 1: Comparison of mean fasting blood glucose, serum sialic acid, and serum uric acid values between the case and control groups

Parameters	Group	n	Mean	Standard deviation	t-value	p-value
Fasting blood glucose (mg/dl)	Case	35	174.77	30.12	15.625	<0.001
	Control	35	90.97	9.98		
Serum sialic acid (mg/dl)	Case	35	76.60	7.89	17.644	<0.001
	Control	35	39.66	9.55		
Serum uric acid (mg/dl)	Case	35	4.48	0.79	0.995	0.323
	Control	35	4.28	0.89		

p<0.001 highly significant, p<0.05 significant, and p<0.1 non-significant

Table 2: Correlation between fasting blood glucose, serum sialic acid, and serum uric acid in the case group

Correlation	Fasting blood glucose	Serum sialic acid	Serum uric acid
Fasting blood glucose (mg/dl)			
Pearson correlation	1	0.941**	0.148
Sig. (two tailed)		<0.001	0.396
Serum sialic acid (mg/dl)			
Pearson correlation	0.941**	1	0.156
Sig. (two tailed)	<0.001		0.37
Serum uric acid (mg/dl)			
Pearson correlation	0.148	0.156	1
Sig. (two tailed)	0.396	0.37	

**Correlation is significant at < 0.001 level (two tailed)

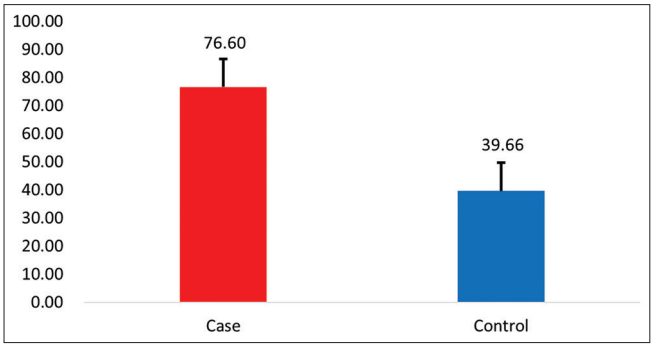

Fig. 1: The mean level of serum sialic acid in the case and control groups. Case: Type-2 diabetes mellitus, control: Non-diabetics

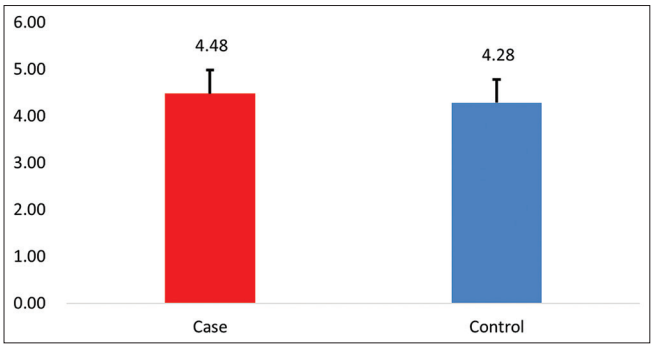

Fig. 2: The mean level of serum uric acid in the case and control groups. Case: Type-2 diabetes mellitus, control: Non-diabetics

to assess the levels of sialic acid in individuals with type-2 diabetes mellitus and non-diabetics.

As shown in Table 1, the serum sialic acid levels of type-2 diabetes mellitus have been shown to be increased in the present study (76.60 ± 7.89) when compared to non-diabetics (39.66 ± 9.55) with a statistically significant, $p < 0.001$. Several researchers have found elevated sialic acid concentration in type-2 diabetes. The tissue injury caused by vascular complications of the diabetes mellitus activates the local cytokine production from cellular infiltrations. This triggers an acute-phase response which leads to the release of acute-phase glycoproteins from the liver with sialic acid into the bloodstream, resulting in increased concentrations of serum sialic acid [27].

Uric acid, although one of the main antioxidants in circulation, it can cause oxidative stress in a number of cells including vascular smooth muscle cells, mediating on cardiovascular disease progression [28]. The correlation between uric acid levels and diabetes mellitus has been a hot topic of research over the years. The current study was conducted to determine the levels of the serum uric acid in type-2 diabetes mellitus. In our present analysis, serum uric acid levels were found to be increased in type-2 diabetes mellitus (4.48 ± 0.79) when compared to non-diabetics (4.28 ± 0.89) with a statistically non-significant, $p = 0.323$, as shown in Table 1.

The causal link between hyperuricemia and type-2 diabetes can be mediated by both kidney dysfunction and insulin resistance. Nonetheless, not many researchers have reached the same conclusion; a broad prospective study did not show a correlation between uric acid levels and type 2 diabetes, and an inverse association was also found between serum uric acid levels and diabetes mellitus. In type-2 diabetes mellitus, hyperuricemia typically results from under excretion of uric acid as a secondary response to hyperinsulinemia. The diabetes condition can also have a direct effect on the oxidation of purine nucleotides, resulting in increased levels of uric acid. In addition, hyperinsulinemia might also lead to hyperuricemia by increasing the xanthine oxidase activity [29]. Uric acid also prevents the bioavailability of nitric oxide, necessary for the absorption of insulin-stimulated glucose. This eventually leads to worsen insulin resistance [30]. However, our study shows an increase in serum uric acid levels in type-2 diabetes mellitus cases but non-significant increase which may be probably due to not having data on variable such as duration of diabetes mellitus in these patients. In future, a long-term study may be conducted by increasing the sample size including the duration of diabetes mellitus to conclude an association between the severity of diabetes mellitus and uric acid levels.

In the present study, serum sialic acid concentration increases with increase in fasting blood glucose concentration in type-2 diabetes patients, which is concomitant with the other studies. However, the results of serum uric acid also show slight elevation in type-2 diabetics when compared to the non-diabetics. Therefore, serum sialic acid and serum uric acid could be considered as an early marker of type-2 diabetes mellitus.

CONCLUSION

It is concluded from the present study that serum sialic acid and serum uric acid levels were found to be positively associated with type-2 diabetes mellitus in both men and women, indicating the risk that these patients may develop microvascular complications. Hence, estimating the levels of serum sialic acid and serum uric acid aids in early diagnosis and the prevention of microvascular complications caused by type-2 diabetes mellitus.

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AUTHORS' CONTRIBUTIONS

All the above-mentioned authors contributed significantly, directly, and intellectually to the work and authorized it for publication.

CONFLICTS OF INTEREST

There are no conflicts of interest connected with this article.

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