

Correlation Of Serum And Urine Sialic Acid Levels With Lipid Profile And Anthropometric Indices In Type 2 Diabetes Mellitus And Diabetic Nephropathy

ABSTRACT

INTRODUCTION : SIALIC ACID IS A COMPONENT OF VASCULAR CELL MEMBRANES; THE ELEVATED LEVELS INDICATE EXCESSIVE VASCULAR DAMAGE LEADING TO DIABETIC COMPLICATIONS. THEREFORE SIALIC ACID CAN BE CONSIDERED TO BE NEWLY ESTABLISHED POTENTIAL RISK FACTOR FOR THE DEVELOPMENT OF DIABETIC NEPHROPATHY.

AIMS:TO STUDY THE CORRELATION BETWEEN SIALIC ACID LEVELS WITH LIPID PROFILE AND ANTHROPOMETRIC VARIABLES IN TYPE 2 DIABETES MELLITUS AND TYPE 2 DIABETICS WITH NEPHROPATHY.

STUDY DESIGN: CASE CONTROL STUDY

PLACE AND DURATION OF STUDY: STUDY WAS CONDUCTED AT DEPARTMENT OF BIOCHEMISTRY AND DEPARTMENT OF MEDICINE AT AJ INSTITUTE OF MEDICAL SCIENCES, MANGALORE FOR A PERIOD OF 2 YEARS.

METHODOLOGY: STUDY POPULATION INCLUDED 75 SUBJECTS IN THE AGE GROUP OF 40-70 YEARS OUT OF WHOM 25 SUBJECTS WERE TYPE 2 DIABETICS (NEWLY DIAGNOSED OR KNOWN DIABETICS ON TREATMENT WITHOUT ANY COMPLICATIONS), 25 SUBJECTS WERE TYPE 2 DIABETICS WITH NEPHROPATHY AND 25 WERE AGE AND SEX MATCHED NORMAL CONTROLS. SERUM AND URINE SIALIC ACID, LIPID PROFILE AND ANTHROPOMETRIC VARIABLES WERE MEASURED IN STUDY SUBJECTS.

RESULTS. SERUM AND URINE SIALIC ACID SHOWED A POSITIVE CORRELATION WITH TOTAL CHOLESTEROL TRIGLYCERIDES, LDL-C AND BODY MASS INDEX (P VALUE <0.001) WHICH WAS STATISTICALLY SIGNIFICANT IN BOTH TYPE 2 DIABETICS AND DIABETICS WITH NEPHROPATHY WHEN COMPARED WITH CONTROLS. SERUM AND URINE SIALIC ACID SHOWED A NEGATIVE CORRELATION WITH HDL-C(P VALUE <0.001) WHICH WAS STATISTICALLY SIGNIFICANT IN BOTH TYPE 2 DIABETICS AND DIABETICS WITH NEPHROPATHY WHEN COMPARED WITH

CONTROLS . SERUM AND URINE SIALIC ACID SHOWED NO CORRELATION WITH WAIST HIP RATIO IN BOTH TYPE 2 DIABETICS AND TYPE 2 DIABETICS WITH NEPHROPATHY.

CONCLUSION: LOW GRADE INFLAMMATION IS IMPLICATED IN THE CAUSATION AND PROGRESSION OF TYPE 2 DM AND ITS COMPLCATIONS. THE ESTIMATION OF SERUM AND URINE SIALIC ACID WILL INDICATE TISSUE DAMAGE AND THUS AID EARLY INTERVENTION IN HELPING TO PREVENT MICROVASCULAR COMPLICATIONS IN PEOPLE WITH TYPE 2 DIABETES MELLITUS.

KEYWORDS: DIABETES MELITUS, DIABETIC NEPHROPATHY, SIALIC ACID, BODY MASS INDEX, WAIST HIP RATIO

Introduction

Type 2 DM (Diabetes Mellitus) is a disorder resulting from deficiency of insulin secretion or decrease in its biological action or both and is associated with chronic hyperglycemia. ⁽¹⁾ Hyperglycemia observed in type 2 dm results in significant damage of different target organs ⁽²⁾

Low grade inflammation plays a potential role in the causation and progression of complications in type 2 DM. ⁽³⁾

Sialic acid [sa], a derivative of neuraminic acid, is an important constituent of glycolipids and glycoproteins. It acts as a co-factor of different cell receptors and is positively associated with most of the serum acute phase reactants which are considered as the indicators of microvascular angiopathy in type 2 DM ⁽⁴⁾ Sialic acid is present as the terminal sugar of the oligosaccharide chain in majority of the acute phase proteins (e.g. fibrinogen and haptoglobin) , thus sialic acid can be used as a measure of acute-phase response.⁽⁵⁾

“Serum sialic acid” is a recently recognized possible risk factor for the rise of “macro and microvascular complications of type 2 DM.”⁽⁶⁾

The present study aimed to correlate sialic acid levels with lipid profile, body mass index (BMI) and waist hip ratio (WHR) in type 2 diabetics and type 2 diabetics with nephropathy.

