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Serum Sialic Acid Levels in Diabetic Subjects: A Promising Screening Tool for Microvascular & Macrovascular Complications in Diabetes

Anirban Poddar[1], Subhashree Ray[2]

PGT, Department of Biochemistry, IMS& SUM Hospital, Bhubaneswar, Odisha, India

Professor &HOD, Department of Biochemistry, IMS& SUM Hospital, Bhubaneswar, Odisha, India

Abstract: ***Diabetes meliitus has been emerging as a deadly killer in the past decade & is found to be associated with a lot of complications such as nephropathy, neuropathy, retinopathyetc. Sialic acid is a component of the erythrocyte membrane & has been identified as an acute phase reactant which is indicated to be associated with the pathophysiology of diabetes mellitus & its associated complications. Serumsialic acid levels were measured in 30 cases each of type 2 diabetes with & without long term complications. Sialic acid levels were found to be grossly elevated in diabetics without complications as compared to the controls. The values were found to be even higher in diabetics with longterm complications. Hence an assay of this new serum marker in diabetic population can help in explaining the inflammatory process implicated in the development of complications such as cardiovascular comorbidities, microangiopathies& thereby helping in a timely intervention.***

Keywords: Diabetes Mellitus, Sialic Acid, Diabetic Nephropathy, Retinopathy

1. Introduction

Diabetes mellitus is a conglomeration of several chronic metabolic disorders which are believed to evolve from an interaction of genetic and environmental factors.[1]A patient with diabetes mellitus invariably presents with a jeopardy in lipid metabolism which results in elevation of free fatty acids & triglycerides in blood[2].Sialic acid presents as the terminal sugar moeity of oligosaccharide sidechains of various tissue glycoproteins & glycolipids, which act as cofactors of various cell surface receptors such as insulin receptor-2 & these are found to be increased in various pathological states such as diabetes mellitus.[3,4].Sialic acid alongwith C-reactive protein &homocysteine which are considered as reputed cardiovascular markers have been found to be elevated in diabetics with cardiovascular compromise.[5,6] A rise in the serum sialic acid levels alongwith a concomitant rise in the urinary albumin excretion rate explains the vascular damage caused to the renal endothelium resulting in shredding of sialic acid of the renal endothelium & consequent increased permeability to plasma proteins.[7,8]It has been substantiated by several studies previously that both sialic acid and lipid bound sialic acid concentrations were found to be elevated in clinically established cases of diabetic retinopathy,[9]this in turn justifies the role of sialic acid as a risk marker for development of diabetic angiopathy.Several population-based studies conducted across the world have clearly demonstrated that an elevated serum sialic acid level is linked directly to various cardiovascular risk factors like increased body mass index (BMI) and lipid profile levels in diabetic subjects suggesting the potential use of this parameter as a marker for cardiovascular disease in diabetes mellitus[10,11].

2. Literature Survey

In the past decade with the progressive increase in incidence of diabetes mellitus & its associated complications,the healthcare burden on many developing & developed economies has significantly increased.This called for extensive research in the field of diabetes in order to devise new cost effective tools for diagnosis & management of the same.The inflammatory markers such as serum sialic acid & adenosine deaminase have been of special interest to researchers & several studies have provided evidence suggestive of a strong role in the pathogenesis of diabetes mellitus[2].More studies by researchers and subsequent data from studies carried out in different parts of the world on these parameters are required to substantiate the findings & draw an inference regarding their role in pathogenesis of diabetes.Our study is a little step in this direction to contribute our two cents worth.

3. Methods & Approach

This comparative observational cohort study was carried out at IMS & SUM Hospital, Bhubaneswar, Odisha. The subjects involved in the study were divided into 3 groups.

- **Group A:**-This group comprised of 30 patients who had history of diabetes mellitus >10 years & presented with known complications associated with diabetes mellitus in the endocrinology opd.
- **Group B:**-This group consisted of 30 newly diagnosed cases of diabetes mellitus(i.e history of diabetes <2 years) & did not complain of any obvious symptoms associated with diabetes mellitus.
- **Group C:**-This group comprised of 30 healthy subjects with no obvious complains of any kind.They presented to the institutional OPD for regular health check up.

An informed written consent was obtained from all the subjects in the three groups. The entire procedure was explained to them in their local language before seeking consent. The study was approved by the institutional ethical committee which follows the "Helsinki guidelines for human research". Analysis of all the blood samples of the

subjects was sponsored by a NABL accredited private lab in kolkata namely" CHIKITSA MEDICARE PVT LTD". The authors declare that no conflict of interest exist whatsoever.

Measurement of Sialic Acid
Sialic acid was estimated by the modified Aminoff's method[12].A wide range of variationin sialic acid levels has been observed in various studies ranging from 0.6 µmol/ml done HPLC[13]to 7 µmol/ml done by Aminoff's method[12].This wide variability may be due to the different methods employed or interfering substances or due to racial differences.

