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ORIGINAL RESEARCH

STUDY OF SIALIC ACID AND NITRIC OXIDE IN TYPE 2 DIABETES MELLITUS WITH AND WITHOUT DIABETICNEPHROPATHY

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ABSTRACT

Background:In diabetes, acute phase reactants are taken into consideration to be diagnostic indications of both microvascular angiopathy and cardiovascular mortality. The chemical sialic acid is an example of one of these acute phase reactants. A deficiency in the amount of bioavailable nitric oxide has been hypothesised to be responsible for the endothelial dysfunction that is commonly linked with diabetes. It has been demonstrated that the vasodilatation that is dependent on NO plays a crucial role in the regulation and maintenance of vascular tone in renal microcirculation.Objectives:1.To evaluate and compare concentrations of serum sialic acid, nitric oxide, glycated haemoglobin, serum lipid profile (TC, TG, LDL, HDL), Urinary Albumin Creatinine Ratio (UACR) in diabetic patients with and without nephropathy and healthy controls.2.To correlate serum sialic acid with glycated haemoglobin, lipid profile, and UACR in diabetics with and without nephropathy.3.To correlate serum nitric oxide with glycated haemoglobin, lipid profile, UACR in diabetics with and without nephropathy.

Materials and Methods: 80 subjects participated. 40 healthy individuals and 80 diabetics were studied. Diabetes with nephropathy and diabetes without nephropathy were each 40 cases. Serum sialic acid was quantified by Ehrlich's reagent, serum nitric oxide by Kinetic cadmium reduction, serum glycated haemoglobin and urine microalbumin by immunoturbidimetric, urinary creatinine by modified Jaffee's method, and TC, TG, HDL by enzymatic methods. Friedewald's formula found LDL.

Results: Age of controls was 51.0 6.8 years, diabetic cases were 53.0 7.5 years, and diabetic nephropathy was 52.5 7.5 years. In the 40 controls, 22 were male and 18 were female. 19 of the 40 diabetic patients were male and 21 were female. 19 of the 40 diabetic nephropathy patients were male and 21 were female. There was no significant difference between the sex distribution of controls and cases ($p>0.05$). The mean concentrations of all the parameters except serum nitric oxide and HDL were

significantly increased in cases when compared with healthy controls. Sialic acid showed a positive correlation with glycated haemoglobin, lipid profile, and UACR. HDL showed a negative correlation. Nitric oxide showed a negative correlation with glycated haemoglobin, lipid profile, UACR. HDL showed a positive correlation.

Conclusion: Serum sialic acid and nitric oxide are indicators of diabetes and diabetic nephropathy, according to the study. Dyslipidemia and glycemic control are affected. Early measurement of sialic acid and nitric oxide helps reduce diabetes complications.

Keywords: Sialic acid; nitric oxide; endothelial dysfunction; UACR.

INTRODUCTION

Diabetes is a diverse set of conditions that are characterised by varying degrees of insulin resistance, decreased insulin secretion, and elevated glucose production. Diabetes is classified as a heterogeneous range of ailments.[1] Diabetes affects 31.7 million people in India. Diabetes is a major health problem in India. Patients with diabetes typically have type 2 diabetes mellitus. This accounts for 90% of all diabetic patients. Nephropathy caused by diabetes is the leading cause of end-stage renal disease and the morbidity and death associated with it.[2-4]

The inflammatory processes play a significant part in the progression of diabetes as well as the late consequences of the disease. The evaluation of diabetic patients' microvascular problems, such as diabetic nephropathy and cardiovascular risk factors, can benefit from the measurement of inflammation-sensitive markers.[5] The markers of inflammation are called acute phase reactants, or APRs for short. They are produced as a reaction to the inflammation and damage that has occurred to the tissue. During an inflammatory response, the typical levels of their concentration are multiplied by a factor of a thousand.[6]

Because many acute phase proteins are glycoproteins, and glycoproteins have sialic acid as the terminal sugar of their oligosaccharide chains, serum sialic acid can be used as a marker of the acute phase response. It is generated in the liver as a response to the stimulation of pro-inflammatory markers.[7] For the reason that the vascular endothelium carries a high concentration of sialic acid, significant microvascular damage brought on by diabetes may be responsible for its release into the circulation. Because of this, there is an increase in vascular permeability as well as an overall increase in the quantities of serum sialic acid.[7]

