

Serum Adiponectin Level in Type 2 Diabetes Mellitus in Urban South Indian Population

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Abstract

Diabetes mellitus is a chronic non-communicable disease which not only increases morbidity, mortality and decreases quality of life, but also leads to a heavy economic burden for the patient, family and the society at large. Adiponectin is a peptide hormone, specifically expressed and produced by adipocytes and plays an important part in glucose metabolism, insulin resistance and it also has anti inflammatory and anti-atherosclerotic properties. This study has been conducted to find out the relationship of adiponectin between healthy controls and with cases of type 2 diabetes mellitus in urban South Indian population. This is a case – control study where cases were already diagnosed cases of type 2 diabetes and were under treatment. Controls were normal healthy individuals who came for routine health check up. This study suggested there is a significant decrease in serum adiponectin level in cases compared to controls (10.37 ± 7.68 vs. 7.53 ± 4.83 $\mu\text{g/ml}$; $P = 0.000$). A highly significant correlation was observed between fasting blood glucose and serum adiponectin ($r = 0.304$, P value = .001) was observed in the study. So the current study shows that decrease of adiponectin decreases the insulin sensitivity which may lead to type 2 diabetes mellitus and its vascular complications like hypertension.

Keywords: Adiponectin, Adipocyte, Diabetes Mellitus, Fasting Plasma Glucose, Globular form of adiponectin

Introduction

Worldwide diabetes mellitus is no more an epidemic; rather it has turned into a pandemic health hazard. As per W.H.O projection global burden of type 2 diabetes mellitus may increase from 366 million in 2011 to 552 million by 2030. Similarly the incidence in India is estimated to rise from 51 million in 2010 to 87 million by 2030^[1].

Diabetes mellitus is a most common endocrine disorder characterized by defect in secretion, action or both of insulin resulting in chronic hyperglycemia with disturbance of carbohydrate, fat and protein metabolism. Out of various causes of diabetes, recent studies show adiponectin play one of the most important role in not only development of diabetes as well as various complications of it^[2]. Adiponectin is one of the adipokines secreted from adipose tissue. It is a polypeptide of molecular weight of 30kDa having 244 amino acids. It also termed as Acrp 30, Adipo Q, apM1 or, GBP28 as was originally identified independently by four groups by different approaches. It has homologous chemistry of other peptides like collagen III, collagen IX and complement c1q. The concentration of adiponectin in circulation in healthy individuals ranges from 5 to 30 $\mu\text{g/ml}$ ^[3].

Adiponectin has clearly been shown to regulate glucose and fatty acid metabolism in skeletal muscles. It can increase the concentration of both basal and insulin stimulated glucose uptake by promoting GLUT-4

translocation to the cell membrane and increase fatty acid uptake and oxidation through the activation of AMPK, PPAR- α pathways. In the liver it causes reduction of hepatic glucose output, decreased free fatty acids (FFA) influx to the hepatocytes, increased fatty acid oxidation and promotion of insulin sensitivity. Various studies show globular form of adiponectin (gAd) administration improves insulin sensitivity in muscle by increasing fatty acid oxidation with a reduction in myocellular lipid accumulation^[4]. As adiponectin play important role in insulin sensitization, so this study was conducted to find out adiponectin level and it correlation to blood glucose in type -2 diabetes mellitus cases who are under treatment with oral hypoglycemic drugs.

Materials and Methods

This case - control study was conducted at Sri Ramachandra Medical College & Research Institute which included 160 subjects of South Indian population in the age group of 40 to 70 years. A total of 50 healthy non-diabetic subjects were taken from people attending Master Health Check-up programme in Sri Ramachandra Medical Centre as control group. The study group included 110 patients attending Diabetology OPD in Sri Ramachandra Medical College Hospital, who were known cases of diabetes mellitus type 2 in accordance with the established diagnostic criteria laid by American Diabetes Association. A written informed consent was obtained from each participant before commencement of the study. The study was performed in agreement with consideration as recommended by Institutional Ethical Committee, Sri Ramachandra Medical College and Research Institute.

The data were collected through a standard questionnaire. All subjects were interviewed regarding a full medical history that included age, sex, occupation, duration, systolic and diastolic blood pressure and family history of diabetes mellitus. The biochemical parameters such as fasting plasma glucose level, serum adiponectin were measured. The material for the study was the peripheral venous blood. Samples were drawn after an 8 to 12 hour of overnight fast. Sample for plasma glucose estimation was collected in grey capped vacutainer containing EDTA and others in yellow topped gel tube. All the tubes were subjected to centrifugation at 3000 rpm for 10 minutes followed by storage at -40°C until assayed.

