Biochemistry: An Indian Journal

BioChemistry
ISSN: 0974-7427

Research | Vol 15 Iss 1

Study of Serum Adiponectin and Oxidative Stress Levels in Patients with Type 2 Diabetes Mellitus

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Received: July 12, 2021; **Accepted:** July 27, 2021; **Published:** August 5, 2021

Abstract

Background: Serum Adiponectin is a specific protein synthesized from the adipocytes and kidney. Some of the recent studiesfound that increased level of serum adiponectin for early detection of nephropathy in Type 2 Diabetes Mellitus (T2DM). This protein has anti-diabetic, anti-oxidative properties and anti-inflammatory. Increased oxidative stress in patients with T2DM lead to some micro and macro vascular complications particularly kidney dysfunction. Estimation of serum adiponectin level may help to predict early detection of nephropathy in T2DM and the role of this protein complex. Therefore, we designed to evaluate the determinant serum adiponectin than urinary microalbuminuria for nephropathy in T2DM. Methods: This is a case control study, included 100 T2DM patients and further divided into two groups according to albumin-to-Creatinine ratio, T2DM patients with Normoalbuminuria (N=50), and Microalbuminuria (N=50), and 50 age and sex matched healthy controls also included. Urinary Albuminuria was analyzed by Albumin Creatinine Ratio (ACR), Serum Adiponectin Enzyme-Linked Immunosorbent Assay (ELISA) and serum MDA was analyzed by using TBARS Method. Results: The mean valuesof serum adiponectin (8.24 ± 2.36, 19.43 ± 3.08 and 23.94 ± 8.40) was significantly higher in T2DM patients with normoalbuminuria, Microalbuminuria, and Microalbuminuria, respectively. The serum MDA levels also elevated in three groups of T2DM patients compared to healthy controls. The significantly elevated levels of serum adiponectin observed in T2DM with Normoalbuminuria when compared to T2DM with Microalbuminuria and T2DM with Microalbuminuria. Conclusion: Elevated levels of serum adiponectin in T2DM with Normoalbuminuria and these levels are associated with renal insufficiency. Hence this study suggests that the estimation of adiponectin may useful for early detection and progression of nephropathy in T2DM patients.

Keywords: Adiponectin, Type 2 Diabetes Mellitus, MDA, TBARS

Introduction

Type 2 Diabetes mellitus (T2DM) is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin action. Hyperglycemia is associated with long-term damage, dysfunction, and failure of the normal functioning of various organs, especially kidneys. Poor lifestyle, obesity, aging, stress, and several other factors are implicated in the prevalence of the disease [1-2]. The prevalence of T2DM is globally 171 million according to 2018 this number is expected to reach 366 million by the year 2030, in the Indian scenario 50.8 million according to 2015 and it reaches 80.0 million by the year 2030 [3-4]. Nephropathy (DN) is a common and severe microvascular complication of T2DM. Microalbuminuria is a gold standard and the earliest clinically available marker for the

Citation: Ganesh V. Study of Serum Adiponectin and Oxidative Stress Levels in Patients With Type 2 Diabetes Mellitus. Biochem Ind J. 2021;15(1):142.

detection of DN [5]. Serum adiponectin is an adipocytokine synthesized particularly in white adipose tissue and also synthesized from other tissues like kidneys, liver, bones, salivary glands, pancreas, and colonial mucosal cells [6]. The physiological action of adiponectin includes anti-diabetic, anti-oxidative, and anti-inflammatory, and also it acts as a renoprotective action by activating AMP kinase and NADPH oxidase activity [7].

In T2DM, increased sugar level in blood circulation due to insulin resistance and reduced uptake of sugar by cells and leads to hypoglycemia in cells [8]. To maintain energy, cells utilize lipids and proteins by degradation [9]. Continuously increased lipolysis and proteolysis lead to the production of free radicals and reactive oxygen species, these will damage tissues in the body. Malondialdehyde (MDA) is one of the oxidative stress markers produced from the peroxidation of polyunsaturated fatty acids. Increased level of MDA in the blood circulation was observed in diabetic patients [10]. Hence, we aimed to evaluate the serum adiponectin and urinary albuminuria levels in patients with type 2 diabetes mellitus.