A recently discovered possible risk factor for the development of macro- and microvascular complications of diabetes is serum sialic acid. These issues can arise from diabetes. In addition to this, it is a very reliable indicator of passing away from cardiovascular disorders.[8]Nitric oxide isthe most powerful endogenous vasodilator that may be produced by the body. In the kidney, it regulates the vascular tone of both the afferent and efferent blood vessels, as well as the ultrafiltration coefficient and medullary blood flow.[9] Due to insulin exerting its influence over the activation of nitric oxide synthase (NOS) via the Akt pathway, the proper regulation of this metabolic process is essential in the management of type 2 diabetes (Activated tyrosine kinase B transfer pathway). Consequently, diabetes is associated with a dysfunction in the metabolism of nitric oxide.[10]

This particular study is being carried out to evaluate the levels of serum sialic acid and nitric oxide concerning glycated haemoglobin, microalbuminuria, and lipid profile (total

cholesterol, triglycerides, low-density lipoproteins, and high-density lipoproteins) in diabetic patients with and without nephropathy.

Aims and objectives

1. To evaluate and compare concentrations of serum sialic acid, nitric oxide, glycated haemoglobin, serum lipid profile (TC, TG, LDL, HDL), and Urinary Albumin Creatinine Ratio between diabetic patients with and without nephropathy and healthy controls.
2. To correlate serum sialic acid with glycated haemoglobin, Lipid profile, UACR in diabetes with and without nephropathy patients.
3. To correlate serum nitric oxide with glycated haemoglobin, Lipid profile, UACR in diabetes with and without nephropathy patients.

MATERIALS & METHODS

A cross-sectional study was carried out for 1 year. This study was done to compare the levels of serum sialic acid, nitric oxide, HbA1c, and lipid profile in type 2 diabetes mellitus with and without nephropathy and healthy controls.

Type 2 diabetes mellitus patients were selected from M.G.M Hospital (Both the hospitals were attached to Kakatiya Medical College and healthy controls from the general population. Written informed consent was taken from the study subjects.

A. Selection of Study Subjects:

Based on inclusion and exclusion criteria a total number of 80 subjects (30 controls and 60 cases) were selected for the present study.

Inclusion criteria:

The present study included 80 subjects of which 30 were controls and 60 were cases. There were three groups in the study.

- Group1 - Normal healthy controls
- Group 2 - Diabetes patients without nephropathy
- Group 3 - Diabetes patients with nephropathy

Type 2 diabetics with microalbuminuria were included in the diabetic nephropathy.

Exclusion criteria:

Patients with the following diseases were excluded from the study

- Type1 diabetes mellitus
- Inflammatory disorders like eczema
- Secondary hyperglycemic states like hypothyroidism
- Proteinuric conditions like congestive cardiac failure, renal failure, pregnancy,
- Female patients with menstrual disorders,
- Heavy smokers (more than one pack of cigarettes per day)

Collection of blood and urine samples:

5 ml of venous blood was drawn from all the subjects (from a large peripheral vein) in fasting condition under aseptic precautions, using a sterile disposable syringe. Out of 5ml, 4 ml of blood was transferred to plain vacutainer and the remaining 1ml into EDTA containing vaccutainer. 4 ml of blood in plain vaccutainer was allowed to clot, centrifuged and then serum was separated. Morning sample of urine was also collected under aseptic precautions in sterile containers and centrifuged.

B. Parameters measured in the study subjects:

Following parameters were measured in the present study

- Serum sialic acid by Ehrlich‟s reagent method.
- Serum nitric oxide by Kinetic Cadmium-Reduction method
- Serumglycatedhaemoglobinandurinary microalbumin by Immunoturbidimetric method.
- Serum total cholesterol & triglycerides by Enzymatic cholesterol oxidase – Phenol aminoantipyrine method.
- Serum HDL by Phosphotungstic acid and enzymatic cholesterol oxidase- phenol aminoantipyrine (CHOD-PAP) method
- Serum LDL by using Friedewald‟s formula
- Urinary creatinine by modified Jaffe‟s method
- Urinary albumin creatinine ratio