Materials and methods

The study population included the following groups:

Group I: Known cases of Type 2 DM without any complications (25)

Group II: Known cases of Type 2 diabetes mellitus with nephropathy (25)

Group III: Healthy controls who were age and sex matched (25)

Selection criteria:

Inclusion criteria: Known cases of type 2 dm without any complications and type 2 diabetics with nephropathy aged between 40-70 years.

Exclusion criteria: Subjects with history of inflammatory disorders, malignancy, alcohol intake, smoking , pregnancy and cardiac disease

Ethical considerations: Approval by the AJ Institute of Medical Sciences institutional ethical committee was obtained. The objectives of the study were explained to all eligible subjects who participated in the study. Informed consent was sought from all participants.

Sample collection: In all selected individuals 7 ml of blood was collected after 8-12 hours of fasting.

Blood was collected in EDTA vacutainer (2ml) and plain vacutainer (5ml). Serum was obtained after processing the blood collected in plain vacutainer. Urine (5ml) sample was also collected in a clean, dry and sterile container. - spot urine sample (single untimed urine sample voided spontaneously by the patient/anytime)

Serum and urine sialic acid: Measured by ehrlich's reagent in spectrophotometer using commercially available kits⁽⁷⁾

Total cholesterol (TC): Measured by enzymatic method chod-pap (cholesterol oxidase-peroxidase 4-aminoantipyrine) in semiautoanalyzer using commercially available kit⁽⁸⁾.

Triglycerides: Measured by enzymatic method GPO-ESPAS (glycerol 3 phosphate oxidase-peroxidase n-ethyl-n-sulfopropyl-n-anisidine) using commercially available kit in semiautoanalyser⁽⁹⁾

HDL-Cholesterol: Measured by enzymatic method after precipitation with polyanions in a semiautoanalyzer using commercially available kit⁽¹⁰⁾

LDL-c : Calculated by Friedewald formula⁽¹⁰⁾

LDL cholesterol mg/dl = Total cholesterol – [HDL cholesterol + Triglycerides/5]

BMI: Calculated as weight (kg)/ height² (m)

Waist circumference (WC): Measured in the midway section between the iliac crests and the lower margin of the ribs at minimal respiration.

Hip circumference (HC): Measured at the level of greater trochanter.

WHR: WC divided by the HC

Statistical analysis:

- Karl pearson correlation test was used to find the correlation sialic acid levels with lipid profile and anthropometric variables in type 2 diabetics without complications and in dn
- SPSS vs16 was used for the analysis of the data and Microsoft word and Excel have been used to generate tables .

Results and Discussion:

Table 1: Age distribution of the study groups

Groups	n	Mean age	S.D	Minimum	Maximum	F	P
Type 2 DM without any complications	25	49.8	±4.56	43	63	0.78	
Type 2	25	61.8	±4.16	53	68	<0.001	

diabetics with nephropathy							
Controls	25	53.2	±7.44	45	63	30.53	0.000

The mean age of type 2 diabetics without any complications was 49.8 ± 4.5 years with the range between 43- 63 years.

The mean age of subjects with type 2 diabetics with nephropathy was 61.8 ± 4.1 years with the range between 53- 68 years.

Mean age of healthy Controls was 53.2 ± 7.4 years with the range between 45- 68 years. Statistical significant difference in the mean age group was found between all the 3 groups ($p = 0.000$)

Table 2: Comparison of GLYCATED HAEMOGLOBIN between the study groups

Study groups	n	Mean	S.D	F	P
Type 2 DM without any complications	25	6.92	±1.40		
Type 2 diabetics with nephropathy	25	8.93	±2.35		
Controls	25	5.45	±0.50	29.62	<0.001

Glycated Haemoglobin levels in type 2 diabetics without any complications was 6.92 ± 1.40 , in type 2 diabetics with nephropathy was 8.93 ± 2.35 and in controls was 5.45 ± 0.50 .

Glycated Haemoglobin 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 ($p < 0.001$)

Table 3: Correlation between Serum sialic acid with lipid profile, BMI and WHR.in type 2 diabetics without complications.

Parameters correlated	r value	P value
Serum sialic acid Total cholesterol	0.96	<0.001
Serum sialic acid Triglycerides	0.92	<0.001
Serum sialic acid HDL Cholesterol	-0.73	<0.001
Serum sialic acid LDL Cholesterol	0.95	<0.001
Serum sialic acid BMI	0.78	<0.001
Serum sialic acid WHR	0.35	0.087

In type 2 DM, it showed a positive correlation between serum sialic acid and TC, TG, LDL-c and BMI which was statistically significant. Serum sialic acid showed a negative correlation with HDL-c which was statistically significant. Serum sialic acid showed no correlation with WHR (Table 3).

