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Original Article

Biochemistry Section

Predictive Value of Serum Sialic Acid in Type-2 Diabetes Mellitus and Its Complication (Nephropathy)

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ABSTRACT

Introduction: Sialic acid levels are increased in type-2 diabetes mellitus and its estimation helps in predicting the occurrence of microvascular complication such as diabetic nephropathy. The present study compared the levels of sialic acid, glycated haemoglobin, serum creatinine and urine microalbumin: in type-2 diabetics without any complications; in type-2 diabetics with nephropathy; and in age and sex matched healthy individual (controls).

Results: The study observed an increased level of sialic acid in type-2 diabetics without any complications and type-2 diabetics with nephropathy. Serum sialic acid levels in type-2 diabetics without any complications was 64.44 ± 3.93 mg/dl, in type-2 diabetics with nephropathy was 73.88 ± 4.41 mg/dl, and in controls it was 53.16 ± 3.40 mg/dl. Urine sialic acid levels in type-2 diabetics without any complications was 6.62 ± 0.70 mg/dl, in type-2 diabetics with nephropathy was 8.46 ± 0.97 mg/dl, and in controls it was 4.44 ± 0.62 mg/dl. Correlation of sialic acid levels with glycated haemoglobin and urine microalbumin was statistically significant but with serum creatinine was not statistically significant.

Conclusion: Sialic acid is an important component of vascular cell membrane. Their increased levels indicate extensive vascular damage in type-2 DM. Therefore, estimation of sialic acid levels help in early prediction and prevention of microvascular complications occurring due to diabetics, thereby decreasing the mortality and morbidity in them.

Keywords: Sialic acid, Diabetes Mellitus type-2

INTRODUCTION

Diabetes Mellitus (DM) is a disorder of multiple aetiologies, where alteration is characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action or both. Diabetes mellitus affects more than 230 million people worldwide and this number is expected to reach 350 million by 2025. Type-2 diabetes mellitus is the most common form of diabetes accounting for 90% of the cases. The chronic hyperglycemia of diabetes is associated with significant long-term sequelae, particularly damage and/or dysfunction and failure of various organs, especially the kidneys, eyes, nerves, heart and blood vessels [1].

Sialic acid [SA], a generic term for a family of acetylated derivatives of neuraminic acid, is an essential component of glycoproteins and glycolipids. It acts as a co-factor of many cell receptors and is positively associated with most of the serum acute phase reactants. In patients with type-2 diabetes mellitus the levels of sialic acid are increased [2].

Sialic acid is a component of cell membranes and vascular permeability is regulated by sialic acid moieties. The vascular endothelium carries a high concentration of sialic acid, hence extensive microvascular damage accounts for its shedding into the circulation leading to increased vascular permeability and overall increased sialic acid concentration. Thus, elevated levels indicate excessive damage of the vascular cells of retina of the eyes, kidneys, heart and brain. This leads to conditions like retinopathy, nephropathy and neuropathy.

Tissue injury caused by diabetic vascular complications stimulates local cytokine secretion from cellular infiltrates, such as macrophages and endothelial cells. This induces an acute phase response with release of acute phase glycoproteins with sialic acid from liver into general circulation leading to their increased levels [3].

In diabetic nephropathy, there is greater increase in sialic acid due to the damage of the vascular endothelial cells of the kidney and it is considered as a newly established potential risk factor for the development of diabetic nephropathy. Therefore, the estimation of sialic acid levels may prove to have predictive value and may have a role in prevention of microvascular diseases and their complications, in people with type-2 diabetes mellitus [4].

The aim of the present study was, to evaluate the sialic acid levels in subjects with type-2 diabetics without any complications and type-2 diabetics with nephropathy. The effect of the type-2 diabetes and diabetic nephropathy on other parameters i.e. creatinine, microalbumin, glycated haemoglobin was also studied.