RESULTS

The present study included 80 subjects of which 40 were normal healthy controls and 40 were cases. There were three groups in this study

- Group1 - Normal healthy controls
- Group 2 - Diabetic patients without nephropathy
- Group 3 - Diabetic patients with nephropathy

Table 1: Age distribution among controls and cases

Groups	**Mean ± SD**	**Range**
1.Controls	51.0 ± 6.8	40 - 65
2.Diabetes	53.0 ± 7.5	40 - 68
3.Diab.Nepphropathy	52.5 ± 5.5	45 -63
ANOVA	F	0.78
	p	0.47, ns

Age of controls was 51.0 ± 6.8 years, diabetic cases was 53.0 ± 7.5 years, diabetic nephropathy was 52.5 ± 7.5 years. There was no significant difference between the age of controls and cases (p value>0.05).

Table 2: Sex distribution among controls and cases.

Groups	Males	Females	Total
	n (%)	n (%)	n (%)
1.Controls	22 (56.7)	18 (43.3)	40 (100)
2.Diabetes	19 (46.7)	21 (53.3)	40 (100)
3.Diab.Nepphropathy	24 (63.3)	16 (36.7)	40 (100)

Among the 40 controls 22 were males and 18 were females. Among the 40 diabetic patients 19 were males and 21 were females. Among the 40 diabetic nephropathy patients 19 were males and 21 were females. There was no significant difference between the sex distribution of controls and cases (p value>0.05).

Table 3: Comparison of Serum Sialic acid, Serum Nitric Oxide, Urinary Albumin Creatinine Ratio among controls and cases

			Serumsialic acid mmol/l	Serum Nitric Oxide µmol/l	UACRmg/gm of creatinine	Serum HBA1c%
1.Controls		Mean ±SD	1.95 ± 0.65	40.42 ± 8.70	14.25 ± 4.12	5.06±0.65
		Range	0.76-2.55	23.3 – 57.5	2.05 - 24.51	3.69-6.05
		Mean ±SD	2.61±0.014	27.25 ± 0.65	18.03 ± 5.46	6.45±0.65
2. Dibetes		Range	2.61-2.65	26.5 -29.2	7.88 -27.22	5.24-7.65
3. Diabeticnephropathy		Mean±SD	3.51±0.32	22.56 ± 2.45	141.28 ±66.00	8.50±1.25
		Range	2.5-3.59	17.7 - 26.55	42.1 – 28.12	6.0-10.3
ANOVA		F	67.55	89.87	102.90	124.161
		p	P < 0.001	P < 0.001	P < 0.001	P < 0.001
Groups Compared	1 v/s 2	Mean diff	0.67	11.50	3.55	1.28
		p Value	P < 0.001	P < 0.001	0.92 (p > 0.05)	P < 0.001
	1 v/s 3	Mean diff	1.12	17.55	126.89	3.71
		p Value	P < 0.001	P < 0.001	P < 0.001	P < 0.001
	2 v/s 3	Mean diff	0.68	5.25	121.85	2.55
		p Value	p < 0.001	P < 0.05	P < 0.001	P < 0.001

Concentration of serum sialic acid in controls (Group 1) is 1.95 ± 0.65 mmol/l, in diabetic patients without nephropathy (group 2) is 2.61 ± 0.014 mmol/l and in diabetic patients with nephropathy (group 3) is 3.51±0.32 mmol/l.

There is highly significant raise in serum sialic acid when comparisons made between all the three groups (P < 0.001).

Concentration of serum nitric oxide in group 1 is 40.42 ± 8.70 µmol/l, in group 2 it is 28.12 ±0.66 µmol/l and in group 3 it is 22.96 ± 2.45 µmol/l.

There is highly significant decrease in levels of serum nitric oxide in group 2 and 3 as compared to group 1 (P < 0.001). But the decrease is only significant when compared between group 2 and 3. (p < 0.05).Concentration of Urinary Albumin Creatinine Ratio (UACR) in group 1 is 14.25 ± 4.12 mg/gm of creatinine, in group 2 is 18.23 ± 5.96 mg/ gm of creatinine andin group 3 is 141.28 ±66.00 mg/ gm of creatinine.

