

## Original Research Article

# Study on Adiponectin Uric acid and CRP in pre-diabetic and diabetic subjects

Rachna Sharma 1, Pallavi Anand 2, , Shravan Kumar 3

1- Research Scholar, Department of Biochemistry, Rama Medical College and Hospital, Rama University, Mandhana, Kanpur, U.P. India.

2- Professor and Head , Department of Biochemistry, Rama Medical College and Hospital, Rama University, Mandhana, Kanpur, U.P. India.

3. Professor and Head , Department of Medicine, Rama Medical College and Hospital, Rama University, Mandhana, Kanpur, U.P. India.

**Corresponding Author:** Dr. Rachna Sharma, Email: drrachna99@gmail.com

## ABSTRACT

**Background:** Diabetes and pre-diabetes are always on the rise over the past decade, but little is known about the development of type 2 diabetes mellitus dysfunction in young adults. The study was conducted in prediabetic and diabetic patients in order to belong to anti-inflammatory hormone adiponectin, proinflammatory marker uric acid in these patients, and also to determine the role of these markers in future CVD risk.

**Material & Methods-** This case-control study was conducted at Rama Medical College & Hospital, Mandhana Kanpur. Out of 400 participants recruited, 140 subjects were control, 140 were pre-diabetics, and the remaining 120 were controlled. The detailed history of the patients regarding age, gender, height, weight, and family history regarding obesity and other chronic illness was taken. Patients with medical complications or diseases and conditions that may affect levels of biochemical markers were excluded from the study. The data analysis was done using SPSS 16 and the results were reported as mean  $\pm$  SD where  $p < 0.05$  has been considered as statistically significant.

**Results-** The adiponectin level was significantly decreased and CRP, Uric acid levels were significantly increased in both the groups (Pre-diabetes and diabetes) as compared to control. Similarly, basic parameters including WHR, BMI, HbA1c, fasting blood glucose were also increased.

**Conclusion-** The study showed that pre-diabetes and diabetes are diseases of inflammatory origin with a high level of proinflammatory molecules. These mediators are not only the potent risk factors for pre-diabetes and diabetes but also mediate significant future CVD risk in these patients.

**Key Word:** Adiponectin, Uric acid, CRP, Pre-diabetic, Diabetes Mellitus.

## INTRODUCTION

On the basis of various studies conducted among diabetic subjects, it is clear that it is an inflammatory disorder. <sup>[1]</sup> The normoglycemic individual experiences a stage of latent hyperglycemia i.e. prediabetic phase before developing disease. Developments of phases from normoglycemia, to prediabetic and further to diabetic state, are all manifested by insulin resistance status. And that is also hallmark of the inflammatory response. Uric acid which is one of the purine catabolic products synthesized in vivo from glutamate and 5-phosphoribosyl pyrophosphate <sup>[2]</sup> and several epidemiological studies have implicated strong influence of UA in several conditions like insulin resistance, obesity, hypertension, metabolic syndrome, diabetes and renal diseases. <sup>[2]</sup> Raised level of

UA level has also been seen in prediabetic subjects and the offspring of diabetes patient too. Current few studies have shown the important role of UA in immune activation and thereby release of cytokines.<sup>[3]</sup> These molecules potentially mediate both endothelial dysfunction and phase of inflammation and oxidative stress in metabolic syndrome. Higher level of UA may pose individual with higher risk of diabetes as per literature search.<sup>[4]</sup> Antioxidant and pro-oxidant role of UA is well studied and established.<sup>[5]</sup> Raised UA level has also been reported to show its effect on pancreatic B cell apoptosis via activating several signal transduction pathways.<sup>[6]</sup> The study was planned in prediabetic and diabetic patients in order to pertain an anti-inflammatory hormone adiponectin, proinflammatory marker uric acid in these patients and also to determine role of these markers in future CVD risk.