MATERIAL AND METHODS

Study was conducted on 75 individuals between the age group of 40-70 years, during the year 2010-2012. The study group consisted of 25 individuals who were diagnosed as type-2 diabetics without any complications (newly diagnosed or known diabetics on treatment), 25 individuals with type-2 diabetics with diabetic nephropathy and 25 age and sex matched healthy individuals (controls). Subjects with history of cardiac diseases, smoking, alcohol intake, pregnancy, malignancy or any inflammatory disorders are excluded from the study group. Study was approved by Institutional ethical committee.

After obtaining the informed consent, by aseptic precautions 7 ml of blood was collected from anticubital vein after 8-12 hours of fasting. Blood was collected in EDTA vacutainer (2ml) and plain vacutainer (5ml). Urine sample (5ml) was also collected in a clean, dry and sterile container. Blood collected in plain vacutainer was processed to obtain serum. Serum and urine sialic acid [5] was measured by Ehrlich's reagent in spectrophotometer using commercially available kits. Free sialic acid in serum and urine reacts with paradimethyl aminobenzaldehyde (Ehrlich's reagent) to form pink coloured solution. The absorbance of the colour developed in the sample at 525 nm was proportional to the total sialic acid concentration in the serum and urine.

Blood collected in EDTA tube was used for estimation of glycated haemoglobin [6] measured by Ion Exchange Resin method using commercially available kit. Serum creatinine was estimated [7] by modified Jaffe's method in semi-autoanalyzer using commercially available kit. Urine microalbumin was estimated [8] by turbidimetric immunoassay.

RESULTS

Serum sialic acid levels and Urine sialic acid levels were found to be increased, in type-2 diabetics without any complications and type-2 diabetics with nephropathy, when compared to controls, which was statistically significant [Table/Fig-1].

The data of type-2 diabetics without any complications were analysed using Pearson correlation, had shown a statistically significant positive correlation of sialic acid level with glycated haemoglobin and urine microalbumin, but with serum creatinine was not statistically significant [Table/Fig-2].

The data of type-2 diabetics with nephropathy were analysed using Pearson correlation, and had shown statistically significant positive correlation of sialic acid level with glycated haemoglobin and urine microalbumin, but with serum creatinine was not statistically significant [Table/Fig-3].

Study Groups	Serum Sialic acid Mean ± SD (mg/dl)	Urine sialic acid Mean ±SD (mg/dl)
Type-2 diabetics without any complications	64.44 ± 3.93	6.62 ± 0.70
Type-2 diabetics with with nephropathy	73.88 ± 4.4	8.46 ± 0.97
Controls	53.16± 3.4	4.44 ± 0.62
F	173.23	170.12
p value	< 0.001	< 0.001

[Table/Fig-1]: Comparison of serum and urine sialic acid (mg/dl) between the study groups. p = < 0.05 significant

Parameters correlated	r-value	p-value
Serum sialic acid Glycated Haemoglobin	r = 0.90	p = < 0.001
Serum sialic acid Serum Creatinine	r = 0.32	p = 0.116
Serum sialic acid Urine microalbumin	r = 0.79	p = < 0.001
Urine sialic acid Glycated Haemoglobin	r = 0.91	p = < 0.001
Urine sialic acid Serum Creatinine	r = 0.27	p = 0.184
Urine sialic acid Urine microalbumin	r = 0.71	p = < 0.001

[Table/Fig-2]: Correlation between Serum and urine sialic acid with glycated haemoglobin, serum creatinine, and urine microalbumin in type 2 diabetics without complication. p = < 0.05 significant

Parameters correlated	r-value	p-value
Serum sialic acid Glycated Haemoglobin	r = 0.60	p = 0.002
Serum sialic acid Serum Creatinine	r = 0.26	p = 0.206
Serum sialic acid Urine microalbumin	r = 0.61	p = < 0.001
Urine sialic acid Glycated Haemoglobin	r = 0.55	p = 0.004
Urine sialic acid Serum Creatinine	r = 0.23	p = 0.273
Urine sialic acid Urine microalbumin	r = 0.59	p = 0.002

