

Correlation of Serum Adiponectin with Uric Acid in Prediabetes and Type -2 Diabetes Mellitus

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ABSTRACT

Background: Many researches have implicated most of the prediabetic individuals to finally end up with the progression to diabetes and increase the risk of other life-threatening diseases. In progression of disease obesity plays a major role. This study earlier interventions involving changes in lifestyle dietary habits and physical activity (decreases production of proinflammatory molecules by reducing visceral fat and increases insulin sensitivity) in conjunction with the treatment modalities involving anti-inflammatory mechanisms that not only prevent the development and progression of diabetes (among high-risk groups) its associated complications, but also reduce the financial burden imposed on the diabetic patients

Methodology: A total of 690 subjects, including 230 diagnosed T2DM cases, 230 pre diabetes mellitus and 230 healthy controls were selected for the research after the imposition of specific inclusion and exclusion criteria for controls, T2DM, and prediabetes.

Fasting blood glucose level was the glucose oxidase- peroxidase (GOD-POD) method, using commercially available kit with semi-autoanalyzer machine. uric acid level was the uricase /POD method, using commercially available kit with semi-autoanalyzer machine. HbA1c level was the high-performance liquid chromatography (HPLC) and adiponectin, interleukin-6 level was the sandwich ELISA.

Results: The FBG, HbA1c, BMI, uric acid and IL-6 level were significantly higher in prediabetes and diabetes group compared with the those in the control group. The FBG, HbA1c, BMI, uric acid and IL-6 level were significantly higher in prediabetes and diabetes group compared with the those in the control group.

There was no significant correlation between adiponectin level and FBG, HbA1c, BMI, uric acid and IL-6 in diabetes individuals. prediabetes individuals only significant correlation was between IL-6 and uric acid, BMI as well as FBG and BMI.

Conclusion: Biochemical markers helpful for marking severity of disease in an early phase of prediabetes. The early diagnosis of prediabetes is important in order to avoid long-term micro- and macro vascular complications in individuals at high risk of diabetes.

Keywords: HbA1c, FBG, Adiponectin, Uric acid, Interleukin-6

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INTRODUCTION

Diabetes mellitus is a collection of metabolic disorders marked by elevated blood sugar levels brought on by deficiencies in either the production or action of insulin, or both. The eyes, kidneys, nerves, heart, and blood vessels are among the organs that are most often affected by chronic hyperglycemia, which is linked to

long-term harm, malfunction, and failure of normal functioning.^{1,2}

Individuals with impaired fasting glucose (IFG) do not have diabetes mellitus (DM) but are at significant risk for acquiring type 2 DM and cardiovascular disease in the future. The hemoglobin A1c (HbA1c) level is

beneficial for assessing therapeutic responses but is not advised for the screening or diagnosis of diabetes mellitus (DM).³

Factors posing risks for the development of T2DM are related with genetic and metabolic etiologies. These risk factors may be modifiable and non-modifiable factors. Obesity, sedentary living, nutritional factors, inflammation, prediabetes and insulin resistance represent modifiable risk factors while age, gender, genetic factor and gestational diabetes denote non modifiable factors.⁴

The adiponectin protein is subject to proteolytic cleavage, leading to the production of globular adiponectin, which comprises just the globular head domain. The therapeutic impact of this globular fragment of adiponectin seems to stimulate β -oxidation in skeletal muscle, whereas full-length adiponectin reduces hepatic glucose production.⁵

Adiponectin activates AMP-activated protein kinase and several other protein kinases. The AMPK pathway enhances glucose uptake and utilization, as well as free fatty acid (FFA) oxidation in numerous tissues, including skeletal muscle cells, hepatocytes, and adipose tissue, hence regulating metabolic rate and insulin levels. Sensitivity: 6.7 Adiponectin may also inhibit damage to blood vessels, particularly the vascular endothelial cells, caused by inflammatory agents, so protecting the cardiovascular system.^{8,9}

Adiponectin is associated with several disorders, as research indicates its correlation with obesity, insulin resistance, type 2 diabetes mellitus, etc.¹⁰ Adiponectin, a plasma protein exclusive to adipose tissue, has recently been identified as possessing anti-inflammatory and anti-atherogenic characteristics.¹¹ It functions by diminishing the production of adhesion molecule-1, decreasing macrophage chemotaxis essential for adipogenesis, and inhibiting inflammatory signaling in endothelial tissue¹²

