

Serum sialic acid and microalbuminuria in non insulin dependent diabetes mellitus

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Abstract

Serum sialic acid, an acute phase reactant and urinary albumin excretion are found to be increased in various conditions like diabetes mellitus, cardiovascular diseases, cancer etc. In diabetes mellitus, acute phase reactants are considered as the indicators of microvascular angiopathy. Therefore, the present study was undertaken to understand the potential association of serum sialic acid levels in diabetic process and to assess the correlation between serum sialic acid concentration and microalbuminuria. 85 non-insulin dependent diabetes mellitus (NIDDM) patients were studied for their urinary albumin, serum sialic acid, fasting serum glucose and serum creatinine levels. Analysis was performed by categorizing them based on their albumin excretion (normoalbuminuric & microalbuminuric). 40 non-diabetic healthy subjects were chosen as a control group.

Analysis showed 49 (57.6%) subjects had normoalbuminuria and 36 (42.3%) had microalbuminuria. Serum sialic acid concentrations found to be elevated in NIDDM (2.58 mmol/L) patients when compared to controls (1.95 mmol/L) and more so with microalbuminuric (2.77 mmol/L). There is a progressive rise in serum sialic acid levels with increase in urinary albumin excretion in NIDDM patients. Therefore, sialic acid can be of useful parameter to follow up the diabetic process.

Key words: Microalbuminuria, Serum sialic acid, Diabetes mellitus.

Accepted September 21 2010

Introduction

Diabetes mellitus is the most common endocrine disorder, the prevalence of which is rising alarmingly in India [1]. The International Diabetes Federation (IDF) estimates the total number of diabetic subjects in India to be around 40.9 million and this is further set to rise to 69.9 million by the year 2025 [2]. Diabetes mellitus is characterized by metabolic abnormalities and on long term with micro and macro vascular complications that cause significant morbidity and mortality among diabetic subjects [3]. Various acute phase reactants are being studied in diabetic process as indicators or predictors of diabetic microvascular complications. Serum sialic acid has been found to be an acute phase reactant [4] and its estimation in NIDDM is very little emphasized. Hence this study was undertaken to find the levels of serum sialic acid in NIDDM.

Diabetic nephropathy occurs in about 25-30% of diabetic patients. However, there is an early phase of diabetic renal disease called incipient diabetic nephropathy characterized by increased albumin excretion in the

range of 30-200 mg/l (microalbuminuria). At this stage urine is negative for standard dipsticks and renal function is normal by standard clinical tests but can be detectable only by the use of sensitive assay [5]. Incipient diabetic nephropathy has been proved to be reversible with tight glycemic control and ACE inhibitors [6]. Therefore, we intended to correlate serum sialic acid with microalbuminuria which is a marker of early renal damage to establish the role of estimation of serum sialic acid in NIDDM.

Materials and Methods

This study was under taken in the department of biochemistry, J J M medical college, Davangere, after the approval of the research and ethical committees. The established NIDDM patients attending the OPD of the Bapuji hospital, Davangere were tested for urinary albumin by albustix method. Urinary albumin positive subjects were excluded and albustix negative NIDDM patients which constituted 85 were recruited into the study. Patients with inflammatory disorders like eczema, secondary hyperglycemic states like hypothyroidism,

proteinuric conditions like congestive cardiac failure, renal failure and pregnancy were excluded. Female patients with menstrual disorders were also excluded anticipating the presence of non specific inflammation. 40 healthy age matched volunteers were chosen as controls. A total of 125 subjects were studied. Fasting serum samples and urinary samples were collected from all the study subjects. Urinary albumin was quantitated using an ELISA kit [7] (UBI MAGIWEL, Enzyme Immuno Assay Microalbumin, US). Serum sialic acid was estimated by Thiobarbituric acid assay of Warren [8]. Fasting serum glucose and serum creatinine was estimated in an autoanalyser by glucose oxidase method [9] and Jaffe's method [10] respectively. Quantitative data summarized to test the difference in mean values obtained for NIDDM patients and controls using student 't' test, p value < 0.05 is taken as the level of significance. Further, Pearson's correlation was used to correlate between the different parameters.

Results

The study included 40 controls (21 males, 19 females) and 85 diabetics (50 males, 35 females). Both cases and controls were aged between 30 to 70 years. Results are shown in the tables 1, 2 and 3. Table 1 shows the Mean croalbumin excretion and sialic acid.

± SD of serum sialic acid levels, albumin excretion, mean fasting serum glucose and serum creatinine in controls and NIDDM patients. All the parameters were found to be elevated in NIDDM patients. Table 2 shows the categorization of NIDDM patients into normo and microalbuminurics based on their albumin excretion. Among 85 NIDDM patients, 49 (57.6%) subjects had normoalbuminuria and 36 (42.3%) had microalbuminuria. Serum sialic acid levels show a progressive rise with the urinary albumin excretion (1.95 ± 0.28 , 2.45 ± 0.32 & 2.77 ± 0.39 in controls, normoalbuminurics & microalbuminurics respectively), where as serum creatinine showed significant increase only in microalbuminuric patients. It can also be noted that serum sialic levels show significant difference between controls and normoalbuminuric patients ($p < 0.001$) where as serum creatinine and albumin excretion levels shows no statistical difference. It is also seen that diabetic duration was more with microalbuminurics (12.0 ± 4.4 years vs 6.3 ± 4.4 years in normoalbuminurics). Fasting glucose levels showed no significant difference in their levels when compared between the normo & microalbuminurics (2.45 ± 0.32 & 2.77 ± 0.39 mg/dl respectively). Table 3 show the Pearson's correlation between the parameters. There is a significant positive correlation between mi

