

A Study on the Serum Adiponectin and Lipid Profile Levels in Type 2 Diabetes

Vineetha K R¹, Periyasamy S.², Inmozhi R³, Santha K⁴, Ashok Kumar P⁵, Kanakasabai G⁶

ABSTRACT

Introduction: Adiponectin (Ad) is one of the main cytokines produced by adipose tissue. Low serum adiponectin levels were associated with atherogenic lipoproteins (elevated triglycerides, small dense LDL cholesterol, and low HDL cholesterol), increased plaque volume, suggesting an antiatherogenic role in the early stages of lesion development and coronary artery disease. Some studies reported anti-atherogenic properties of adiponectin showed an increase in circulating levels of adiponectin in cardiovascular disease. The aim of this study was to find out the association of serum adiponectin with lipid profile levels in type 2 diabetic patients.

Material and methods: 100 controls and 100 type 2 diabetic patients on oral hypoglycemic drugs between 35-55 years of age without any cardiac, renal, liver, and thyroid dysfunction were selected for this study. Baseline investigations, blood sugar, HbA1C, lipid profile parameters were assessed by standardized procedures and adiponectin levels were analyzed by the ELISA method.

Results: Serum Total cholesterol, Triglycerides, LDL cholesterol levels were increased in type 2 diabetic patients compared with controls. Serum adiponectin level was found to be low which showed a significant negative correlation with HbA1C ($r = -0.775$, $P < 0.001$). We also observed negative correlation of serum adiponectin with total cholesterol ($r = -0.449$, $P < 0.001$), triglycerides ($r = -0.632$, $P < 0.001$), LDL cholesterol ($r = -0.299$, $P < 0.001$) and positive correlation with HDL -cholesterol ($r = 0.176$, $P < 0.001$).

Conclusion: Serum Adiponectin level was significantly low in type 2 diabetics and associated with borderline dyslipidemia in our study. Further longitudinal studies are needed to find out the role of adiponectin as an early marker of atherosclerosis.

Keywords: Adiponectin, Cardiovascular Disease, Dyslipidemia

INTRODUCTION

Adiponectin (Ad) is one of the main cytokines produced by adipose tissue. It acts on peripheral target tissues through specific receptors, so it can be classified as a hormone.¹ Evidence showed that low Ad values are associated with the presence of coronary artery disease.² Several studies reported that adipokines play an important role in glucose and lipid metabolisms and the development of cardiovascular and metabolic complications of obesity.³ The metabolic effect of Ad decreases liver glucose production, circulating glucose, and insulin.⁴ Initially, low levels of adiponectin were also found in patients with coronary artery disease independently of other risk factors.⁵

The down-regulation of AdipoR1/2 may play a role in the

development of insulin resistance, type 2 diabetes, metabolic syndrome, and atherosclerosis.⁶ Cross-sectional studies reported that low serum adiponectin has been associated with obesity, IR, T2D, dyslipidemia, hypertension, and coronary heart disease.⁷ Serum adiponectin levels are also influenced by modifiable factors such as physical activity, diet, and genetic factors.^{8,9}

Steven P.et.al., reported that low adiponectin levels are associated with atherogenic lipoproteins (elevated triglycerides, small dense LDL cholesterol, and low HDL cholesterol), increased plaque volume, lipid-rich plaque, in the nondiabetic population, suggesting an antiatherogenic role in the early stages of lesion development.¹⁰ Adiponectin is a unique adipokine, downregulated in the presence of increasing central adiposity and associated with insulin resistance, inflammation, the risk for metabolic syndrome, type 2 diabetes, decreased LDL particle size, and small dense HDL.¹¹ Increased levels have also been associated with reduced risk of myocardial infarction even after adjustment for traditional cardiovascular risk factors.¹² However, the association between serum adiponectin and coronary events remains controversial.¹³⁻¹⁶

Prior studies have shown a significant inverse correlation between coronary lumen narrowing as assessed by angiography and plasma adiponectin levels.^{17,18} Recent studies indicate that elevated adiponectin levels are associated with adverse outcomes in patients with established coronary atherosclerosis.^{16,19-21} So the aim of this study is to explore the association of serum adiponectin and lipid profile levels in type 2 diabetic patients compared with healthy volunteers.