Material and Methods

This is a case-control study conducted at "Akash Institute of Medical Sciences and Research Centre", Karnataka for a period of 3 years (2017-2019). A total of 150 subjects were included in the present study, 100 cases are diagnosed with T2DMwith age of 30-63 years according to American diabetes association (ADA) criteria [11]. The cases are further divided into 2 groups based on albumin-creatinine ratio, 50 T2DM with normoalbuminuria (ACR Ratio: < 30 mg/dL) and 50 T2DM with Microalbuminuria (ACR Ratio: 30-300 mg/dL) along with that the present study also included 50 age and gender-matched healthy controls. All the subjects were recruited in the study after obtaining informed consent after obtaining ethical clearance from the institute (IEC No-508). Patients with a history of hypertension, hypercholesterolemia, cardiovascular disease, hepatic disorders, acute and chronic renal insufficiency, and alcohol abuse were excluded from this study. Five milliliters of venous blood were collected from each patient after 12 hrs of overnight fasting, 2 mL transferred into fluoride tube and 3 mL transferred into the plain tube. The second sample was collected for PPBS from all subjects. Urine samples were also collected from all the subjects. The collected samples were separated by centrifugation at 3000 rpm for 5 min and stored at -200C in a deep freezer until biochemical analysis was done. Estimation of FBS, PPBS, Serum Urea, Creatinine, Uric Acid was done by well-established laboratory standard methods, Urinary Albuminuria was analyzed by Albumin Creatinine Ratio (ACR), Serum Adiponectin was analyzed by Enzyme-Linked Immunosorbent Assay (ELISA) and Serum Malondialdehyde was analyzed by TBARS Method.

Statistical Analysis

The normal distribution of data was done by using the Kolmogorov Smirnov test. All the characters are descriptively summarized. Microsoft Excel was used for mean and standard deviation. The significant difference between the groups of variables was done by ANOVA. The Pearson correlation was used to correlate between the variables in the study. The Data has compiled in Microsoft Excel spreadsheets and analyzed by using SPSS for windows version 21.0. 'p' value <0.05 was considered as statistically significant.

Results

Distribution of demographic and biochemical parameters in between the study group. The plasma fasting blood sugar, postprandial blood sugar, serum urea, creatinine, uric acid, adiponectin, and Malondialdehyde levels were increased in two groups of T2DM Patients when compared to healthy controls. A significant difference in the level of all parameters in the present study was observed between two groups of T2DM patients **(TABLE 1).**

Pearson correlation between the variables in the study subjects. The serum adiponectin was positively correlated with plasma fasting blood sugar, postprandial blood sugar, serum urea, creatinine, uric acid, urinary albumin, and Malondialdehyde **(TABLE 2).**

Pearson correlation between the variables in the study subjects. The serum Malondialdehyde was positively correlated with plasma fasting blood sugar, postprandial blood sugar, serum urea, creatinine, uric acid, adiponectin, and urinary albumin **(TABLE 3).**

Pearson correlation between the variables in the study subjects. The urinary Microalbumin was positively correlated with plasma fasting blood sugar, postprandial blood sugar, serum urea, creatinine, uric acid, adiponectin, and Malondialdehyde **(TABLE 4).**

TABLE 1. **Clinical biochemical parameters between the study groups.**

Parameter	Controls	T2DM Patients with Normoalbuminuria	T2DM Patients with Microalbuminuria	P value
Age (Years)	47.34 ± 13.42	51.30 ± 11.73	49.58 ± 11.29	0.069
Fasting Blood Sugar (mg/dL)	88.22 ± 24.10	163.16 ± 27.76	184.46 ± 48.11	0.0001**
Post Prandial Blood Sugar (mg/dL)	127.14 ± 28.10	240.56 ± 52.81	260.66 ± 79.65	0.0001**
Serum Urea (mg/dL)	22.06 ± 8.01	21.24 ± 6.90	90.68 ± 10.10	0.0001**
Serum Creatinine (mg/dL)	0.75 ± 0.21	0.744 ± 0.19	8.56 ± 1.24	0.0001**
Serum Uric Acid (mg/dL)	3.64 ± 1.35	4.13 ± 1.16	8.69 ± 0.43	0.0001**
Serum Adiponectin (ng/dL)	3.24 ± 1.71	19.43 ± 6.72	23.94 ± 17.87	0.0001**
Urinary Albuminuria (mg/dL)	10.13 ± 0.88	22.16 ± 1.09	118.66 ± 47.45	0.0001**
Serum MDA (mg/dL)	4.66 ± 0.30	8.67 ± 0.52	10.84 ± 2.81	0.0001**