Serum adiponectin was measured in the laboratory of Department of Biochemistry (SRMC & RI) using sensitive ELISA by Assay Max Human adiponectin Elisa Kit (Catalog No: EA2500-1)). Fasting plasma glucose was measured by Hexokinase–glucose-6-phosphate dehydrogenase method.

Results

All the results obtained were statistically analyzed using SPSS software version 15.0. Mean and standard deviation were found for all the parameters. Independent sample t-test and ANOVA were performed to check for the statistical test of significance for differences in means between the parameters. The serum adiponectin was highly significantly decreased in type -2 diabetes mellitus group compared to healthy control group. In diabetic group Fasting blood glucose was increased but it was not significant. On correlating adiponectin with fasting plasma glucose there was no correlation in control group but highly significant correlation was observed in study group.

Table – 1: Comparison of physical parameters of the study and control groups

Parameter	Control (n=50)	Study group (n=110)	P value
Age	52.2 ± 7.58	55.24 ± 6.4	0.010
Sex	25 / 25	44 / 66	---
SBP	118 ± 9.48	137 ± 24.6	0.000
DBP	75 ± 7.18	83 ± 10.2	0.000

Table – 2: Comparison of biochemical parameters of the study and control groups

Parameter	Control (n=50)	Study group (n=110)	P value
Adiponectin	10.37 ± 7.68	7.53 ± 4.83	0.000
FBG	100 ± 9.03	143 ± 66.7	0.079

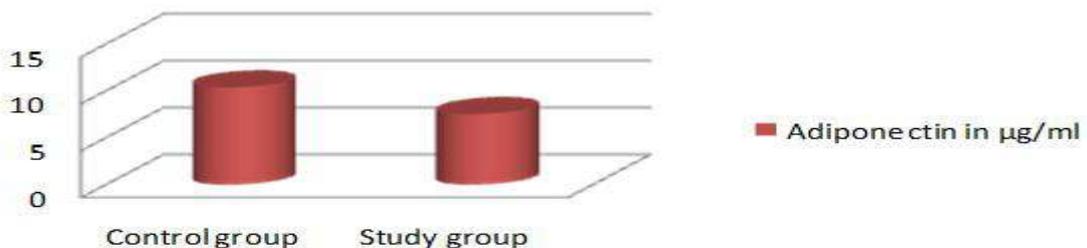
Table – 3: Comparison of parameters in control group based on sex

Parameter	Males (n = 25)	Females (n = 25)	P value
SBP	117 ± 8.49	118 ± 10.5	0.659
DBP	74 ± 7.1	76 ± 7.2	0.330
Adiponectin	9.37 ± 6.16	11.37 ± 8.97	0.364
FBG	99 ± 8.9	100 ± 9	0.805

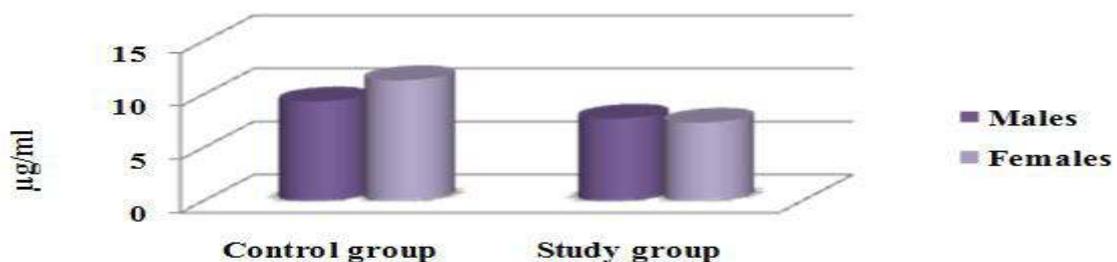
Table – 4: Comparison of parameters in study group based on sex

Parameters	Males (n = 44)	Females (n = 66)	P value
SBP	139 ± 23.7	136 ± 25.3	0.642
DBP	84 ± 11	81.7 ± 9.4	0.202
Adiponectin	7.75 ± 4.7	7.38 ± 4.94	0.692

Serum adiponectin levels



Comparison of serum adiponectin based on sex



Discussion

Obesity is a current growing public health problem and its prevalence has increased dramatically in recent years. It is associated with several chronic diseases such as coronary artery disease, hypertension, metabolic syndrome and type 2 diabetes mellitus in particular. The main function of adipose tissue is to store energy in the form of fat, but recent studies show it also functions as an endocrine tissue that secretes several bioactive molecules like cytokines and peptide hormones, which collectively known as adipokines. These adipokines are responsible for regulating metabolism and inflammation and are implicated in some chronic diseases^[5].