¹Research Scholar, Department of Biochemistry, Rajah Muthiah Medical College, Annamalai University, ²Professor, Department of Medicine, Rajah Muthiah Medical College, Annamalai University, ³Professor, Department of Biochemistry, Rajah Muthiah Medical College, Annamalai University, ⁴Professor & HOD, Department of Biochemistry, Rajah Muthiah Medical College, Annamalai University, ⁵Professor, Department of Biochemistry, Rajah Muthiah Medical College, Annamalai University, ⁶Biochemist, Department of Biochemistry, Rajah Muthiah Medical College, Annamalai University, India

Corresponding author: Dr.K.Santha, M.D., Ph.D., Professor & HOD, Department of Biochemistry, Rajah Muthiah Medical College, Annamalai University, India

How to cite this article: Vineetha KR, Periyasamy S, Inmozhi R, Santha K, Ashok Kumar P, Kanakasabai G. A study on the serum adiponectin and lipid profile levels in type 2 diabetes. International Journal of Contemporary Medical Research 2020;7(11):K1-K4.

DOI: <http://dx.doi.org/10.21276/ijcmr.2020.7.11.2>



MATERIAL AND METHODS

The experimental study was done in the Department of Biochemistry at Rajah Muthiah Medical College and Hospital, Annamalai University, Chidambaram, Tamil Nadu, India. The study was approved by the Institutional Ethics Committee (IHEC/0385/2018). Written informed consent was obtained from all subjects after clearly explaining the nature, purpose, and duration of the study.

One hundred types 2 diabetic Patients on oral hypoglycemic drugs, in the age group 35-55 years without any other organic diseases were selected for our study. Diabetes is confirmed based on fasting and postprandial blood glucose levels. ECG was done to rule out the cardiac problem. 100 control subjects in the same age group were also selected for this study.

Fasting blood samples were collected from study subjects. Blood samples were centrifuged at 3000×g for 10 min. The routine investigations glucose, lipid profile (Total Cholesterol, HDL, LDL, triglycerides) carried out by ERBA

semi-automated analyzer. Samples were separated and kept in a deep freezer at -20 degree C for special parameter analysis. Serum Adiponectin was analyzed by Enzyme-Linked Immunosorbent Assay (ELISA).

STATISTICAL ANALYSIS

The data were expressed as mean ± SD. Statistical analysis was carried out by SYSTAT. The comparison of parameters in the study groups was done by the student's 't' test, while the correlation was determined by Pearson's correlation coefficients. P < 0.001, P < 0.05 indicated statistical significance.

RESULTS

Table 1 shows the baseline parameters in control and diabetic patients. Baseline parameters like height, weight, BMI, waist-hip ratio, systolic BP, Diastolic BP were within the normal range in the control and diabetic group.

Table 2 shows the FBS, PPBS, and HbA1C in controls and diabetes. There was an increase in the level of FBS,

Parameters	Controls (n=100) Mean ± SD	Type 2 diabetic patients (n=100) Mean ± SD	p-value
Age (year)	45.53 ± 5.33	46.21 ± 5.24	0.365
Height (cm)	163.90 ± 6.43	169.77 ± 7.40	0.001
Weight (cm)	62.17 ± 6.31	76.21 ± 7.12	0.001
BMI (Kg/m ²)	23.17 ± 2.54	26.48 ± 2.24	0.001
Waist Hip ratio	0.895 ± 0.02	0.916 ± 0.02	0.001
Systolic BP (mm of Hg)	113.94 ± 5.08	126.22 ± 8.97	0.001
Diastolic BP (mm of Hg)	76.38 ± 3.0	79.88 ± 3.96	0.001