Uric acid may function as a prooxidant, perhaps serving as a signal for oxidative stress, while simultaneously possessing a therapeutic effect as an antioxidant.¹³

Hyperuricemia has been included among the metabolic abnormalities linked to insulin resistance and/or hyperinsulinemia in metabolic syndrome.¹⁴ Hyperuricemia has been associated with the onset of diabetic nephropathy.¹⁵ Some studies have shown an elevation in uric acid levels in prediabetes and diabetes, whereas other researchers have reported a decreasing tendency in serum uric acid levels with rising blood glucose levels.¹⁶

It is a common outcome for tissues to have IL-6. Long-term exposure and irregular production cause

inflammation, which in turn causes insulin resistance and overt Type 2 diabetes. There is a molecular connection between insulin resistance and IL-6 activation. The current investigation elucidated potential associations between adiponectin levels and uric acid, interleukin-6, fasting blood glucose, and HbA1c in individuals with diabetes mellitus, prediabetes, and good health.

MATERIALS AND METHODS

Study design and subject selection

The present case-control investigation was conducted at the Index Medical College and Research Department of Biochemistry in Indore, India. After applying specific inclusion and exclusion criteria for T2DM, Prediabetes, and controls, a total of 690 subjects were selected for the study. This included 230 diagnosed type-2 DM cases, 230 cases of pre-diabetes, and 230 healthy controls. Subjects diagnosed with diabetes mellitus according to the American Diabetes Association Criteria were included in the type 2 diabetes mellitus cases group. Patients were aged 30-60 years. Control group subjects were composed of healthy individuals aged 30-60. Subjects with a history of patient on drugs, insulin, corticosteroids and vitamin D supplements are excluded from study. Patients with cardiac disease, renal disease are excluded from study. gout and arthritis or any inflammatory conditions are excluded from study. were excluded from the prediabetes and diabetes cases. Meanwhile, the control group did not include participants with a history of acute or chronic illness.

Every participant had their clinical history gathered using a data collection form. In Indore, Madhya Pradesh, the Index Medical College and Research Center's Institutional Ethics Committee gave its approval for the collecting of blood samples from human subjects.

Sample Collection and Separation of Serum

7 ml of blood will be collected from the individuals under the aseptic condition in a 1ml fluoride vial, 2ml in EDTA vial and 4 plain vials. The Blood Sample will be allowed to clots at room temperature for 10 minutes. The blood sample will then be centrifuged at 3000 rpm for 10 minutes to separate the serum. Which was then used to estimation the concentration of FBG, HbA1c, adiponectin, uric acid and interleukin-6.

Estimation of FBG, HbA1c, adiponectin, uric acid and interleukin-6

Fasting blood glucose level was the glucose oxidase-peroxidase GOD-POD method, using available kit with semi-autoanalyzer machine. uric acid level was the uricase/POD method, using available kit with semi-autoanalyzer machine. HbA1c level was the high-performance liquid chromatography (HPLC) and

adiponectin, interleukin-6 level was the sandwich ELISA.

The statistical analysis will be using SPSS version 28.0. All data were expressed as mean ± SD. Continuous normal distributed variables will be compared by using the un-paired t-test. Correlation was used to find the significance. of study parameters between the two group of patients. A P value less than 0.05 will be consider as statistically significant and less than 0.001 will be consider as highly significant

RESULTS

Gender Distribution

In the study we can clearly see that majority the population consists of male and female across all the groups (male control= 53.48%, pre- diabetes 49.57%, diabetes 52.61%) and female 46.53%, pre- diabetes 50.43%, diabetes 47.40%). In case group, as shown in table 1 and figure 1, indicate a male predominance with T2DM.

Table 1. Gender wise distribution of study groups

Gender	Control N (%)		Pre- Diabetes N (%)		Diabetes N (%)	
	Frequency	%	frequency	%	frequency	%
Male	123	53.48	114	49.57	121	52.61
Female	107	46.53	116	50.43	109	47.40
Total	230	100	230	100	230	100