## MATERIAL AND METHODS

Our study was a case control study which was approved by ethical committee of Rama Medical College & Hospital Kanpur, UP India. Out of 400 participants recruited, of whom 140 subjects were control, 140 were pre-diabetics and remaining 120 were control. Detailed history of the patients regarding age, gender, height, weight and family history regarding obesity and other chronic illness was taken. Patients suffering from any medical complications or diseases or any other conditions that may affect levels of inflammatory markers were not considered in the study. Blood samples from the recruited study subjects were collected and the separated serum or plasma was used for biochemical analysis. All the parameters including routine (FBG, HbA1c) and inflammatory parameters (Adiponectins, Uric acid & CRP) were analyzed appropriately using standard kits. The data analysis was done using SPSS 16 and the results were calculated as mean  $\pm$  SD where  $p < 0.05$  has been taken as statistically significant. The comparison of assayed parameters among control & prediabetic group, control & diabetic group and prediabetic & diabetic group was done by student – t test (unpaired). To determine the association, Pearson's correlation test was applied.

## RESULT

In this study, the adiponectin level was significantly decreased and CRP, Uric acid levels were significantly increased in both the groups (Pre-diabetes and diabetes) as compared to control. Similarly basic parameters including WHR, BMI, HbA1c, Fasting blood glucose were increased. In the study cardiac risk indices were also estimated and significantly high risk was documented in patient group with profoundly raised levels in diabetic group (**Table 1&2**). Regarding correlation analysis, adiponectin in both prediabetic and diabetic groups correlated inversely with CRP ( $r/p = -0.32 / < 0.001$ ,  $0.6 / < 0.001$ ), uric acid ( $r/p = -0.14 / 0.09$ ,  $-0.2 / 0.024$ ) respectively. Similarly the Indices for cardiac risk CRR, A1, AC & AIP showed inverse association to adiponectin ( $r/p = -0.31 / < 0.001$ ,  $-0.29 / < 0.001$ ,  $-0.29 / < 0.001$ ,  $-0.29 / < 0.001$  in prediabetic group;  $-0.45 / < 0.001$  &  $-0.41 / < 0.001$ ,  $-0.45 / < 0.001$  &  $-0.49 / < 0.001$  in diabetes respectively); and the linear association with CRP ( $r/p = 0.24 / 0.004$ ,  $0.22 / 0.008$ ,  $0.24 / 0.004$  and  $0.19 / 0.22$  in pre-diabetes and  $0.71 / < 0.001$ ,  $0.67 / < 0.001$ ,  $0.71 / < 0.59 / < 0.001$ ) in diabetes respectively, uric acid ( $r/p = 0.13 / 0.119$ ,  $0.12 / 0.15$ ,  $0.13 / 0.119$  and  $0.1 / 0.231$  in pre-diabetes;  $0.29 / < 0.001$ ,  $0.28 / < 0.001$ ,  $0.29 / < 0.001$  and  $0.22 / 0.013$  in diabetes respectively).

**Table 1- Basic parameter among control, pre-diabetic, diabetic group**

Parameters	Control	Pre-diabetes	Diabetes	p ivalue
BMI	23.23±1.97 <sup>a*</sup>	23.98±2.39 <sup>c</sup>	24.35±2.72 <sup>b**</sup>	<0.001
WHR	0.85±0.08 <sup>a**</sup>	0.91±0.12 <sup>c</sup>	0.91±0.12 <sup>b**</sup>	<0.001
Fasting iBlood iGlucose	0.840±6.99 <sup>a**</sup>	116.63±5.15 <sup>c**</sup>	160.49±40.15 <sup>b**</sup>	<0.001
HbA1c	5.06±0.44 <sup>a**</sup>	5.97±0.2 <sup>c**</sup>	8.63±1.18 <sup>b**</sup>	<0.001