Values are shown as mean ± SD. p<0.05 was considered statistically significant

Table-1: Baseline parameters in Controls and Type 2 diabetic patients

Parameters	Controls (n=100) Mean±SD	Type 2 Diabetic patients (n=100) Mean±SD	p-value
FBS (mg/dl)	94.64 ± 9.14	155.14 ± 33.93	0.001
PPBS (mg/dl)	115.29 ± 10.74	252.14 ± 44.20	0.001
HbA1C (%)	5.87 ± 0.30	8.29 ± 0.51	0.001
Adiponectin (ng/ml)	19.48 ± 5.34	7.46 ± 2.54	0.001

Values are shown as mean ± SD .p<0.05 was considered statistically significant

Table-2: Blood sugar, HbA1c and serum Adiponectin in controls and type 2 diabetics

Parameters	Control (n=100) Mean±SD	Type 2Diabetic patients (n=100) Mean±SD	p-value
Total cholesterol (mg/dl)	176.34 ± 12.97	202.38 ± 26.97	0.001
Triglycerides (mg/dl)	99.31 ± 15.42	155.44 ± 30.19	0.001
HDL (mg/dl)	39.75 ± 3.94	38.27 ± 3.20	0.004
LDL (mg/dl)	106.20 ± 16.36	136.17 ± 29.46	0.001

Values are shown as mean ± SD .p<0.05 was considered statistically significant

Table-3: Lipid profile parameters in controls and Type 2 diabetic patients

Parameter	Pearson correlation coefficient (r)	p-Value
Adiponectin (ng/ml) Vs Total Cholesterol (mg/dl)	-0.449	<0.001
Triglyceride (mg/dl)	-0.632	<0.001
HDL (mg/dl)	0.176	<0.001
LDL Cholesterol (mg/dl)	-0.299	<0.001
HbA1C (%)	-0.775	<0.001

Data values representing the Pearson Correlation Coefficient(r), Correlation is significant at the 0.01 level (2-tailed).

Table-4: Correlation between Adiponectin and HbA1C, lipid profile

PPBS, and HbA1C in diabetic patients compared to control statistically significant subjects. ($P < 0.001$).

Table -3 shows the levels of serum cholesterol, triglyceride, HDL cholesterol, and LDL cholesterol. The level of serum cholesterol, triglycerides, and LDL-C were increased in diabetics compared to controls and statistically significant ($p < 0.01$). HDL cholesterol was within the normal range in both control and diabetic patients.

Table 4 shows serum Adiponectin negatively correlated with total cholesterol, triglycerides, serum LDL - cholesterol, HbA1C, and positively correlated with HDL cholesterol.

DISCUSSION

The prevalence of obesity has been increasing worldwide in recent years, in adults, children, and adolescents.²² In India, more than 135 million individuals were affected by obesity. The prevalence of obesity in India varies due to age, gender, geographical environment, socio-economic status, etc. In India, abdominal obesity is one of the major risk factors for cardiovascular disease (CVDs).²³ Obesity is associated with type 2 diabetes, hypertension, dyslipidemia, and metabolic syndrome.^{24,25,26,27}

Our study showed a high BMI in type 2 diabetics compared to controls. Several studies have proved links between obesity and T2DM, relating to insulin resistance, pro-inflammatory cytokines, endothelial dysfunction, altered fatty acid metabolism, mitochondrial dysfunction, and endoplasmic reticulum stress.²⁸ We found that serum cholesterol, triglycerides, and LDL cholesterol levels were high and statistically significant in type 2 diabetic patients compared to the control group. Dyslipidemia in individuals with type 2 diabetes is very common, with a prevalence of 72–85%. This is associated with a significantly increased risk of coronary artery disease compared to individuals without diabetes.²⁹ Increased triacylglycerols and reduced HDL-cholesterol are the main quantitative lipid abnormalities of diabetic dyslipidemia.³⁰

It is believed that transport of lipoproteins across the endothelial cell monolayer is an initial step in atherogenesis and is also probably enhanced in the presence of oxidized LDL. In our study, we observed adiponectin levels were significantly decreased in type 2 diabetics compared to controls. Also, adiponectin levels are negatively correlated with serum total cholesterol, triglycerides, and positively correlated with high-density lipoprotein as reported earlier.

