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Research article

SERUM ADIPONECTIN LEVEL IN OBESE AND NON OBESE TYPE 2 DIABETES MELLITUS

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ABSTRACT

Back ground: Worldwide diabetes mellitus is no more an epidemic; rather it has turned into a pandemic health hazard. Association of obesity in type 2 diabetes mellitus is an established fact. This association could be partly mediated by altered secretion of adipokines by adipose tissue. Among all adipokines, adiponectin has been considered as an important factor in obesity induced insulin resistance. This new hormone produced exclusively by adipocytes differs from its predecessors in at least one important feature. While all of the other adipose tissue derived hormones related to insulin resistance are increased in obesity, adiponectin production and concentration actually decreases in obese subjects. **Objective:** the study was taken up to investigate the relationship between adiponectin in obese and non obese type 2 diabetes, and also to find out the correlation between adiponectin and serum lipids in urban south Indian population. **Method:** The cases chosen for the study group were already diagnosed cases of type 2 diabetes mellitus undergoing treatment. All subjects were interviewed regarding a full medical history that included age, sex, occupation, duration and family history of diabetes mellitus. The general physical examination procedure included measurement of height, weight, waist circumference and hip circumference. The biochemical parameters such as fasting plasma glucose, serum adiponectin, HDL and triglyceride were measured. **Result:** The reduction of serum adiponectin in study group was highly significant as compared to control group but its difference between the two subgroups divided based on BMI did not give a statistically significant result. But on correlation of BMI with adiponectin in study group, the correlation co-efficient was found to statistically highly significant. Similar correlation of waist-hip ratio (W/H) with adiponectin did not give a significant result. **Conclusion:** Adiponectin is lowered in obese non-diabetics affecting lipid metabolism showed by increase of LDL and TG and decrease of HDL. In obese diabetics adiponectin is high but dyslipidemia is still present possibly due to improper function of existing serum adiponectin.

KEYWORDS: Adiponectin, Diabetes mellitus, Obesity, Dyslipidemia.

INTRODUCTION

Diabetes mellitus (DM) is a metabolic disorder characterized by defect in secretion, action or both of insulin resulting in chronic hyperglycemia with disturbance of carbohydrate, fat and protein metabolism. DM and obesity are closely interrelated in terms of pathogenesis and pathophysiology. Moreover, the prevention and control of these diseases have become prominent public health issues. Both DM and obesity result in vascular complications, such as coronary artery disease, cerebrovascular disease, and peripheral vascular disease, caused by arteriosclerosis. Obesity is defined as an increase in body fat mass. Visceral fat plays a more important role in a variety of metabolic abnormalities associated with obesity than subcutaneous fat and that increases in visceral fat both raise concentrations of hepatic portal blood free fatty acids and reduce insulin sensitivity [1]. While it has long been apparent that obesity is a major risk factor for type 2 diabetes, it has recently been appreciated that adipose tissue, in addition to its role as an energy reservoir, modulates energy metabolism via secretion of circulating adipocytokines. Variety of adipocytokines including leptin, adipsin and tumor necrosis factor etc are produced by adipose tissue. Adiponectin, recently identified most abundant among them is a 30 kDa protein. It plays an important role in the regulation of glucose and lipid

metabolism [2, 3]. Adiponectin increases insulin sensitivity and improves glucose tolerance. Plasma adiponectin concentrations are positively correlated with whole-body insulin sensitivity. Adiponectin is found to be antidiabetic, anti-atherosclerotic and it also plays an important role in inflammation [4, 5]. Because of various metabolic effects of adiponectin, this study was designed to find out variation of adiponectin in obese and non obese type 2 diabetic patients and relation of adiponectin with lipid profile in type 2 diabetic patients.

The aim of the present work was to study the adiponectin concentration between obese and non-obese diabetic and non diabetic and also association of plasma adiponectin levels and lipid profile in type-2 diabetic patients in urban south Indian population.

METHODOLOGY

Study design: The present study is analytical case - control study

Place of research: The study was conducted at Sri Ramachandra Medical College & Research Institute.

Ethical approval: Written informed consent was obtained from each participant before commencement of the study. The study was performed in agreement with considerations as recommended by the Institutional Ethical Committee, Sri Ramachandra Medical College and Research Institute.

Inclusion criteria: ages ranging between 40 and 70 years including both genders were stratified according to diabetes mellitus and obesity into two categories each.

1) In the first category, the subjects were divided into two groups as diabetic / cases (n=110) and non diabetic / control (n=50)
2) In the second category, both the case and control group were further subdivided as obese (BMI> 25 Kg/m2) and non obese (BMI < 25Kg/m2) respectively.

Exclusion criteria: Type 1 diabetes mellitus, gestational diabetes, any other cause of glucose intolerance, malignancies

Sample size: A total of 160 subjects

Grouping: The control group consisted of 50 normal healthy individuals and the study group comprised of 110 known cases of type 2 Diabetes Mellitus.