There is highly significant raise in the UACR in group 3 as compared to group 1 and 2 (p <0.001). But there is no significant difference between group1 and group 2 (p > 0.05).Concentration of serum HbA1c in group 1 is 5.06±0.65%, in group 2 it is 6.45±0.65% and in group 3 it is 8.50±1.25 %. There is highly significant raise in HbA1c when comparisons made between all the three groups (p < 0.001).

Table 4: Comparison of TC, TG, LDL, HDL among controls and cases

			Ser. Total Cholesterol mg/dl	**Ser. Triglycerides mg/dl**	**Ser. High density Lipoprotein mg/dl**	**Ser. low Density Lipoproteins mg/dl**
1.Controls	Mean±SD		156.48 ±10.11	119.55 ± 7.67	71.15 ± 6.18	61.21±11.65
	Range		136.24-182.88	105.9 - 136.06	57.27-71.06	41.55 -92.68
2.Dibetes	Mean±SD		218.08 ± 6.25	235.38 ± 15.26	41.61 ± 2.40	126.72±6.35
	Range		205.2 - 230.67	219.98 - 265.45	35.00 -46.75	110.11-137.06
3.Diaetc nephropathy	Mean±SD		252.84 ± 15.55	316.98 ±5.22	36.02 ± 3.03	156.56±17.05
	Range		240-245.98	303.7 – 325.81	30.0 - 45.59	133.6 - 199.66
ANOVA	F		556.30	2868.029	569.82	457.269
	p		< 0.001	< 0.001	< 0.001	< 0.001
Groups compared	1 v/s 2	Mean diff	60.00	125.7	28.94	63.81
		P Value	< 0.001	< 0.001	< 0.001	< 0.001
	1 v/s 3	Mean diff	99.25	197.29	35.55	95.42
		P Value	< 0.001	< 0.001	< 0.001	< 0.001
	2 v/s 3	Mean diff	39.36	71.6	6.51	31.55
		P Value	< 0.001	< 0.001	< 0.001	< 0.001

p > 0.05 Nothing Significant, p < 0.05 Significant, p< 0.001 Highly Significant

Concentration of serum total cholesterol in controls (group 1) is 156.48 ±10.11 mg/dl, in diabetic patients without nephropathy (group 2) it is 218.08 ± 6.25 mg/dl and in diabetic patients with nephropathy (group 3) it is 252.84 ±15.55 mg/dl.Concentration of serum triglycerides in group1 is 119.55 ± 7.67 mg/dl, in group 2 it is 235.38 ± 15.26 mg/dl and in group 3 it is 316.98±5.22 mg/dl.Concentration of serum High density Lipoprotein (HDL) in group 1 is 71.15 ± 6.18 mg/dl, in group 2 it is 41.61 ± 2.40 mg/dl and in group 3 it is 36.02 ± 3.03 mg/dl.Concentration of serum Low density Lipoprotein (LDL) in group 1 is 61.21 ±11.65 mg/dl, in group 2 it is 126.72 ±6.35 mg/dl and in group 3 it is 156.56±17.05 mg/dl.

There is highly significant raise in Serum TC, TG, LDL when comparisons aremade between all the three groups (p < 0.001). There is highly significant decrease in serum HDL in group 3 as compared to group 1 and 2 (p < 0.001).

Table 5: Correlation of serum sialic acid and nitric oxide with different parameters.

Correlation Analysis: Diabetic Group (With & Without Nephropathy)				
Variable	**Relationship with Sialic Acid**		**Relationship with Nitric Oxide**	
	rvalue	**p value**	**rvalue**	**p value**
S.HbA1c%	0.72	$p < 0.001$	-0.78	$p < 0.001$
STCmg/dl	0.75	$p < 0.001$	-0.86	$p < 0.001$
S Tri mg/dl	0.89	$p < 0.001$	-0.85	$p < 0.001$
S. HDL mg/dl	-0.75	$p < 0.001$	0.83	$p < 0.001$
S.LDLmg/dl	0.69	$p < 0.001$	-0.85	$p < 0.001$
UACRmg/gm	0.98	$p < 0.001$	-0.92	$p < 0.001$

r: Pearson's Correlation Coefficient, $p < 0.05$ – Significant, $p < 0.001$ - Highly Significant, -ve sign indicates inverse relationship

Serum sialic acid is positively correlated with all the parameters except HDL which shows negative correlation.

