A STUDY OF SERUM SIALIC ACID LEVELS IN DIABETIC NEPHROPATHY

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ABSTRACT

Background: Diabetic Nephropathy is a major microvascular complication of Diabetes mellitus and the most common cause of End Stage Age Renal Disease (ESRD). Serum sialic acid, an acute phase reactant and acute phase reactants are considered as indicators of microvascular angiopathy. Microalbuminuria is a predictor of incipient nepropathy in Diabetic patients. Aim: The study was under taken to evaluate Serum Sialic acid and Microalbuminuria levels and to assess to correlation of serum sialic acid and Microalbuminuria in Diabetic Nephropathy patients.

Materials & Methods: The study population consists of two groups. Group-I, 50 clinically diagnosed cases of Diabetic Nephropathy. Group-II, 50 individuals with age and sex matched healthy persons were taken as control. Blood samples were analysed for Fasting blood sugar, blood urea, and serum creatinine, glycated HbA1C and serum sialic acid levels. Urine samples were analysed for microalbumin levels.

Results: Serum Sialic acid levels were found to be significantly increased in Diabetic Nephropathy compared to controls. Serum sialic acid level was statistically correlated with glycated HbA1C and serum sialic acid levels. Urine albumin was also increased in the diabetic group.

Conclusion: Estimation of Serum sialic acid levels will help in early prediction and prevention of microvascular complications like Diabetic Nephropathy.

Keywords: Diabetic Nephropathy, End Stage Age Renal Disease (ESRD).

INTRODUCTION

Diabetes mellitus is the major healthcare problem occurring all over the world. "Diabetes mellitus", the most common endocrine disease is represented by "metabolic abnormalities" due to relative or absolute deficiency of insulin and or insulin resistance resulting in "hyperglycemia" and associated with "micro and macrovascular complications".[1]

"Diabetes mellitus" presents with characteristic symptoms such as "polydipsia, polyuria, polyphagia, weight loss and the long-term effects include progressive development of microvascular complications, particularly in the eye and kidney, and an increased frequency of macrovascular disease such as peripheral vascular and coronary heart disease". [2] "Diabetes mellitus" is the most important reason of "End Stage Renal Disease (ESRD)”. It is responsible for 30-40% of all ESRD. Even though "Type 1 and Type 2 DM" lead to ESRD, most of the patients are those with "Type 2 DM". [3] "Diabetic renal disease" is categorized by an increase in the "flow of protein, predominantly albumin", "An early and continuing rise in blood pressure" and decrease in the rate of filtration in the "glomerulus" most important ultimately to "End Stage Renal Disease".[3] "Reactive oxygen species (ROS)" increase is caused by "Hyperglycemia". "Poly ADP-ribose polymerase (PARP)" is activated by stand breaks in DNA. Decreased "glyceraldehyde-3-phosphate dehydrogenase (GAPDH)" activity causes augmented "polyl pathway flux, intracellular advanced glycation end product formation, activation of protein kinase C and hexosamine pathway flux".[4] These pathways in combination, finally results in high renal albumin permeability and extracellular matrix growth.
resulting in "proteinuria, glomerulosclerosis and tubular interstitial fibrosis". [6]

"Serum sialic acid" is a recently recognized possible risk factor for the rise of "macro and microvascular complications of diabetes". [7] "Serum sialic acid" is a part of "glycoprotein" such as acute phase proteins which are increased in diabetes. The possible mechanism linked with the function of sialic acid is to maintain the "negative charge of renal glomerular basement membrane". Due to increased "vascular permeability" there is shedding of "vascular endothelial sialic acid into circulation". [8]

"Microalbuminuria" is the earliest manifestation of "diabetic nephropathy" and it is the predictor of incipient nephropathy in diabetic patients. "Glycated haemoglobin" is a standard measure of severity of diabetes mellitus and gives an idea about long term "glycemic control". "Microalbuminuria" arise from the amplified passage of albumin throughout the "glomerular filtration" wall resulting in ultrastructural changes fairly in "glomerular pressure". [9]

The present study was intended to explore the role of "serum static acid" as a Predictor in the progress of "diabetic nephropathy" and to associate the clinical relationship of "serum sialic acid with glycated haemoglobin and the indicator of diabetes nephropathy such as microalbuminuria".

**Aim of The Study**
- To estimate the serum sialic acid levels in diabetic nephropathy patients.
- To know the correlation between serum sialic acid and microalbuminuria in diabetic nephropathy patients.
- To know the correlation between serum sialic acid and glycated hemoglobin in diabetic nephropathy patients.

**MATERIAL AND METHODS**

The study population consist of two groups.

**Inclusion Criteria**

**Group-I:** Clinically diagnos cases of Diabetic Nephropathy, who attend outpatient department and admitted cases of Government General Hospital, Ongole, in the period between April 2022 to March 2024 were taken for case study.