Methodology

All subjects were interviewed regarding a full medical history that included age, sex, occupation, duration and family history of diabetes mellitus. The general physical examination procedure included measurement of height, weight, waist circumference and hip circumference. Waist circumference at the umbilical level and hip circumference at the level of maximum girth were measured and waist –hip ratio (W/H) [6] were calculated, so also the Body Mass Index (BMI) [7] in each subject. The material for the study was the peripheral venous blood. Samples were drawn after 8 to 12 hour of overnight fast. Sample for plasma glucose estimation was collected in grey capped vaccutainer 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^{o}C until assayed.

Serum adiponectin was measured using sensitive ELISA (Assay Max Human adiponectin Elisa Kit (Catalog No: EA2500-1)) [8] . Fasting plasma glucose was measured by Hexokinase–glucose-6-phosphate dehydrogenase method [9]. Triglyceride was measured by enzymatic method i.e. GPO - PAP (Glycerol phosphate oxidase – peroxidase – amidopyrine method) [10]. HDL cholesterol was measured by enzymatic end point method (Accelerator Selective Detergent methodology) [11].

RESULTS

A highly significant reduction of serum adiponectin level in diabetic group (cases) compared to control / healthy group ($p < 0.01$) was observed. There was highly significant difference of BMI & W/H between these two groups. A significant decrease in HDL –C ($p < 0.010$) in diabetic group was noticed. Triglyceride and fasting blood glucose were high in diabetic group but not statistically significant. [Table – 1]

Table 1. Comparison of parameters of the study and control groups

Parameter	Control (n=50)	Study group (n=110)	P value
Age(Year)	52.2 ± 7.6	55.24± 6.4	0.01*
Sex (M/F)	25 / 25	44 / 66	---
BMI(Kg/m^2)	25.63 ± 3.2	26.75 ± 4.2	0.001**
W/H	0.89 ± .16	0.97 ± .1	0.004**
Adiponectin (µg/ml)	10.37 ± 7.7	7.53 ± 4.8	0.000**
FBG (mg/dl)	100 ± 9.0	143 ± 66.7	0.079
HDL(mg/dl)	36 ± 7.4	33 ± 11.8	0.01*
TG(mg/dl)	114 ± 46.5	192± 100.4	0.163

**highly significant (P < 0.01) * significant (P < 0.05)

All the subjects in the study and control groups were further subdivided into two subgroups based on BMI (<25 and ≥25). As shown in Table – 2, waist hip ratio was higher in obese group which is statistically highly significant ($p<0.000$). Adiponectin was decreased in obese group but not statistically significant. On analyzing by Pearson correlation there was no correlation between BMI and the biochemical parameters such as serum adiponectin, FBG, serum HDL and TG in control group.

Table 2. Comparison of parameters of control group based on BMI

Parameter	BMI < 25 (n= 20)	BMI ≥ 25 (n= 30)	P value
W/H	0.79 ± 0.1	0.96 ± 0.2	0.000**
Adiponectin	10.8 ± 9.4	10.08 ± 6.4	0.904
FBG	97.8 ± 7.5	101.46± 9.7	0.190
HDL	36 ± 8.7	36 ± 6.5	0.634
TG	104 ± 46	121 ± 46	0.329

**highly significant (P < 0.01) * significant (P < 0.05)

On comparing the parameters in study group based on BMI, as shown in Table – 3, it was observed that waist hip ratio and serum triglyceride were significantly high in obese diabetic group. The adiponectin concentration was increased

in obese diabetic group compared to non obese diabetics but was not statistically significant attributed to high standard deviation and sample size. There was increase in TG and decrease in HDL between two groups but was not statistically significant.

Table 3. Comparison of parameters of study group based on BMI

Parameter	BMI < 25 (n = 39)	BMI ≥ 25 (n = 71)	P value
W/H	0.93 ± 0.1	0.99 ± 0.09	0.034*
Adiponectin	6.44 ± 3.9	8.13 ± 5.19	0.079
FBG	144 ± 69.8	143.5 ± 65.5	0.967
HDL	36 ± 13	31.7 ± 10.8	0.067
TG	159.6±65.9	210.1 ± 111	0.011

**highly significant (P < 0.01) * significant (P < 0.05)

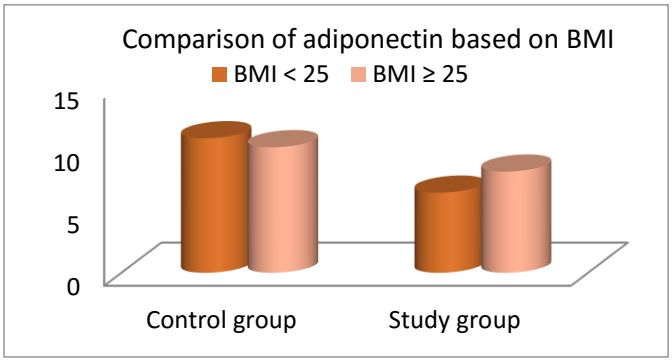

Figure 1. Comparison of adiponectin based on BMI

On correlation of BMI with biochemical parameters in control group, a negative correlation was obtained between BMI and serum adiponectin (R = - 0.023, P = 0.872). Analyzing the study group, a significant but positive correlation (R = 0.302, P = 0.001) was observed between BMI and serum adiponectin. But a significant negative correlation of BMI with serum HDL- C was noted although it was non-significant with FBG and TG.