Serum nitric oxide is inversely correlated with all the parameters except HDL which shows positive correlation. All the correlations are highly significant ($p < 0.001$).

DISCUSSION

Nephropathy caused by diabetes is the major cause of death among patients with end-stage renal disease (ESRD).[7]The inflammatory process is a significant contributor to the progression of diabetes and the development of its late consequences. In diabetic patients, measuring inflammatory markers can be helpful in determining the extent of their risk for cardiovascular disease.[5]Acute phase reactants, often known as APRs, are indicators of inflammation. They are produced as a reaction to the damage done to the tissue and the inflammation that it causes. 6Because many acute phase proteins are glycoproteins, and sialic acid serves as the terminal sugar of their oligosaccharide chain, serum sialic acid can be used as a marker for the acute phase response.[7]Nitric oxide is the most powerful vasodilator that the body naturally produces. In the kidney, it regulates ultrafiltration coefficient and medullary blood flow in addition to controlling the afferent and efferent vascular tone.[9]Because insulin controls the activation of NO oxide synthase via the Akt pathway, the regulation of this metabolic process is critical in type 2 diabetes.

(Activated Tyrosine Kinase B Transfer pathway). Thus an impaired metabolism of nitric oxide is found in diabetes.[10]

This study is undertaken for assessment of sialic acid, nitric oxide, glycated hemoglobin, serum lipid profile (TC, TG, HDL, LDL) and urinary microalbumin and creatinine in diabetes and diabetic nephropathy patients. The present study included 80 subjects of which 30 are normal healthy controls and 60 are cases. There are three groups in the present study

- Group 1 - Normal healthy controls
- Group 2 – Diabetic patients without nephropathy
- Group 3 – Diabetic patients with nephropathy

Serum Sialic Acid

Concentration of serum sialic acid in group 1 is 1.95±0.65 mmol/l, in group 2 it is 2.61 ±0.014 mmol/l and in group 3 it is 3.11 ± 0.34 mmol/l.

In the present study it is found that the mean levels of serum sialic acid is significantly increased in diabetic nephropathy as compared to diabetic patients without nephropathy and controls. It is also significantly raised in diabetic people without nephropathy as compared to controls ($p<0.001$ in 1 v/s 2, 1 v/s 3, 2 v/s 3 comparisons). These findings are in accordance with the studies by Mahajan V V et al 6.

Serum Nitric Oxide

Concentration of serum nitric oxide in group 1 is 40.42 ± 8.70 μmol/l ; in the group 2 it is27.25 ± 0.65 μmol/l and in the group 3 it is22.56 ± 2.45 μmol/l.

In this study it is found that serum nitric oxide is very significantly decreased in diabetics without nephropathy and diabetics with nephropathy when compared with healthy controls ($p<0.001$ in group 1 v/s group 2 and group 1 v/s group 3 comparison) But the decrease is onlysignificant in diabetics with nephropathy when compared with diabetics without nephropathy ($p<0.05$ in group 2 v/s group 3 comparison). These findings are in accordance with the studies by TessariPet al.[10]

The NO is a paracrine mediator acting as a potent vasodilator in various vascular beds. In the kidney, NO controls both afferent and efferent vascular tone, the ultrafiltration coefficient and medullary blood flow.[9]

The low production of nitric oxide during diabetes and diabetic nephropathy is supposed to be the consequence of

- Reduced production by NOS
- Inactivation of nitric oxide by reactive oxygen species (ROS) produced by glycosylated proteins.[9]

In diabetes and diabetic nephropathy NO dependent vasodilatation is unresponsive in both renal cortical and papillary microcirculations of the kidney. Thisleads to the higher susceptibility of diabetic kidney to vasoconstrictor stimuli leading to pappillary necrosis and proteinuria. The causes for unresponsiveness are lower sensitivity of vascular smooth muscle cells to nitric oxide, increased production of nitric oxide antagonists such as endothelin 1 and quenching of nitric oxide by advanced glycation products.[9]

