



## ORIGINAL ARTICLE

# Correlation of Serum Adiponectin, Ceruloplasmin and C-reactive Protein with Fasting Blood Glucose Levels and Glycosylated Hemoglobin Levels in Type 2 Diabetes

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## Abstract

**Introduction:** The correlation of the levels of acute phase reactants ceruloplasmin, C-reactive protein (CRP) and adiponectin with fasting blood glucose (FBG) and glycosylated haemoglobin (HbA1c) were assessed in type 2 diabetes mellitus patients. **Material and Methods:** This descriptive cross-sectional study was conducted in Department of Biochemistry, Pathology and Medicine at School of Medical Sciences and Research, Greater Noida. 100 cases of Type II Diabetes mellitus patients with age sex matched controls were included in the study. Blood samples were collected in plain vacutainer for adiponectin, ceruloplasmin, CRP; sodium fluoride vacutainer for plasma blood glucose and EDTA sample for HbA1c. The results thus obtained were analysed statistically by SPSS software version 22.0. **Results:** High serum ceruloplasmin and CRP levels were seen in Type 2 diabetic patients. The levels were directly proportional to blood plasma glucose levels and HbA1c. The adiponectin levels are inversely proportional to plasma glucose level and HbA1c in the same group. **Conclusion:** There was a significant positive correlation between CRP, ceruloplasmin levels with FBG and HbA1c, while there was inverse correlation of adiponectin with FBG and HbA1c.

## Key Words

Adiponectin, Ceruloplasmin, CRP, Diabetes Mellitus, FBG

## Introduction

Diabetes mellitus is a public health problem worldwide particularly in developing countries like India.<sup>[1]</sup> Adiponectin, a fat-derived hormone, plays a crucial role in protecting against insulin resistance/diabetes and atherosclerosis. Decreased adiponectin levels are thought to play a central role in the development of type 2 diabetes, obesity and cardiovascular disease.<sup>[2]</sup>

Ceruloplasmin, CRP, acute phase reactants are involved in multiple metabolic pathways which are relevant to insulin resistance, including insulin regulation, reactive oxygen species, lipoprotein lipase action and adipocytes function.<sup>[3]</sup>

The aim of this study was to determine serum adiponectin, ceruloplasmin and CRP levels in patients with type 2

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diabetes and their correlation with FBG and HbA1c. This study was carried out to evaluate utility of the said markers in Type II diabetes. The ethical clearance has been taken from the institute for this study.

### Materials and Method

The study was conducted in Department of Biochemistry, Pathology and Medicine at School of Medical Sciences and Research, Greater Noida. Blood samples were collected in plain vacutainer for adiponectin, ceruloplasmin and CRP, sodium fluoride vacutainer for plasma FBG (Vitros FC 500) and EDTA for HbA1c (Bio Rad D10).

#### Inclusion Criteria

*Cases:* a. All patients 20-80 years diagnosed with type II diabetes mellitus based on ADA guidelines (n=100).

b. Patients who gave consent for the study.

*Controls:* Age and sex matched normal healthy adults (n=100).

*Exclusion Criteria:* a. Patients with associated medical disease like hemoglobinopathies, chronic liver disease, chronic kidney disease, chronic inflammatory disease.

b. Patients who did not give consent

### Statistical Analysis:

SPSS version 22.0 software (SPSS Inc. Chicago IL) was used for data collection and analysis. Interpretations were made based on results of ANOVA two factors with replication for multiple comparisons. Student t test for comparing individual parameters. A p-value <0.05 was considered statistically significant.

### Results:

100 cases and equal number of controls were enrolled in the study. The age (mean  $\pm$  S.D.) was  $29.37 \pm 4.76$  years for cases and  $29.30 \pm 4.35$  years for controls.

To evaluate the correlation of serum levels of adiponectin, ceruloplasmin and CRP among cases and controls ANOVA two factor with replication was applied and a significant difference in mean values of serum adiponectin, ceruloplasmin and CRP was noted among cases and controls (F-value= 675.220, p-value<0.0001). Individual analytes were then compared with student t test among cases and controls and significant association was found among each analyte (adiponectin  $t= 7.1299$ ,

p-value<0.001; ceruloplasmin  $t=31.4189$ , p-value<0.0001; CRP  $t=45.345$ , p-value<0.0001) (Table No.1, Fig No.1)

Correlation of analytes with FBG and HbA1c was obtained by Spearman's Rho correlation coefficient. The analysis showed positive correlation of FBG and HbA1c with ceruloplasmin and CRP and inverse correlation of FBG and HbA1c with adiponectin. (Table No.2 & 3)

Further the subjects enrolled in the study were divided in 5 groups (70-110 (controls), 111-160, 161-210, 211-260 and >260 mg/dl) based on FBG.

