Original Research Article

Study of serum adiponectin levels for early detection of type 2 diabetes mellitus and its complications on kidney

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ABSTRACT

Background: Type 2 diabetes mellitus is a chronic metabolic disorder due to insulin resistance caused by destruction of beta cells of pancreas. Insulin resistance in newly diagnosed type 2 diabetes mellitus patients leads to hyperglycemia. Serum adiponectin is a more sensitive and specific biomarker for early detection of diabetic nephropathy than urinary microalbuminuria.

Methods: This is a case-control study conducted in Akash Institute of Medical Sciences, A total 180 subjects (120 cases and 60 controls). All the subjects included after informed consent, blood samples and urine samples are collected from the all the subjects. The serum Adiponectin and was estimated by using enzyme-linked immunoassay (ELISA) and fasting blood sugar (FBS), post prandial blood sugar (PPBS) and renal function test (RFT) was also estimated by laboratory standard methods.

Results: This study was evaluated the FBS, PPBS, RFT and serum adiponectin levels in patients with type 2 diabetes mellitus patients and compare them with healthy controls. The serum adiponectin levels more significantly elevated in newly diagnosed type 2 diabetes mellitus patients and compared with the healthy controls. The study also found that significantly elevated levels of FBS, PPBS and RFT in type 2 diabetes mellitus patients and compared with the healthy controls, The statistically significant levels of serum adiponectin in patients with type 2 diabetes mellitus and when compared with the controls (p= 0.0001).

Conclusions: The study suggesting that the s estimation of serum adiponectin levels in newly diagnosed type 2 diabetes mellitus patients useful for early detection of diabetic nephropathy. Because elevated levels of serum adiponectin in patients with newly diagnosed type 2 diabetes mellitus, this levels are positively correlated with the FBS and PPBS.

Keywords: Type 2 diabetes mellitus, Diabetic nephropathy, Enzyme linked immunosorbent essay, Albumin creatinine ratio

INTRODUCTION

Hyperglycemia is a major cause of type 2 diabetes mellitus due to insulin resistance caused by destruction of beta cells of pancreas.[1] The T2DM prevalence 347 millions in worldwide, in India 73 million peoples my effect by 2030.[2] This leads to micro and macro vascular complications on tissues like " Kidney, heart, brain and retina, abdominal obesity and life style changes are the major causes.[3]

The adiponectin is the adipocytokine majorly synthesized from the adipose tissues and also synthesized from the liver, kidney, bone, mussels, brain cells, this having 244 amino acids and in the circulation 3 forms it will observed.[4-6] The physiological functions of adiponectin in the body are "antidiabetic, anti-oxidative and anti-inflammatory.[7] The adiponectin acts on the insulin gene in the beta cells of pancreas leads to produce insulin and also its act as a anti-oxidative through AMP kinase, NADPH enzymatic pathways.[8] If any pathological changes in the

releated cells this levels are altered in the blood and urine samples.

Microalbuminuria is a one of the gold standard markers for detection of diabetic nephropathy now a days, according to recent researchers urinary microalbuminuria is not an a specific biomarker for detection of nephropathy in Type 2 diabetes mellitus patients because this levels are elevated in other conditions like hypertension, liver and cardiac disorders.[9-11] Some of the research studies found increased levels of adiponectin and also other research studys found decreased levels of serum adiponectin in Type 2 diabetes mellitus patients and compared with healthy controls.[12-15] Based on this background the present study was evaluated study of serum adiponectin levels for early detection of type 2 diabetes mellitus and its complications of kidney.

METHODS

This is a case-control study was conducted at "Akash Institute of Medical Sciences and Research Centre", Karnataka from 2017-2020. A total 180 subjects included in the present study 120 cases diagnosed with T2DM patients (60 T2DM with normoalbuminuria (<30 mg/dL) and 60 T2DM with microalbuminuria (30-300 mg/dL) was included according to American Diabetes Association Criteria (ADA) 16 and 60 age and gender matched Healthy controls also included. All the subjects were recruited in the study after obtaining their informed consent after obtaining of ethical clearance from the institute. Patients with T2DM and age more than 30 years were included in the present study. Whoever has Exclusion criteria's for both cases and controls were patients with history of hypertension, hypercholesterolemia, cardiovascular disease, hepatic disorders, acute and chronic renal insufficiency and alcohol abuse excluded from this study. From the all subjects, after overnight fasting (12 hours), 5 ml of venous blood was collected and 2 mL transferred into anticoagulant Tube contain fluoride and 3 mL transferred into plain tube. The second sample was collected for PPBS. Urine samples also collected from all the subjects. The collected samples were separated by centrifugation at 3000 rpm for 5 min and stored until biochemical analysis was done.