Adiponectin, one such peptide hormone is secreted abundantly by adipose tissue and directly sensitizes the body tissue to insulin. It has a special role as anti-inflammatory, anti-atherogenic and insulin sensitizer. Decrease in the level of serum adiponectin due to genetic or hormonal factors has been strongly implicated that in the development of insulin resistant type 2 diabetes mellitus, metabolic syndrome and other chronic diseases that are associated with obesity.

Comparison of physical parameters of control group versus study group revealed highly significant difference in systolic blood pressure and diastolic blood pressure (Table – 1). The control group serum adiponectin was 10.37 µg/ml and is observed to be quite close to the value reported by Nakano Y et al^[6]. On comparison of biochemical parameters, highly significant difference was found only in adiponectin. The mean difference of serum adiponectin levels was (10.37 ± 7.68 vs. 7.53 ± 4.83 µg/ml; P = 0.000). This result corroborates with the findings of study on Asian Indians by C. Snehalatha et al in 2003^[7] in which the base line adiponectin level in diabetics and non-diabetics was 11.3 ± 5.5 vs. 16.7 ± 7.6 µg/ml, P = 0.0017. Similar results were also reported by Tabak et al in 2009^[8] and Arleta Malecha-Jedraszka et al in 2011^[9] in their respective case-control studies on different populations. Conversely decrease in adiponectin level may be predictive of type 2 diabetes mellitus as suggested by Matsuzawa et al^[10], Kadowaki et al^[11]. A study by Nagwa AEG et al^[12] on Egyptian population shows a highly significant decrease in adiponectin level in type 2 diabetic patients group as compared to control group (10.0 ± 4.8 vs. 9.0 ± 5.1 µg/ml, P = 0.001).

Circulating adiponectin concentrations are higher in female than male, independent of the fact that female usually have more overall adiposity than male. The biological basis of this sexual dimorphism in the circulating levels of adiponectin is unknown. Possible explanation for this may be that sexual hormones regulate the production of adiponectin. But how estrogen and progesterone are involved in the regulation of plasma adiponectin level is controversial, as some study shows estrogen increases adiponectin production; however evidence supporting this hypothesis is limited and contradictory. This also partly accounts for the fact that females are more sensitive to insulin than males. In this study it was observed that there was a difference in the mean of adiponectin between males and females (9.37 ± 6.16 vs. 11.37 ± 8.97) of control group but it is not statistically significant. C. Snehalatha et al^[8] in their study in 2003 also found higher level of serum adiponectin in females which was also not statistically significant in normal healthy population. A non-significant result in control group of this study could be due to high standard deviation and limited sample size.

In this study similar comparison of adiponectin in study group did not show an expected higher level in females. However significant differences were reported by Merja Santaniemi et al in 2006^[13], Peake PW et al in 2005^[14]. The unexpected lower range of serum adiponectin in females of study group may be due to various factors like duration and progression of diabetes, effect of oral hypoglycemics etc.

Role of adiponectin on glucose metabolism is that it increases insulin sensitivity by inhibiting hepatic glucose production and increases glucose uptake in muscles. It also plays an important role in lipid metabolism as it decreases free fatty acid influx to liver and increased free fatty acid oxidation in both liver and muscle. Increased level of plasma adiponectin is strongly suggestive of its association with decrease risk of diabetes mellitus in healthy individuals. Conversely a decreased serum adiponectin level has been observed to be associated with high plasma glucose level as in diabetes mellitus by various studies. On correlating fasting blood glucose (FBG) with serum adiponectin in study group a highly significant ($R = 0.304$, $P = 0.001$) result was obtained. The positive correlation of FBG is in contrast to the accepted notion i.e. serum adiponectin and FBG have an inverse relationship and this finding is well supported by other researchers such as Bruce B. Duncan et al ^[15], Helen C. Looker et al^[16]. The relationship between plasma adiponectin and fasting glucose level may be influenced by presence of oral hypoglycemic drugs which has been taken by study group for the treatment of type 2 diabetes mellitus. The molecular mechanisms underlying the glucose lowering effect of adiponectin has been shown to be partly due to its activation of AMP- activated protein kinase (AMPK) cascade in the liver and skeletal muscle. AMPK is a target for metformin and other oral hypoglycemic agents. Moreover exercise is also a factor to effect the glucose utilization through AMPK mediated mechanism in peripheral tissues. Treatment record and habits like exercise, diet patterns etc were not taken into account in this present study. So it may be inferred that these unseen factors could have influenced the adiponectin levels resulting in a contrasting observation.

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