The fall in serum adiponectin levels was significant between 111-160 mg/dl and 161-210 mg/dl groups of FBG ( $p < 0.05$ ). However, the further decline in serum adiponectin levels in successive groups with increase in FBG was not statistically significant. The rise in serum ceruloplasmin levels was significant between 70-110 mg/dl and 111-160 mg/dl group and thereafter between 111-160 mg/dl and 160-210 mg/dl group of FBG ( $p < 0.05$ ). The subsequent groups with increasing FBG did not exhibit much significant increase in the ceruloplasmin levels. CRP levels exhibited rise from the control group and increased significantly among all the following defined groups thereafter. (Table No. 4)

Based on HbA1c the study group was divided into 3 groups (< 5.7% (controls), 5.7-6.4 % & 6.4%) based on HbA1c. The fall in serum adiponectin levels was significant between 5.7-6.4% and >6.4% groups of HbA1c ( $p < 0.05$ ). No significant difference in serum adiponectin levels in between the controls and 5.7-6.4% group. Statistically significant rise was observed in serum ceruloplasmin and CRP levels in the consecutive groups of HbA1c ( $p < 0.05$ ). (Table No. 5)

### Discussion:

Our study revealed strong inverse relation between plasma adiponectin with FBG and HbA1c. The findings were consistent with study by Okoro et al which reported significantly lower levels of adiponectin in type 2 diabetes and Tabak et al expressed higher adiponectin levels with lower HbA1c at follow-up.<sup>[2, 3]</sup> However Wang et al expressed that adiponectin-type 2 diabetes association remained unchanged after adjusting for inflammation and

**Table No. 1 Comparison of Serum Adiponectin, Ceruloplasmin and CRP Among Cases and Control groups by Student t test**

Parameters	Cases	Controls	Result
Adiponectin Mean ( $\mu\text{g/mL}$ )	4.98 $\pm$ 2.33	7.60 $\pm$ 2.83	t=7.1299 p <0.0001
Ceruloplasmin Mean (ng/ml)	69.69 $\pm$ 8.82	31.03 $\pm$ 8.55	t=31.4189 p <0.0001
CRP Mean (ng/ml)	31.24 $\pm$ 5.288	4.95 $\pm$ 2.37	t=45.345 p <0.0001

**Table No. 2 Spearman's Factor Showing Correlation of Serum Adiponectin, Ceruloplasmin and CRP with FBG**

Parameters	Spearman's Rho (rs)	P value
FBG vs. Adiponectin	-0.95011	<0.001
FBG vs. Ceruloplasmin	0.9127	<0.001
FBG vs. CRP	0.92685	<0.001

**Table No. 3 Spearman's Factor Showing Correlation of Serum Adiponectin, Ceruloplasmin and CRP with HbA1c**

Parameters	Spearman's Rho (rs)	P value
HbA <sub>1c</sub> vs. Adiponectin	-0.93386	<0.001
HbA <sub>1c</sub> vs. Ceruloplasmin	0.89833	<0.001
HbA <sub>1c</sub> vs. CRP	0.92031	<0.001

**Table No. 4. Correlation of Serum Adiponectin, ceruloplasmin and C-reactive protein with Fasting Blood Glucose levels in Cases and Control groups**

Participants	FBG (mg/dl) Range	No. of cases (n)	Adiponectin ( $\mu\text{g/ml}$ )	Ceruloplasmin (ng/ml)	CRP (ng/ml)
Controls (n=100)	70-110	100	7.60 $\pm$ 2.83	31.03 $\pm$ 8.55	4.95 $\pm$ 2.37
Cases (n=100)	111-160	54	6.73 $\pm$ 1.63	63.69 $\pm$ 7.57	27.41 $\pm$ 3.35
	161-210	19	3.64 $\pm$ 1.03	74.15 $\pm$ 3.50	33.25 $\pm$ 2.84
	211-260	15	2.64 $\pm$ 0.21	77.54 $\pm$ 0.76	35.96 $\pm$ 0.76
	> 260	12	2.18 $\pm$ 0.36	79.33 $\pm$ 2.54	39.26 $\pm$ 2.27