**Group-II:** 50 individual with age and sex matched health persons were taken as control.

**Exclusion Creteria**

1. Patients with acute and chronic inflammatory conditions.
2. Pregnant women.
3. Chronic alcoholics

**Laboratory Investigations**

10 ml of blood was collected in fasting state under aseptic precautions and blood is divided 3 testubes marked and 1, 2 and 3. Test tube (1) contains 2 ml of blood with anticoagulant which is used for estimation of fasting blood glucose. (Glucose – Oxidase paroxidase method). Test tube (2) contains 4 ml of blood with no anticoagulant that is allowed to clot and serum is separated. Serum is used for measurement of a) Blood urea (Glotamate dehydrogenase- Urease method) b Serum creatinine (Jaffe’s method), c) Serum sialic acid (modified Thiobarbituric acid assay of WARREN-Principle: Sialic acid is oxidized to FORMYL PYRUVIC ACID which reacts with Thiobarbituric acid to form a pink coloured product, the intensity of colour is measured at 549 nm. Test tube (3) contains whole blood that is used for estimation of Glycated HbA1C by direct method using Minray Semianlyser.

**URINE MICROALBUMIN:** RandomMidstream urine samples (10 ml) were collected in a sterile container without preservative and assayed for microalbumin (immune turbid metric assay).

**RESULTS**

**Figure 1:**

**Figure 2:**

**Figure 3:**
**DISCUSSION**

The present study was carried out to investigate the role of serum sialic acid as predictor the development of diabetic nephropathy and to correlate the clinical relationship of serum sialic acid with glycated hemoglobin. The mean fasting blood sugar in cases and controls was 196.32 ±48.21 mg/dl and 80.62 ±6.82 mg/dl respectively. The association between mean fasting blood sugar in cases and controls was statistically significant P<0.001. 

"Hyperglycemia is a causative factor in the pathogenesis of diabetic nephropathy. Glucose reacts non enzymatically with primary amines of proteins forming glycated compounds. Hyperglycemia exerts toxic effects and results in kidney damage by directly altering intracellular signaling pathways and via many biochemical pathways."

Shows mean values of Glycated haemoglobin among cases and controls. The mean values of Glycated haemoglobin among cases and controls was 10.09 ±0.99% and 6.21 ±0.58% respectively and association between mean values of Glycated haemoglobin among cases and controls was highly significant. (P< 0.001)
The mean blood urea among cases and controls was 56.12 ±12.88 mg/dl and 21.86 ±4.89 mg/dl respectively and association between them was statistically significant (P<0.001). The mean serum creatinine values among cases and controls was 2.54 ±0.51 mg/dl and 1.11 ±0.29 mg/dl respectively and association between them was statistically significant (P<0.001).

"The table no. 4 shows mean values of serum sialic acid among cases and controls. The mean values of serum sialic acid among cases and controls was 3.01 ±0.75 mmol/L and 1.89 ±0.48 mmol/L respectively and association between mean values of serum sialic acid among cases and controls was highly significant, (P<0.001)".

"Sialic acid acts as a cofactor of many cell surface receptors and positively associated with most of the serum acute phase reactants. Sialic acid regulates vascular permeability. The vascular endothelium carries a high concentration of sialic acid hence extensive microvascular damage associated with diabetes result in its shedding into the circulation leading to an increase in vascular permeability and increased serum sialic acid concentration. Tissue injury caused by diabetic vascular complications stimulates local cytokine secretions from cells involved in the 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 the general circulation again leading to increased serum sialic acid concentrations."

The mean value of microalbuminuria among cases and controls was 131.84 ±9.41 mg/L and 10.45 ±2.04 mg/L respectively and association between mean values of microalbuminuria among cases and controls was highly significant, (P< 0.001)."Microalbuminuria is defined as the excretion of 30 to 300 mg of albumin per day in urine. It is a predictor of progressive renal damage. It is a clinically important indicator of deteriorating renal function in diabetic patients. Microalbuminuria is due to widespread endothelial dysfunction arising from the effects of cytokines and other inflammatory mediators which are released during the intense inflammatory responses that are associated with critical illness. The effects of disruption of the integrity of the endothelial barriers is manifested as altered glomerular endothelial permeability in the kidneys, allowing increased amounts of albumin to escape into the glomerular ultrafiltrate. The tubular reabsorptive mechanism for albumin from the ultrafiltrate is exceeded beyond its threshold capacity, leading to increased excretion of albumin in the urine."

"Our study is in accordance with Shivananda Nayak B and Geetha Bhaktha", who demonstrated significantly increased urinary microalbumin levels in diabetic nephropathy patients compared to healthy controls. Melidonis A, Tournis S and Chen JW, Gall MA101 in their study, demonstrated increase in urinary albumin levels in diabetic nephropathy patients compared to controls."

The table no. 6 described correlation between serum sialic acid with FBS. The correlation study revealed a positive correlation between serum sialic acid and both FBS in diabetic nephropathy cases (r=0.78) indicating the role of hyperglycemia towards renal damage.

CONCLUSION

Elevating Serum Sialic acid and Urinary microalbumin levels are strongly associated with the presence of Nephropathy. Therefore, estimation of Serum Sialic acid levels may help in early prediction and prevention of microvascular complications occurring due to Diabetes Mellitus, there by Sialic acid can be used as marker of renal dysfunction in Diabetic Nephropathy, thus decreasing mortality and morbidity.

REFERENCES