[Table/Fig-3]: Correlation between Serum and urine sialic acid with glycated haemoglobin, serum creatinine, and urine microalbumin in type 2 diabetics with nephropathy. p = < 0.05 significant

DISCUSSION

Present study was conducted to evaluate the sialic acid levels in type-2 diabetics without any complications and type-2 diabetics with nephropathy patients. We observed statistically significant increase in serum sialic acid levels, in type-2 diabetics without any complications and type-2 diabetics with nephropathy, when compared to controls. These findings were in accordance to the study of Nayak S.B. et al. Sialic acid is an essential component of glycoproteins and glycolipids. It acts as a co-factor of many cell receptors and is positively associated with most of the serum acute phase reactants. Sialic acid is a component of cell membranes and vascular permeability is regulated by sialic acid moietes. This vascular endothelium carries a high concentration of sialic acid and hence extensive microvascular damage associated with non-insulin dependent diabetes mellitus (NIDDM) accounts for its shedding into the circulation, leading to increased vascular permeability and overall increased sialic acid concentration [2].

Study had shown increased urine sialic acid levels in type-2 diabetics without any complications and type-2 diabetic with nephropathy, when compared to controls which was statistically significant. Nayak S.B. et al., found that urine sialic acid levels were increased in type-2 diabetics without any complications and type-2 diabetic with nephropathy when compared to controls which was not statistically significant [4]. Tissue injury caused by diabetic vascular complications stimulates local cytokine secretions from cells involved in complications such as, macrophages and endothelium. This induces an acute phase response which involves the release of acute phase glycoproteins with sialic acid from the liver into general circulation leading to increased serum sialic acid concentration which in turn increases urinary excretion of sialic acid.

In the present study, the serum creatinine levels were found to be increased in type-2 diabetics without any complications and type-2 diabetics with nephropathy when compared to controls, which was statistically significant. These findings were in accordance to the study of Nayak S.B. et al., [4]. Sialic acid levels showed a positive correlation with serum creatinine in both type-2 diabetics without any complications and type-2 diabetics with nephropathy which was similar to the study of Shahid S.M. et al., [9].

This study showed increased glycated haemoglobin levels in type-2 diabetics without any complications and type-2 diabetics with nephropathy when compared to controls, which was statistically significant. These findings were in accordance to the study of Usman M.K. et al., [10]. In the present study, the sialic acid levels showed a significant positive correlation with glycated haemoglobin. This was in accordance to the study of Chen et al., [11]. As plasma glucose is consistently elevated, there is increase in non-enzymatic glycation of haemoglobin. HbA1C is formed by a non-enzymatic irreversible process with combination of aldehyde group of glucose and the amino terminal valine of β chain of haemoglobin.

The present study showed that the urine microalbumin levels were found to be increased, in type-2 diabetics without any complications and type-2 diabetics with nephropathy when compared to controls, which was statistically significant. These findings were in accordance to the study of Nayak S.B. et al., [4]. The increase in urine albumin in the diabetics can be interpreted as an early sign of nephropathic changes in those individuals. Increase in urine albumin seen with diabetic nephropathy can be attributed to degradation of the glomerular basement membranes and hypertension, both characteristic of diabetic nephropathy. The presence of microalbuminuria is a marker of endothelial dysfunction, and indices an increased risk of generalized atherosclerosis and increased mortality from cardiovascular disease.

Thus, this study showed the presence of increased levels of sialic acid in type-2 diabetics without any complications and type-2

diabetics with nephropathy. Sialic acid levels showed a significant positive correlation with urine microalbumin. There may be shedding of sialic acid into circulation because of the vascular damage. This vascular damage is seen throughout the body including the kidneys especially in diabetic nephropathy. Consequently, there may be increased filtration of albumin via the damaged glomeruli and hence an increased albumin loss in urine.

CONCLUSION

Sialic acid is an important component of vascular cell membrane, their increased levels indicate extensive vascular damage in type-2 DM. Therefore, estimation of sialic acid levels may help in early prediction and prevention of microvascular complications occurring due to diabeties mellitus type-2, thereby decreasing the mortality and morbidity.

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