Table 4: Correlation between Serum sialic acid with lipid profile, BMI and WHR.in type 2 diabetics with nephropathy

Parameters correlated	r value	P value
Serum sialic acid	0.97	<0.001

Total cholesterol		
Serum sialic acid Triglycerides	0.86	<0.001
Serum sialic acid HDL Cholesterol	-0.90	<0.001
Serum sialic acid LDL Cholesterol	0.97	<0.001
Serum sialic acid BMI	0.90	<0.001
Serum sialic acid WHR	0.17	0.396

In type 2 diabetics with nephropathy it showed a positive correlation between serum sialic acid and TC, TG, LDL-c and BMI which was statistically significant. Serum sialic acid showed a negative correlation with HDL-c which was statistically significant. Serum sialic acid showed no correlation with WHR (Table 4)

Table 5: Correlation between urine sialic acid with lipid profile, BMI and WHR in type 2 diabetics without complications.

Parameters correlated	r value	P value
Urine sialic acid Total cholesterol	0.95	<0.001
Urine sialic acid Triglycerides	0.88	<0.001
Urine sialic acid HDL Cholesterol	-0.72	<0.001
Urine sialic acid LDL Cholesterol	0.94	<0.001
Urine sialic acid BMI	0.80	<0.001
Urine sialic acid WHR	0.31	0.128

In type 2 DM it showed a positive correlation with TC, TG, LDL-c and BMI which was statistically significant. Urine sialic acid showed a negative correlation with HDL-c which was statistically significant. Urine sialic acid showed no correlation with WHR. (Table 5)

Table 6: Correlation between urine sialic acid with lipid profile, BMI and WHR in type 2 diabetics with nephropathy.

Parameters correlated	r value	P value
Urine sialic acid Total cholesterol	0.96	<0.001
Urine sialic acid Triglycerides	0.88	<0.001
Urine sialic acid HDL Cholesterol	-0.88	<0.001
Urine sialic acid LDL Cholesterol	0.95	<0.001
Urine sialic acid BMI	0.92	<0.001
Urine sialic acid WHR	0.23	0.279

In type 2 diabetics with nephropathy it showed a positive correlation with TC, TG, LDL-c and BMI which was statistically significant. Urine sialic acid showed a negative correlation with HDL-c which was statistically significant. Urine sialic acid showed no correlation with WHR (Table 6)

DISCUSSION

Recent studies have shown an interrelationship between inflammation, adiposity and diabetes. Inflammatory markers may be used as a sensitive marker for the assessment of microvascular complications in type 2 DM .

In the present study, there was a significant positive correlation of sialic acid levels with TC. It showed a significant negative correlation with HDL-c in both type 2 DM and DN. Similar findings were found in a study conducted by Chen J et al⁽¹¹⁾.

Levels of sialic acid showed a significant positive correlation with TG and LDL-c in both type 2 DM and DN. Similar findings were observed in a study conducted by Nayak SB et al⁽¹²⁾.

Sialic acid also showed a positive correlation with BMI in both type 2 diabetics and type 2 diabetics with nephropathy. Similar observations were found in study conducted by Nayak SB et al⁽⁴⁾.

Serum sialic acid is a protein bound carbohydrate and occurs in combination with monosaccharides like galactose and mannose. Sialic acid can be used as a marker of the acute phase response because many of the proteins of the immune response are glycoproteins and these glycoproteins have sialic acid as terminal sugar on their oligosaccharide chain⁽¹³⁾

Sialic acid levels are elevated in pathological states whenever there is damage to tissues, defect in tissue proliferation and inflammation⁽¹⁴⁾ Sialic acid levels are increased in type 2 diabetes suggesting that these elevations reflect the pathogenic processes involved in diabetes⁽¹⁵⁾ Insulin is known to be an anabolic hormone and one of its actions is to increase acute phase proteins. Therefore in type 2 diabetes the insulin resistance / hyperinsulinemia causes an acute phase response.

Hyperglycemia promotes inflammation by increasing oxidative stress⁽¹⁶⁾

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 liver into general circulation again leading to increased SSA concentration which inturn increases urinary excretion of sialic acid⁽⁵⁾

Dyslipidemia and obesity are the cardiovascular risk factors. Hence these patients may have underlying microvascular complications and this may explain the correlation of sialic acid with lipid profile and anthropometric indices.

CONCLUSION

The present study showed a statistically significant positive correlation between sialic acid levels with TC, TG, LDL-c and BMI. A statistically significant negative correlation was seen between sialic acid level with HDL-c. There was no correlation between sialic acid level with WHR .

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227 ABBREVIATIONS

228 BMI- Body Mass Index

229 DM- Diabetes Mellitus

230 DN- Diabetic Nephropathy

231 HC-Hip Circumference

232 HDL-c -High Density lipoprotein - cholesterol

233 KP-Karl Pearson

234 LDL-c- Low Density Lipoprotein- cholesterol

235 TC- Total Cholesterol

236 TG-Triglycerides

237 WC-Waist Circumference

238 WHR-Waist Hip Ratio