Plasma fasting blood sugar (FBS), plasma post prandial blood sugar (PPBS), serum urea, serum creatinine, serum uric acid were measured by laboratory standard methods and serum adiponectin was measured by Enzyme linked immunosorbent essay (ELISA). Urinary microalbuminuria was measured by urinary albumin and Urinary creatinine ratio (ACR) (normoalbuminuria <30 mg/dL, microalbuminuria 30-300 mg/dl and macroalbuminuria >300 mg/dL).

Statistical analysis

The normal distribution of data checked by using Kolmogorov Smirnov test. All the characters descriptively summarized. The mean and standard deviation about the arithmetic mean were used. The significance difference between FBS, PPBS, serum RFT, adiponectin and urinary albuminuria analysed by using independent student's t-test (2-tailed). The Pearson correlation was used for between the serum Adiponectin and FBS, PPBS, RFT and also we correlated serum microalbuminuria with FBS, PPBS, serum RFT, adiponectin and urinary albuminuria. The data was compiled in Microsoft excel spread sheets and analyzed using statistical package for social sciences (SPSS) for windows version 16.0. A p<0.05 was considered statistically significant.

RESULTS

Table 1 shows the mean and standard deviation (SD) values of subject's characteristics and other biochemical parameters was analysed the Type 2 diabetes mellitus patients and compared with age and gender matched controls. The positive significant difference between Plasma FBS (165.26±41.99 , p=0.0001*), Plasma PPBS (239.24±72.68, p=0.001*) and serum urea (56.14±35.87, p=0.001*) serum creatinine (7.38±6.81, p=0.001*) serum uric acid (6.37±2.51, p=0.0001*), serum adiponectin (11.77±4.51, p=0.0001*) and urinary microalbuminuria (63.33±61.76, p=0.0001**).

Table 1: Comparison of biochemical parameters in patients with type 2 diabetes mellitus and healthy controls.

Parameter	Controls	T2DM Patients	P value
Age (years)	47.03±13.24	50.53±11.43	0.069*
Gender	0.62±0.49	0.66±0.47	0.584
Fasting blood sugar (mg/dl)	90.05±8.31	165.26±41.99	0.0001**
Post prandial blood sugar (mg/dl)	111.73±20.85	239.24±72.68	0.0001**
Serum urea (mg/dl)	18.92±5.76	56.14±35.87	0.0001**
Serum creatinine (mg/dl)	0.73±0.17	7.38±6.81	0.0001**
Serum uric acid (mg/dl)	4.59±1.25	6.37±2.51	0.0001**
Serum adiponectin (ng/ml)	3.69±0.97	11.77±4.51	0.0001**
Urinary albuminuria (mg/dl)	9.61±0.92	63.33±61.76	0.0001**

Data expressed as Mean ± SD; * Median (Inter quartile range), ** More Significant. Fasting Blood Sugar (FBS), Post Prandial Blood Sugar (PPBS), Type 2 Diabetes Mellitus (T2DM), p=Probability Values, Mg/dL : Milligram per Deciliter, ng/mL: Nano grams per Milliliter.

Significantly elevated levels of FBS, PPBS, serum RFT, adiponectin and urinary albuminuria Type 2 diabetes mellitus and compare with age and gender matched healthy controls.

Table 2: Comparison of biochemical parameters in type 2 diabetes mellitus patients with normoalbuminuria and type 2 diabetes mellitus patients with microalbuminuria.

Parameter	Normo albuminuria with T2DM Patients	Micro albuminuria with T2DM Patients	P value
Age (years)	51.83± 11.51	49.21±11.28	0. 211
Gender	0.60±0.49	0.71±0.45	0.181
Fasting blood sugar (mg/dl)	149.26± 29.90	181.25± 46.29	0.0001**
Post prandial blood sugar (mg/dl)	216.85±58.14	261.63± 79.09	0.0001**
Serum urea (mg/dl)	21.43± 7.12	90.85±9.74	0.0001**
Serum creatinine (mg/dl)	0.74±0.19	14.02±2.01	0.0001**
Serum uric acid (mg/dl)	4.03±1.22	8.71±0.43	0.0001**
Serum adiponectin (ng/ml)	8.16±1.35	15.36±3.57	0.0001**
Urinary albuminuria (mg/dl)	10.16± 1.05	116.50± 44.08	0.0001**

Data expressed as Mean ± SD; * Median (Inter quartile range), ** More Significant. Fasting Blood Sugar (FBS), Post Prandial Blood Sugar (PPBS), Type 2 Diabetes Mellitus (T2DM), P=Probability Values, Mg/dL : Milligram per Deciliter, ng/mL: Nano grams per Milliliter.