Table 4. Correlation of BMI with Adiponectin, FBG, serum creatinine, HDL and TG in control group

Parameter	Correlation coefficient	P value
Adiponectin	-.023	0.872
FBG	.206	0.151
HDL	.050	0.729
TG	.167	0.246

Table 5. Correlation of BMI with Adiponectin, FBG, serum creatinine, HDL and TG in study group

Parameter	Correlation coefficient	P value
Adiponectin	.302	0.001**
FBG	.087	0.368
HDL	-.194	0.04*
TG	.144	0.133

**highly significant (P < 0.01) * significant (P < 0.05)

A similar trend was also observed on analyzing W/H ratio with the biochemical parameters in both case and control groups.

Table 6. Correlation of W/H with Adiponectin, FBG, Serum creatinine, HDL, TG in control group

Parameter	Correlation coefficient	P value
Adiponectin	-.096	0.509
FBG	.185	0.199
HDL	.199	0.167
TG	.077	0.593

Table 7. Correlation of W/H with Adiponectin, FBG, Serum creatinine, HDL and TG in study group

Parameter	Correlation coefficient	P value
Adiponectin	.131	0.174
FBG	-.002	0.986
HDL	-.139	0.148
TG	.082	0.396

DISCUSSION

Adipocytes are an endocrine entity and secrete various proteins commonly referred to as adipocytokines. These include tumor necrosis factor, plasminogen-activator inhibitor type 1, adipsin, resistin, leptin, and adiponectin [12]. Most adipocytokines are positively correlated with obesity; however, adiponectin is negatively correlated with obesity and appears to be down-regulated in more obese patients. Adiponectin also plays an important role in glucose metabolism and insulin resistance and is down-regulated in type 2 diabetes patients and in those with cardiovascular disease [13, 14, 15]. In the present study, diabetic patients had a lower concentration of adiponectin compared with that of non-diabetic control group as published in our previous published article.

Analysing the control group, a lower serum adiponectin level was observed in the subgroup with BMI more than 25 but it was not statistically significant possibly due to small sample size for statistical comparison. But the study group (cases) revealed a higher serum adiponectin level in the subgroup with BMI more than 25. This result is in contrast to the studies by Merja Santaniemi et al in 2006 [16], Drazenka Pongrac Barlovic et al in 2010 [17] and Arleta Malecha-Jedraszek et al in 2011 [18]. As all diabetic patients in our study were of different duration of diabetes with or without various complications like hypertension, micro and macroalbuminuria and were under treatment, the excretion of adiponectin could be affected showing higher adiponectin in obese diabetic patients compared to non obese diabetic patients.

The positive correlation observed between BMI and serum adiponectin was in contrast to reports by other authors including Merja Santaniemi et al in 2006 [16], Drazenka Pongrac Barlovic et al in 2010 [18]. The reason may be alteration in the blood concentration of adiponectin by various factors such as medication, exercise, diet, alcohol, smoking etc and most importantly excretion of adiponectin in later stage of diabetic nephropathy.

A negative correlation was observed on analyzing waist hip ratio (W/H) with serum adiponectin in control group but it was not statistically significant. Correlation of waist hip ratio with adiponectin level was found to be non-significant in the study group. A study by Mojtaba Eizadi et al in 2006 [19] also reveals a result similar to this study. But studies by Amir Elokely et al in 2010 [20], showed significant correlation of waist hip ratio with serum adiponectin which could be attributed to similar possible factors as mentioned in the context of BMI above.

Adiponectin augment lipid oxidation with increased glucose uptake. This results in prevention of postprandial elevation of FFA. gAd administration improves insulin sensitivity in muscle by increasing fatty acid oxidation with a reduction in myocellular lipid accumulation. Here in this study adiponectin levels have been positively associated with HDL-C and negatively with low-density lipoprotein-cholesterol and TG (4), suggesting a role not only in obesity but also in dyslipidemia. But in case of obese diabetic group though adiponectin was high but reverse finding may suggest improper function of it on lipid metabolism.

CONCLUSION

Serum adiponectin level decreases with obesity, with W/H and BMI as the comparison tools. But such relation is not seen in obesity with diabetes mellitus which could be due to defect in secretion as well as excretion of adiponectin in diabetic individuals and with diabetic complications. Adiponectin is lowered in obese non-diabetics affecting lipid metabolism showed by increase of LDL and TG and decrease of HDL. In obese diabetics adiponectin is high but dyslipidemia is still present possibly due to improper function of existing serum adiponectin.

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