TABLE 2. **Correlation of Serum Adiponectin with other biochemical parameters.**

Parameter		r value	P value
Adiponectin (ng/dL)	Age (Years)	0.091	0.267
	Fasting Blood Sugar (mg/dL)	0.14	0.088
	Post Prandial Blood Sugar (mg/dL)	0.088	0.285
	Serum Urea (mg/dL)	0.387	0.0001**
	Serum Creatinine (mg/dL)	0.349	0.0001**
	Serum Uric Acid (mg/dL)	0.337	0.0001**
	Urinary Albuminuria (mg/dL)	0.401	0.0001**
	Serum MDA (mg/dL)	0.507	0.0001**

TABLE 3. **Correlation of Urinary Albuminuria with other biochemical parameters**

Parameter		r value	P value
Urinary Albuminuria (mg/dL)	Age (Years)	0.022	0.79
	Fasting Blood Sugar (mg/dL)	0.205	0.012*
	Post Prandial Blood Sugar (mg/dL)	0.132	0.107
	Serum Urea (mg/dL)	0.858	0.0001**
	Serum Creatinine (mg/dL)	0.874	0.0001**
	Serum Uric Acid (mg/dL)	0.79	0.0001**
	Serum Adiponectin (ng/dL)	0.401	0.0001**
	Serum MDA (mg/dL)	0.605	0.0001**

TABLE 4. **Correlation of Serum MDA with other biochemical parameters**

Parameter		r value	P value
Serum MDA (mg/dL)	Age (Years)	0.074	0.368
	Fasting Blood Sugar (mg/dL)	0.303	0.809
	Post Prandial Blood Sugar (mg/dL)	0.234	0.0001**
	Serum Urea (mg/dL)	0.632	0.004*
	Serum Creatinine (mg/dL)	0.649	0.0001**
	Serum Uric Acid (mg/dL)	0.63	0.0001**
	Serum Adiponectin (ng/dL)	0.507	0.0001**
	Urinary Albuminuria (mg/dL)	0.605	0.0001**

Discussion

Type 2 diabetes mellitus is a chronic metabolic disorder due to insulin resistance; it may also cause due to improper secretion of insulin from the beta cells of the pancreas. Insulin resistance was due to beta cells of the pancreas, genetic and metabolic reasons [12-14]. In this condition, energy production is maintained by the degradation of lipids and proteins [15]. Simultaneously this process generates free radicals is more and causes oxidation of polyunsaturated fatty acids results in tissue damage. Malondialdehyde is one of the oxidative stress biomarkers synthesized from lipid peroxidation and other oxidative stress molecules like acrolein, 4-hydroxynonenal (HNE), 4-oxononenal(ONE), and isolevuglandins [16-18]. The present study found that the elevated level of serum MDA in both the groups of type 2

diabetes mellitus, which indicates that hyperglycemia is also one of the triggering factors for the generation of oxidative stress molecules. Similarly, previous studies also found that the serum MDA levels in diabetes mellitus were positively correlated with HbA1C, and also, they reported that poor glycemic control and advanced drug effects cause micro and macrovascular complications in type 2 diabetes mellitus patients [19].

Adiponectin act as a hormone synthesized particularly from adipose tissues and other tissues like the liver, kidney, skeletal muscles, bones, salivary glands, etc. the physiological actions of adiponectin in diabetes mellitus play a good role that stimulates the synthesis of insulin production and activation by its anti-diabetic property, along with that it will prevent the generation of oxidative stress molecules by anti-oxidative properties and also protect the tissues from inflammation by its anti-inflammatory actions [20-22]. The present study also measured serum adiponectin elevated levels in type 2 diabetes mellitus patients when compared to healthy controls. The increased levels of serum adiponectin in type 2 diabetes mellitus Microalbuminuria when compared to type 2 diabetes mellitus normoalbuminuria. The serum adiponectin was positively correlated with FBS, PPBS, Urinary Microalbumin, and Serum MDA. Similarly, other studies found that increased level of serum adiponectin in type 2 diabetes mellitus for improving glycemic control, and protects internal organs from oxidants and inflammatory molecules [23].

Conclusion

The present study suggests that evaluation of serum adiponectin levels is useful for early detection of Type 2 Diabetes Mellitus and its complications due to its anti-diabetic, anti-oxidant, and anti-inflammatory action.

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