Table 2 shows the mean and standard deviation (SD) values of subject's characteristics and other biochemical parameters was analysed the both Type 2 diabetes mellitus patients (T2DM with normoalbuminuria and T2DM with microalbuminuria). The positive significant difference between plasma FBS (149.26±29.90, 181.25±46.29, p=0.0001), Plasma PPBS (216.85±58.14, 261.63±79.09, p=0.001) and serum urea (21.43±7.12, 90.85±9.74, p=0.001) serum creatinine (0.74±0.19, 14.02±2.01, p=0.0001) serum uric acid (4.03±1.22, 8.71±0.43; p=0.0001), serum adiponectin (8.16±1.35, 15.36±3.57, p=0.0001) and urinary microalbuminuria (10.16±1.05, 116.50±44.08, p=0.0001). Significantly elevated levels of FBS, PPBS, serum RFT, adiponectin and urinary albuminuria both the Type 2 diabetes mellitus.

Table 3: Correlation (Pearson) of serum adiponectin with FBS, PPBS, RFT and urinary albuminuria in type 2 diabetes mellitus patients with normoalbuminuria and type 2 diabetes mellitus patients with microalbuminuria.

Parameter		r value	P value
Serum adiponectin (ng/ml)	Age (years)	0.063	0.404
	Gender	0.087	0.244
	Fasting blood sugar (mg/dl)	0.658**	0.0001**
	Post prandial blood sugar (mg/dl)	0.620**	0.0001
	Serum urea (mg/dl)	0.823**	0.0001
	Serum creatinine (mg/dl)	0.824**	0.0001
	Serum uric acid (mg/dl)	0.709**	0.0001
	Urinaryalbuminuria (mg/dl)	0.764**	0.0001

Data expressed as r = Rho Values; ** More Significant. Fasting Blood Sugar (FBS), Post Prandial Blood Sugar (PPBS), Type 2 Diabetes Mellitus (T2DM), P = Probability Values, Mg/dL: Milligram per Deciliter, ng/mL: Nano grams per Milliliter.

Table 4: Correlation (Pearson) of urinary albuminuria with FBS, PPBS, RFT and serum adiponectin in type 2 diabetes mellitus patients with normoalbuminuria and type 2 diabetes mellitus patients with microalbuminuria.

Parameter		r value	P value
Urinary albuminuria (mg/dl)	Age (years)	0.026	0.731
	Gender	0.027	0 .717
	Fasting blood sugar (mg/dl)	0.485**	0.0001**
	Post prandial blood sugar (mg/dl)	0.441**	0.0001**
	Serum urea (mg/dl)	0.871**	0.0001**
	Serum creatinine (mg/dl)	0.882**	0.0001**
	Serum uric acid (mg/dl)	0.785**	0.0001**
	Serum adiponectin (ng/ml)	0.764**	.0001 **

Data expressed as r=Rho Values; ** More Significant. Fasting Blood Sugar (FBS), Post Prandial Blood Sugar (PPBS), Type 2 Diabetes Mellitus (T2DM), P = Probability Values, Mg/dL: Milligram per Deciliter, ng/m: Nano grams per Milliliter.

Table 3 shows the correlation (Pearson Correlation) was done in between the serum adiponectin positively

correlated with biochemical parameters like plasma FBS (r=0.658, p=0.0001), plasma PPBS (r=0.0480.620, p=0.0001), serum urea (r=0.823, p=0.0001), serum creatinine (r=0.824, p=0.0001) and serum uric acid (r=0.709, p=0.0001) and urinary albuminuria (r=0.764, p=0.0001). More significantly elevated levels of serum adiponectin in T2DM patients with normoalbuminuria and compared with urinary albuminuria.

Table 4 shows the correlation (Pearson Correlation) was done in between the urinary albuminuria positively correlated with biochemical parameters like plasma FBS (r=0.658, p=0.0001), plasma PPBS (r=0.0480.620, p=0.0001), serum urea (r= 0.823, p=0.0001), serum creatinine (r=0.824, p=0.0001) and serum uric acid (r=0.709, p=0.0001) and urinary albuminuria (r=0.764, p=0.0001). Significantly elevated levels of urinary albuminuria in T2DM patients with microalbuminuria and compared with T2DM patients with normoalbuminuria.