Measurement of fasting blood glucose & post prandial blood glucose & HbA1C
Blood sugar estimation was done by a commercially available enzymatic assay kit based on the HEXOKINASE method using COBAS –INTEGRA 400 autoanalyser.HbA1C was measured by HPLC method using autoanalyser BIORAD-D10.

Measurement of Lipid Profile
Total cholesterol was estimated using a commercially available kit supplied by Roche Diagnostics which involves the CHOD/PAP enzymatic method. Triglyceride was assessed by kit involving enzymatic GPO/PAP method. HDL, LDL & VLDL were estimated by a commercially available kit supplied by Roche Diagnostics which involves the enzymatic CHOD/PAP method.

Measurement of Serum Creatinine
Serum creatinine was estimated using a commercially available kit using autoanalyser COBAS –INTEGRA 400 which employs the Jaffes's kinetic method.

Statistical Analysis
Data was statistically analysed using the STATISTICAL PACKAGE FOR SOCIAL SCIENCES(SPSS) V17.0. & SYSTAT V8.0. Tests like chi-square & T- tests were applied to analyse the data.

4. Results & Discussion

Relationship Between Serum Sialic Acid & Other Metabolic Variables In Diabetes Mellitus With & Without Complications.

Parameters	*Normal Subjects*	*Diabetics Without Complications*	*Diabetics With Complications*	'p' value
SIALIC ACID(µmol/ml)	0.627±0.0541	0.7819±0.1343	0.7944±0.1418	<0.001
FBS(mg%)	84.46±11.9	137.53±6.6	188.31±26.7	<0.001
PPBS(mg%)	123.7±0.3	219.9±14.37	319.13±39.9	<0.001
HbA1C(%)	4.68±0.7	8.79±1.4	11.58±2.2	<0.001
CHOLESTEROL(mg%)	173.91±37.4	246.33±8.3	270.57±23.6	<0.001
TRIGLYCERIDE(mg%)	121.46±28.7	171.3±45.1	263.13±67.6	<0.001
HDL(mg%)	47.53±3.7	37.46±3.5	29.33±4.5	<0.001
LDL(mg%)	103.03±33.9	174.6±6.3	187.9±23.9	<0.001
CREATININE(mg%)	0.3±0.16	0.7±0.1	1.33±0.8	<0.001

The most important aspect in the diagnosis & management of diabetes mellitus revolves around the reliability of serum markers for diagnosis of the microvascular complications of diabetes mellitus. Amongst latest biochemical inflammatory markers sialic acid & adenosine deaminase has been of special interest. Adenosinedeaminase activity has also been found to have a strong correlation with blood sugar levels & glycosylated haemoglobin levels in some biochemical studies, thus fuelling the probability of it being used as a glycemic marker in type 2 diabetes mellitus in future[14].

As far as our study with sialic acid is concerned, a clear cut elevation in sialic acid levels is evident from the above data in diabetics without complications as compared to the healthy controls.The levels were even higher in diabetic subjects with complications.

Another study conducted over 200 indian diabetic subjects have reported similar findings as ours with clear cut evidence of the existence of a strong positive correlation between serum sialic acid levels & altered lipid levels[6] especially in those with complications as compared to those without complications & healthy controls. Various other studies conducted over diabetic subjects have revealed that serum levels of acute phase reactants like serum sialic acid are actually "hands in gloves"with chronic complications of diabetes.

A significant increasing trend of serum sialic acid concentration with severity of nephropathy has been observed in few studies. Significant rise of serum sialic acid has been observed in cases of diabetic retinopathy as well[5,8,15,16].These findings are similar to our study results reflecting that increased serum sialic acid level may be an inflammatory marker and a possible indicator of angiopathic complications in type 2 diabetic patients.

5. Conclusion

It might be inferred from above discussion that serum sialic acid levels might serve as an important tool in detecting the subclinical inflammatory process in diabetic subjects & in turn may serve as a valuable screening tool for identifying diabetic subjects who are predisposed to suffer from microvascular complications, thus aiding in a timely intervention.

6. Future Scope

The inflammatory markers such as sialicacid hold enormous potential & promise as is evident already from various studies in the past & further research in this field might hold the key to a better understanding of the pathogenesis of various diseases such as diabetes &cancer.A better understanding of their association with the pathogenesis of the aforesaid diseases might also make them lucrative therapeutic targets aimed to cure these diseases.

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Author Profile

Dr. Anirban Poddar PGT (Biochemistry) IMS & SUM Hospital, Bhubaneswar, Odisha, India

Dr. Subhashree Ray is Professor & HOD (Biochemistry) IMS & SUM Hospital, Bhubaneswar, Odisha, India