Serum Glycated Hb

The concentration of HbA1c in the serum of those in group 1 is 5.060.65 percent, whereas those in group 2 have a concentration of 6.450.65 percent, and those in group 3 have a concentration of8.501.25 percent. In the current investigation, it was discovered that diabetic patients, both with and without nephropathy, had considerably higher levels of serum glycated haemoglobin compared with the control group. It is also considerably elevated among diabetics who have nephropathy in comparison to diabetics who do not have nephropathy (the p value for the comparison of group 1 versus group 2, group 1 versus group 3, and group 2 versus group 3 is less than 0.001) Thefindings presented here are consistent with the research carried out by Sabjawari MJ et al.[5] There is a substantial positive association between HbA1c and sialic acid, with a value of r equal to 0.71 and a significance

level of p 0.001. The findings presented here are consistent with the research carried out by Shahid M. Set al.[8] There is a statistically significant inverse relationship between the haemoglobin A1c level and nitric oxide (r value = -0.81, p 0.001) These findings are consistent with the research carried out by Mohamed HM et al.[11]The concentration of glucose in the plasma is the most critical component that plays a role in determining the amount of glycated haemoglobin that is produced. Glycated haemoglobin levels in diabetic individuals increased in tandem with the rise in plasma glucose concentration. Better than fasting blood glucose concentrations or the results of glucose tolerance tests, it shows the mean daily blood sugar concentration and the degree of carbohydrate imbalance.[1]

Serum Lipid Profile

Serum total cholesterol

The concentration of serum total cholesterol in group 1 is 156.48 10.11 mg/dl, the concentration is218.08 6.25 mg/dl in group 2, and the concentration is 252.84 15.55 mg/dl in group 3. In the current investigation, it was discovered that diabetic patients, both with and without nephropathy, have considerably elevated levels of serum TC when compared with controls. It is also considerably elevated among diabetics who have nephropathy in comparison to diabetics who do not have nephropathy (the p value for the comparison of group 1 versus group 2, group 1 versus group 3, and group 2 versus group 3 is less than 0.001) These findings are consistent with those found in the research carried out by J. C. Pickup et al.14. The value of r for this connection is 0.78, and the significance level is more than 0.001. These findings are consistent with the research carried out by Usman K et al.[15]The value of r is -0.85, and the association between TC and NO is statistically significant (p 0.001). Both diabetes and diabetic nephropathy are associated with an increase in serum cholesterol concentration for a number of different reasons. These include an impairment in the overstimulation of the HMG COA reductase enzyme by glucagon, a defect in the catabolism of cholesterol into bile acids, and an increase in the accumulation of VLDL in the blood, which contain 20 percent of the total lipid content as cholesterol.[16]

Serum triglycerides

The concentration of serum triglycerides in group 1 is 119.55 7.67 mg/dl, in group 2 it is 235.3815.26 mg/dl, and in group 3 it is 316.98 5.22 mg/dl. In the present study, it is found that serum triglyceride is significantly raised in diabetics with and without nephropathy when compared withcontrols. It is also significantly raised in diabetics with nephropathy when compared with diabetics without nephropathy (p value is 0.001 in group 1 v/s 2, group 1 v/s 3, group 2 v/s 3 comparison). These findings are in accordance with the studies by Sabjavari MJ et al. There is a significant positive correlation between TG and sialic acid (r value of 0.69, p 0.001). These findings are in accordance with studies by Adullaet al.[17] There is a significant negative correlation between TG and NO (r value is -0.82, p 0.001). The causes of increased serum triglyceride concentration are an increase in hepatic lipase activity and a decrease in lipoprotein lipase activity. The increase in hepatic lipase activity is responsible for the increased synthesis of TG in the liver, whereas the decreased activity of lipoprotein lipase is responsible for the decreased catabolism of TG at the tissue level. Uptake of the

VLDL remnants by the liver is found to be delayed, leading to increased serum TG concentration.[18]

Serum HDL cholesterol:

The concentration of serum High density lipoprotein (HDL) in group 1 is 71.15 6.18 mg/dl, in group 2 it is 41.61 2.40 mg/dl, and in group 3 it is 36.02 3.03 mg/dl. In this study, it is found that serum HDL is significantly decreased in diabetics with and without nephropathy when compared with healthy controls. It is also significantly reduced in diabetics with nephropathy when compared with diabetics without nephropathy. In the comparisons of group 1 vs. 2, group 1 vs. 3, and group 2 vs. 3, the p value is 0.001). These findings are in accordance with studies by J.C. Pickup et al.14. The increase of plasma triglycerides drives the exchange of core lipids between VLDL and HDL particles. There is increased cholesterol ester transfer protein (CETP)-mediated transfer of esterified cholesterol to VLDL and of triglycerides to the HDL particles, resulting in the triglyceride enrichment of the latter. Triglycerides in HDL are a good substrate for hepatic lipase, and the hydrolysis produces smaller HDL particles and free apoAI, which is excreted by the kidneys. The catabolic rate of small HDL particles is faster than that of normal HDL, resulting in a reduced number of circulating HDL particles. 19The protective effect of HDL is attributed mainly to its role in reverse cholesterol transport, but other HDL properties (anti-inflammatory, antioxidant, antithrombotic, etc.) may also be involved. It can be said that the smaller size and lower concentrations of HDL seen in diabetic dyslipidemia contribute to the higher risk of heart disease intype2diabetics.[19]

Serum LDL cholesterol

Low density lipoprotein (LDL) concentration in group 1 is 61.21 11.65 mg/dl, whereas the concentration in group 2 is 126.72 6.35 mg/dl, and the concentration in group 3 is 156.5617.05 mg/dl. When compared with controls, the levels of serum LDL were discovered to be considerably higher in diabetic patients both with and without nephropathy in the current investigation. In diabetic patients who have nephropathy, the level is likewise much higher than in diabetic patients who do not have nephropathy. (the p value for the comparison of group 1 to group 2, group 1 to group 3, and group 2 to group 3 is less than 0.001) These findings agree with those that were found by Sabzwari MJ et al5. The value of r for this connection is 0.79, and the significance level is more than 0.001. According to research carried out by Abdulla et al.[15] and Nayak BS et al,[20] this holds true. There is a statistically significant inverse relationship between LDL and NO (r value = -0.83, p 0.001). The raised LDL cholesterol concentration can be attributed to a number of factors, including increased cholesterol synthesis, decreased HDL cholesterol concentration, and decreased HDL-mediated reverse cholesterol transfer. An increase in triglycerides may be one of the factors that leads to an increase in the development of small dense LDL, an atherogenic variation of the LDL particle.[21]

Microalbuminuria

The concentration of urinary albumin creatinine ratio (UACR) in group 1 is 14.25 4.1 mg/gm of creatinine, while the concentration of UACR in group 2 is 18.03 5.46 mg/gm of creatinine,

and the concentration of UACR in group 3 is 141.28 66.00 mg/gm of creatinine.The findings of this study indicate that the UACR is significantly elevated in diabetic nephropathy as compared to diabetics who did not have nephropathy as well as controls. On the other hand, there is not a discernible difference in UACR between diabetics who do not have nephropathy and controls. (p 0.001 in the comparison of group 1 to group 3, 2 to group 3, and p 0.05 in the comparison of group 1 to group 2) This is consistent with the findings of research conducted by Sabzwari MJ et al.[5] The value of the association betweenmicroalbuminuria and sialic acid is 0.87, and the associated significance level is more thanthe findings of the research done by Mahajan VV et al,[6] align with this conclusion.Microalbuminuria and NO had a statistically significant inverse connection (r-value = -0.92, p 0.001).Microalbuminuria is a significant risk factor for cardiovascular disease as well as increasing kidney damage in people who have diabetes. It is caused by an increase in the amount of albumin that can flow through the glomerular filtration barrier. Disruption of the endothelium glycocalyx is the element of this injury that is considered to be the most significant. The elevated levels of reactive oxygen species (ROS), vascular endothelial growth factor (VEGF), and proinflammatory cytokines that are created as a result of diabetes's hyperglycemia are among the causes.[22]

CONCLUSION

The findings of this research make it abundantly clear that the indicators for diabetes and diabetic nephropathy are elevated levels of serum sialic acid as well as nitric oxide. Controlling one's blood sugar and dyslipidemia are both affected by their levels. Taking readings of sialic acid and nitric oxide early on in the course of diabetes treatment is beneficial for reducing the progression of the disease as well as the development of complications.

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