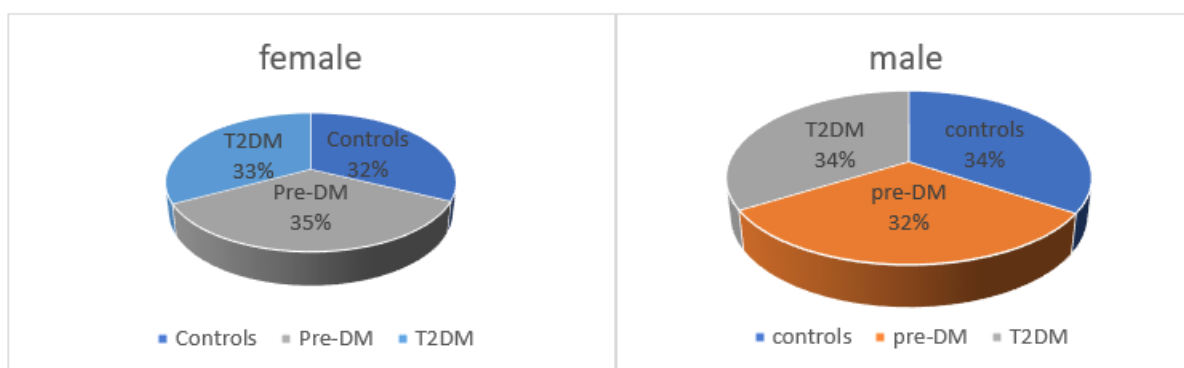


Figure-1 percentage of patients across the gender (male & female) group for the control, pre-diabetes and type-2 diabetes groups

Biochemical parameters

Table 2 shows the biochemical parameters values between the three study groups. The FBG, HbA1c, BMI, uric acid and IL-6 level were significantly higher in prediabetes and diabetes group compared with the those in the control group. Whereas adiponectin level was significantly lower in prediabetes and diabetes group compared with in the control group.

Individuals with diabetes did not exhibit a significant link between their adiponectin levels and their fasting

blood glucose, HbA1c, body mass index, uric acid, or IL-6 levels. In prediabetes individuals only significant was between IL-6 and uric acid, Body mass index as well as FBG and BMI (Table-3). Figure 2-a, b shows the positive correlation between IL-6 and body mass index,

uric acid while figure 3 show the negative correlation between FBG and BMI. Whereas in significant correlation b/w adiponectin level and FBG, HbA1c level in prediabetes individuals.

Table 2: characteristics of subjects

Parameters	Control	Prediabetes	Diabetes	ANOVA (p)
FBG	81.42±7.64	118.5±14.97	145.94±25.41	0.001**
HbA1c	4.43±.56	5.99±0.45	8.87±1.76	0.001**
BMI	22.65±.5.84	24.95±3.04	25.90±4.20	0.001**
ADIPONECTIN	6.94±2.5	5.73±1.49	4.50±0.81	0.001**
URIC ACID	4.63±0.66	4.93±1.06	6.48±1.66	0.001**
IL-6	5.48±1.18	5.44±1.14	7.5±1.86	0.001**

* $p < 0.05$ significant, ** $p < 0.01$ significant

Table 3: correlation between variables in prediabetes cases:

Parameters	FBG	HbA1c	BMI	ADIPONECTIN	IL-6	UA
FBG	1.000	.028	-.142*	.111	-.122	-.010
HbA1c	-	1.000	.034	-.081	-.038	.032
BMI	-	-	1.000	-.087	.141*	.108
ADIPONECTIN	-	-	-	1.000	-.110	.108
IL-6	-	-	-	-	1.000	.161*
URIC ACID	-	-	-	-	-	1.000