Statically significant-\* p<0.05

a- Control & pre-diabetes b- Control & diabetes c- Pre-diabetes & diabetes

**Table 2- Correlation among adiponectin, CRP & UA in pre- diabetes, Diabetes and control subjects**

Parameters	Pre-diabetic	Diabetic	P ivalue
Adiponectin	8.21±1.97	6.74±2.04	<0.001
CRP	4.29±3.2	5.25±1.85	<0.001
Uric iAcid	4.58±0.95	6.36±1.9	<0.001

p<0.001= Significant

## DISCUSSION

Diabetes mellitus, one of the important health issue of 21<sup>st</sup> century, affecting millions of life which is mainly attributed to physical inactivity, stress, changes in living habit. Basic parameters including BMI, WHR, FBG, HbA1c were evaluated between different groups and found to be significantly raised pre-diabetic and diabetic group (>0.05 in both the groups). The outcome of study was in support of previous studies done. Adela et al also reported raised FBG in subjects compared to control. [7] Similarly Upadhyay S et al [8] and Jagmohangaihi D et al., [9] Also documented significantly high BMI, HbA1c, FBG. Differences were more significant in diabetics as compared to pre-diabetic group.

Adiponectin is an anti-inflammatory adipokine. The level of adiponectin was apparently less in both the groups (pre & diabetes) in comparison to healthy control. Supporting evidences to the observation of study were provided by Upadhyaya et al, [8] who also showed significantly low adiponectin level in IFG and hyperglycemic group as compared to normoglycemic group. Further supporting evidences were given by jiang Y et al [10] who showed significant differences in adiponectin level in both the subject groups as compared to control group. Fisher MF [11] et al also reported similar results. According to Yaturu S et al [12] adiponectin is one of the important factors predicting pre-diabetes. Protective role of adiponectin against hyperglycemia can be correlated with its insulin sensitizing effects<sup>13</sup>. Mechanistic approaches demonstrate that adiponectin stimulates AMP dependent protein kinases, [14] Thereby trigger insulin sensitivity by enhancing glucose cellular uptake, fatty acids oxidation in the liver. According to Okada IM et al, oral supplementation of Adipo R agonist can serve as a promising therapeutic option insulin resistance and diabetes. [15]

CRP is most common acute phase inflammatory marker generated by liver. Several observational studies have demonstrated well diabetes incidence and association with CRP. Results of our study

were in alliance with that of Shreshtha et al <sup>[16]</sup> and many others who showed orderly increase of CRP levels from control group to prediabetic and to diabetic group. Consistent results were also observed in the study of Sabnayagam C et al <sup>[17]</sup> and Gupta et al,<sup>[18]</sup> who showed high CRP level in prediabetic group. Though fewer studies have focused on ethnic variations with regard to association of CRP with pre-diabetes.<sup>[19]</sup>The elaborated mechanism that links hyperglycemia with CRP level may be explained in parts with insulin resistance.<sup>[20]</sup> Uric acid has been reported to serve as a marker for blood glucose metabolic alterations.<sup>[2]</sup> This study documented significantly high uric acid concentration in diabetic subjects (with respect to prediabetic, diabetic and control group). Study conducted by Khan SA et al reported similar results. <sup>[21]</sup> The level progressively increased from control group to IFG to hyperglycemic group thereby highlighting the significance of uric acid function in the pathogenesis of diabetes. Rao et al and a number of other workers also reported similar results.<sup>[22]</sup> Some studies suggested, though uric acid level is low in diabetes, raises again due to renal insufficiency.<sup>[23]</sup> Possible mechanism of such variations in uric acid level may be reduced synthesis and altered excretion of and increased consumption as an antioxidant.<sup>[23]</sup>

As per correlation analysis all the basic parameters were significantly and inversely correlated with adiponectins. These reports were analogous with many researches including Hina et al,<sup>[24]</sup> Uslu S et al, <sup>[25]</sup> Alam R et al,<sup>[26]</sup> reported significant inverse correlation of adiponectin with HbA1c and BMI but the correlation was insignificant in case of age, diabetes duration, insulin and glucose level.

## CONCLUSION

The study showed that pre-diabetes and diabetes are diseases of inflammatory origin with high level of proinflammatory molecules. These mediators are not only are potent risk factors to pre-diabetes and diabetes but also mediate significant future CVD risk in these patients. Therefore earlier screening of high risk individuals is suggested so as to prevent onset of diabetes development.

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