**Table No. 5. Correlation of Serum Adiponectin, Ceruloplasmin and CRP with HbA1c levels in Cases and Control Groups**

Participants	HbA <sub>1c</sub> (%) Range	No. of cases	Adiponectin Mean ( $\mu\text{g/mL}$ )	Ceruloplasmin Mean (ng/ml)	CRP Mean (ng/ml)
Controls (n=100)	<5.7	100	7.60 $\pm$ 2.83	31.03 $\pm$ 8.55	4.95 $\pm$ 2.37
Cases (n=100)	5.7- 6.4	17	7.96 $\pm$ 1.32	58.08 $\pm$ 6.33	25.25 $\pm$ 3.25
	>6.4	83	4.37 $\pm$ 1.99	72.00 $\pm$ 7.18	32.47 $\pm$ 4.72

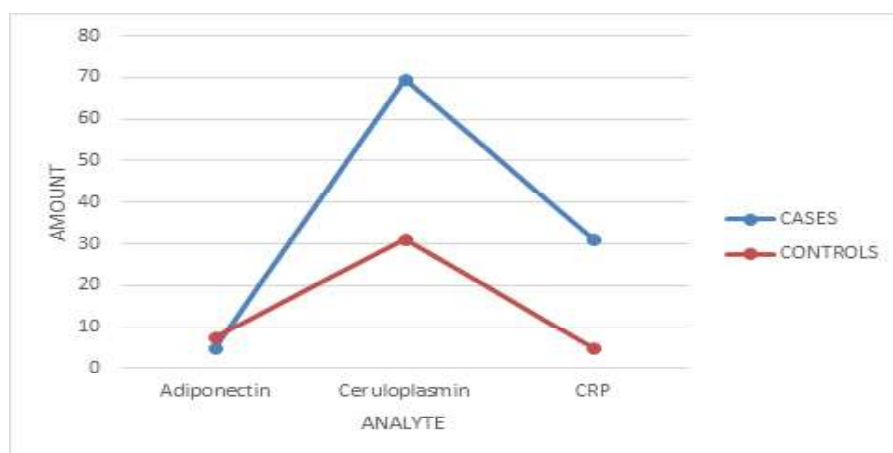
dyslipidemia markers but attenuated with adjustment for insulin sensitivity and/or glycaemia markers.<sup>14</sup> Where as in our study dyslipidemia markers were not taken into consideration. The inflammatory markers ceruloplasmin and CRP were analysed in the present study however no adjustment in inflammation was carried out.

CRP levels were higher with increase in FBG. Tabassum R et al reported higher CRP levels in diabetic compared to non-diabetic patients (16.48 $\pm$ 12.69, 6.00  $\pm$  0.00 mg/L in diabetics and non diabetics respectively).<sup>15</sup>

Vikram NV et al found that adiponectin levels (p =0.01) were lower whereas those of fasting insulin (p =0.01) and hs-CRP (p=0.02) were higher in overweight subjects.<sup>16</sup> Adiponectin levels inversely correlated insulin resistance measured by the homeostasis model of assessment (HOMA-IR; r = -0.31, p < .05), but not with hs-CRP levels. These studies were in agreement to the results of our study.

We found significant increase in serum ceruloplasmin in cases compared to controls. Daimon M *et al* reported

**Figure No.1 Mean values of serum adiponectin, ceruloplasmin and CRP levels among cases and controls.**



serum ceruloplasmin levels in the Type 2 diabetes were significantly higher than controls ( $p= 0.351$ )<sup>171</sup>. Sharma M *et al* reported a significant association between the raised serum ceruloplasmin levels and elevated plasma glucose levels in type-2 diabetes.<sup>181</sup> Indra S *et al* did not found association between serum ceruloplasmin levels and plasma glucose levels in type-2 diabetes.<sup>191</sup> Our study was concordant to Daimon M *et al*, Sharma M *et al* and discordant with Indra S *et al*.<sup>17-91</sup>

**Conclusion**

This study suggests adiponectin as an independent marker and acute phase reactants (ceruloplasmin and CRP) as inflammatory biomarkers in diabetogenesis.

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Nil.

**Conflicts of Interest**

There are no conflicts of interest.

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