$p < 0.05$ significant, **

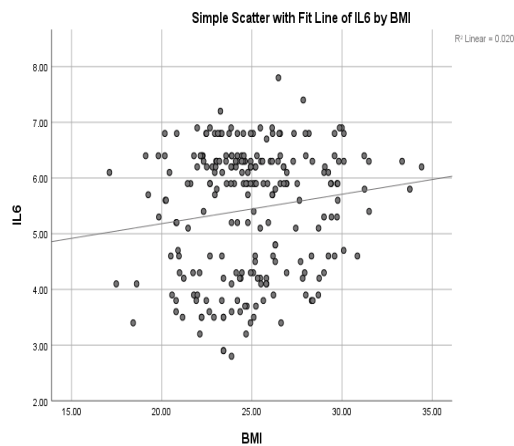


Figure 2 a: correlation between IL-6 and BMI

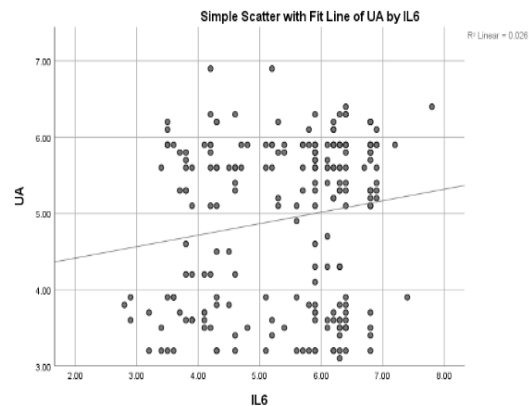


Figure 2 b: correlation between IL-6 and uric acid

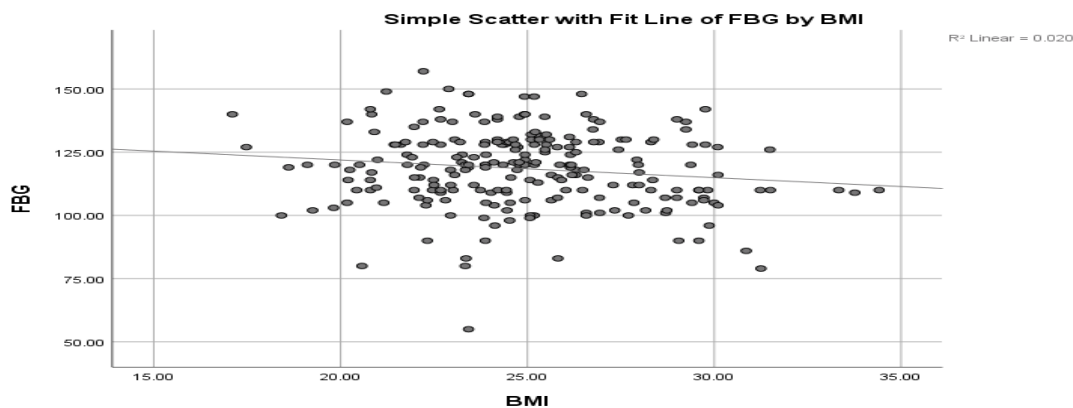


Figure 3: the correlation between FBG and BMI levels.

DISCUSSION

In the present study FBG, HbA1c, IL-6 and uric acid levels were shown higher while adiponectin levels were lower in prediabetes and diabetes patients compared to the healthy controls. These findings are consistent with previous study that found adiponectin secretion in prediabetic state leading to further reduced levels in overt diabetes, thus suggesting adiponectin to be an indicator of energy status of the body. Lower adiponectin level leads to abnormal metabolism of glucose and increases diabetic risk. 17

The protective role of adiponectin against hyperglycemia can be correlated with its insulin sensitizing effects. Mechanistic approaches demonstrate that adiponectin stimulates AMP dependent protein kinase, increases insulin sensitivity by enhancing glucose uptake, oxidation of fatty acids in liver and skeletal muscle. 18

The uric acid may also serve as a marker for alteration in blood glucose metabolism. In the present study documented significantly high uric acid concentration in diabetic patients with respect to prediabetes and control groups.

Proinflammatory cytokines (IL-6) released from adipocytes are capable of inducing insulin resistance in hepatocytes, myocytes and adipocytes. They have been shown to appear at the early stages of diabetes. IL-6 via its autocrine and paracrine action alters the metabolic process in adipose tissue and is found to locally influence insulin sensitivity. 19

It is shown that IL-6 production increases in obesity and diabetes thereby indicating IL-6 mediated decrease in insulin sensitivity. But in some researches, it has been shown that IL-6 has dual roles. It promotes insulin resistance in hepatocytes and adipocytes while it enhances insulin sensitivity in skeletal muscles and stimulates influx and efflux of glucose and lipids. Another study showed that weight reduction in obese

females caused reduction in both IL-6 gene expression and its serum levels. 20

Consequently, adiponectin, uric acid, and IL-6 are significant factors to consider when treating persons with prediabetes and type 2 diabetes. And also, lifestyle changes and increased physical activity also has beneficial role in preventing T2DM via modulation of inflammatory markers.

CONCLUSION

Our findings revealed an inverse relationship between adiponectin and HbA1c levels, as well as all other diabetes markers. The prediabetes and diabetes show the elevated HbA1c, FBG, uric acid and IL-6 and decrease level of adiponectin which can be interpreted as poor glycemic control and more extensive and increase cardiovascular risk. All biochemical markers helpful for marking severity of disease in an early phase of prediabetes. Early detection of prediabetes is critical for preventing long-term micro- and macrovascular problems in those at high risk of diabetes.

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