Table 1. Comparison of parameters between diabetic patients and healthy controls

Parameters	Groups		p value
	Controls	Diabetics	
Microalbumin (mg/l)	10.3 ± 5.3	48.8 ± 49.8	< 0.001 (HS)
Fasting serum glucose (mg/dl)	90.9 ± 11.3	186.5 ± 62.5	< 0.001 (HS)
Serum creatinine (mg/dl)	1.24 ± 0.33	1.60 ± 0.50	< 0.01 (S)
Serum sialic acid (mmol/l)	1.95 ± 0.28	2.58 ± 0.40	< 0.001 (HS)

The values are expressed as their Mean ± SD

HS – Highly significant; S – Significant; NS – Not significant

Table 2: Showing the comparison of parameters between controls, normo- and microalbuminurics

Parameters	Groups			p-value		
	Controls (n = 40)	Normo-albuminurics (n = 49)	Micro-Albuminurics (n = 36)	Controls v/s Normoalbuminurics	Controls v/s Microalbuminurics	Normoalbuminurics v/s Microalbuminurics
Microalbumin (mg/l)	10.3 ± 5.3	10.9 ± 5.3	100.5 ± 33.8	0.55 (NS)	< 0.001 (HS)	< 0.001 (HS)
Fasting serum glucose (mg/dl)	90.9 ± 11.3	182.7 ± 63.9	188.8 ± 59.2	< 0.001 (HS)	< 0.001 (HS)	0.65 (NS)
Serum creatinine (mg/dl)	1.24 ± 0.33	1.40 ± 0.47	1.81 ± 0.45	0.08 (NS)	< 0.001 (HS)	< 0.001 (HS)
Serum sialic acid (mmol/l)	1.95 ± 0.28	2.45 ± 0.32	2.77 ± 0.39	< 0.001 (HS)	< 0.001 (HS)	< 0.001 (HS).
Diabetic duration	-	6.3 ± 4.4	12.0 ± 4.4	-	-	< 0.001 (HS).

The values are expressed as their Mean ± SD; HS – Highly significant ($p < 0.001$); S – Significant ($p < 0.05$)

NS – Not significant ($p > 0.05$)

Table 3: Pearson's correlation between the parameters

Relationship between	r - Values	p - Value	Significance
Microalb. Vs Sialic acid	+ 0.43	< 0.01	S
FSG Vs. Sialic acid	+ 0.43	0.07	NS
Serum creatinine Vs. Sialic acid	+ 0.14	0.22	NS
Microalb. Vs. FSG	+ 0.95	< 0.001	HS
Microalb. Vs. Serum creatinine	+ 0.34	< 0.01	S
FSG Vs. Serum creatinine	+ 0.09	0.40	NS

r = Pearson's correlation co-efficient.

HS – Highly significant ($p < 0.001$)

S – Significant ($p < 0.05$)

NS – Not significant ($p > 0.05$)

Discussion

Inflammation plays a major role in the pathogenesis of type 2 diabetes mellitus and its complications [11]. Hence inflammatory markers or acute phase markers have gained the importance as indicators and predictors of diabetic process. Serum sialic acid is one of the acute phase response markers that is found to be associated with diabetes mellitus [12]. In our study we observed a progressive rise in serum sialic acid levels with the urinary albumin excretion and a significant positive correlation between them. It is noted that there is significant difference in serum sialic levels between controls and normoalbuminuric patients, which was not shown with serum creatinine and albumin excretion levels. Serum creatinine showed significant increase only in microalbuminuric patients suggesting its importance only after the onset of nephropathy. Therefore, sialic acid may act as an indicator for early diabetic process. Crook MA, et al attribute the increase in serum sialic acid concentrations in diabetes to cytokine induced, which is produced in excess in diabetic process [13]. Microalbuminuria a resultant of hyperglycemia induced glycation of glomerular membrane [14]. Jorgensen et al [15] and Mayurasakorn K et al [16] have shown that tight glycemetic control reverses the microalbuminuric state and may delay the onset of complications but does not halt the ongoing microvascular damage. Therefore, monitoring of diabetic patients with serum sialic acid levels may help in predicting the onset of microvascular changes. Since this is a cross sectional study, follow up studies and interventional studies are required to emphasize the importance of sialic acid estimation. Since the underlying inflammation is the cause for establishing the diabetes and its complications, our study would have been strengthened if we had measured the inflammatory marker like hsCRP and correlated with serum sialic acid levels.

In conclusion, estimation of both microalbuminuria and serum sialic acid levels in NIDDM is helpful in assessing the diabetic process and identifying the risk category for

complications which are the main causes for mortality and morbidity among diabetes mellitus patients.

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