Figure 1 shows the liner regression between serum adiponectin and urinary albuminuria compared with both T2DM patients. The serum adiponectin is more significantly elevated in T2DM patients with normoalbuminuria compared to T2DM patients with microalbuminuria.
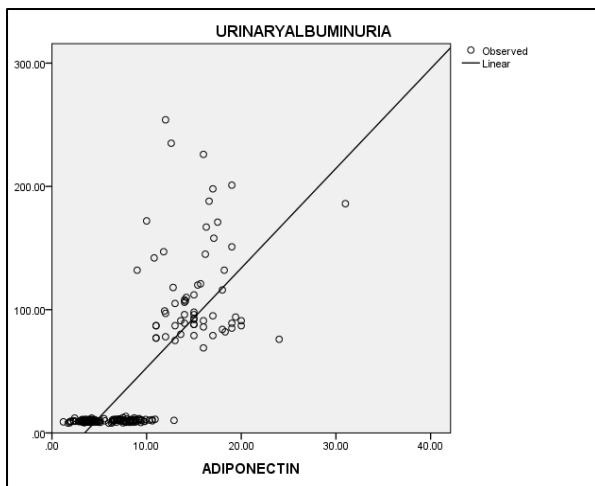

Figure 1: Association of serum adiponectin with albuminuria in type 2 diabetes mellitus patients with normoalbuminuria and type 2 diabetes mellitus patients with microalbuminuria.

DISCUSSION

Adipose tissue is an a storage organ in the body and also act as a endocrine tissue that secrets several biological compounds like cytokines and peptide hormones which is known as a adipokines.[17] This adipokines are involves in physiological functions like regulates metabolism and inflammation in some of the chronic diseases.[18] The adiponectin is also one of the adipocytokine has anti-inflammatory, anti- atherogenic and anti- diabetic properties, reduced levels of adiponectin strongly correlated with insulin resistance leads to Type 2 diabetes mellitus, metabolic syndrome and other chronic diseases.[19]

T2DM is one of the major metabolic disorders caused by insulin resistance due to improper secretion and activation of insulin leads to hyperglycemia. In T2DM patients significantly increased proteolysis and lipolysis and increased oxidants levels caused by micro and macrovascular complications particularly diabetic nephropathy.[20] For detection of diabetic nephropathy urinary microalbuminuria gold standard method, based on levels T2DM with normoalbuminuria, T2DM with microalbuminuria and T2DM with macroalbuminuria.[21] Some of the recent studys found that urinary albuminuria is not a specific and sensitive method for detection of nephropathy in T2DM.[22]

Recent study found adiponectin is the specific and sensitive biomarker for early detection of diabetes mellitus and its complications particularly nephropathy.[23] The present study also significantly increased levels of serum adiponectin levels was observed in both the types 2 diabetes mellitus and compared with the healthy controls. similar results previous studys also found that significantly elevated serum adiponectin levels was triggers insulin sensitivity and reduced the risk oxidants, inflammatory compounds in type 2 diabetes mellitus patients.[24-25]

The serum adiponectin levels and urinary albuminuria with two different groups of type 2 diabetes mellitus patients and healthy controls, significantly elevated levels of serum adiponectin levels in type 2 diabetes mellitus with normoalbuminuria it is useful for early detection of nephropathy in type 2 diabetes mellitus patients. Along with that serum adiponectin positively correlated with FBS, PPBS, Urea, creatinine and uric acid when compared to both groups of T2DM patients and healthy controls. Previous studys also identified similar results serum adiponectin levels are significantly elevated than urinary albuminuria in T2DM patients with normoalbuminuria.[26-27] In this study also correlated serum adiponectin with urinary albuminuria significantly elevated levels observed in type 2 diabetes mellitus patients with microalbuminuria when compared to type 2 diabetes mellitus patients with normoalbuminuria and healthy controls.

Limitations

This study didn't followed up and also less sample size, large sample size and follow up studies are required.

CONCLUSION

The significantly increased levels of serum adiponectin in Type 2 diabetes mellitus with normoalbuminuria is more sensitive and specific biomarker than urinary albuminuria for early detection and progression of diabetic nephropathy in type 2 diabetes mellitus because it is positively correlated with FBS, PPBS, Urea, Creatinine and Uric acid.

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