Rangasamy S. et al. reported that an inverse association of adiponectin levels with a higher prevalence of small dense LDL particles. Small dense LDL is associated with endothelial cell injury and increased permeability.³¹ In a cohort of patients with coronary artery disease, lower adiponectin levels are associated with small dense LDL cholesterol, increased plaque volume as measured by lipid-rich atheroma, and a higher prevalence of intravenous ultrasound (IVUS) -derived pathological intimal thickening in nondiabetic patients, suggesting an antiatherogenic role for adiponectin.¹⁰ Further, adiponectin may play a regulatory role in foam cell maturation. At physiologic concentrations of

adiponectin, the expression of class A macrophage scavenger receptor is suppressed. Adiponectin also dose-dependently decreases class A macrophage scavenger receptor-ligand binding and uptake activities, suggesting a preventive role in foam cell maturation and subsequent atherosclerosis progression.³²

CONCLUSION

In our study serum, Adiponectin level was significantly low in type 2 diabetics and associated with high total cholesterol, triglycerides, and low HDL cholesterol. Adiponectin is a unique adipokine, downregulated in the presence of increasing central adiposity and associated with insulin resistance, inflammation, the risk for metabolic syndrome, type 2 diabetes. Further longitudinal studies are needed to find out the role of adiponectin as an early marker of atherosclerosis.

REFERENCES

1. Antonina Orlando, Elisa Nava, Marco Giussani, and Simonetta Genovesi. Adiponectin and Cardiovascular Risk. From Pathophysiology to Clinic: Focus on Children and adolescents *Int J Mol Sci* 2019; 20: 3228.1-14.
2. Sattar N, Wannamethee G, Sarwar N, Tchernova J, Cherry L, Wallace A.M. Adiponectin and coronary heart disease: A prospective study and meta-analysis. *Circulation* 2006;114:623-629.
3. Jain V, Kumar A, Agarwala A, Vikram N, Ramakrishnan L. Adiponectin; Interleukin-6 and High-sensitivity C-reactive Protein Levels in Overweight/Obese Indian children. *Indian Pediatr* 2017;54:848-850.
4. Weyer C, Funahashi T, Tanaka S, Hotta K, Matsuzawa Y, Pratley R.E., Tataranni P.A. Hypoadiponectinemia in obesity and type 2 diabetes: close association with insulin resistance and hyperinsulinemia. *J. Clin. Endocrinol. Metab* 2001;86:1930-1935.
5. David Karasek, Helena Vaverkova, Milan Halenka, Dagmar Jackuliakova, Zdenek Frysak, Dalibor Novotny. Total Adiponectin levels in dyslipidemic individuals: Relationship to metabolic parameters and Intima Media Thickness. *Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub* 2011;155:55-62.
6. Ouchi N, Kihara S, Arita Y, Okamoto Y, Maeda K, Kuriyama H. Adiponectin; an adipocyte-derived plasma protein; inhibits endothelial NF-B signaling through a cAMP-dependent pathway. *Circulation* 2000;102:1296-1301.
7. Andrew Mente, David Meyre, Matthew B Lanktree, Mahyar Heydarpour, A Darlene Davis, Ruby Miller, Hertzler Gerstein, et al. Causal Relationship between Adiponectin and Metabolic Traits: A Mendelian Randomization Study in a Multiethnic Population. *PLoS One*. 2013; 8: e66808.1-8.
8. Katherine Esposito, Alessandro Pontillo, Carmen Di Palo, Giovanni Giugliano, Mariangela Masella et al. Effect of weight loss and lifestyle changes on vascular inflammatory markers in obese women: a randomized trial. *JAMA*. 2003;289:1799-1804.
9. Vasseur F, Meyre D. & Froguel, P. Adiponectin, type

- 2 diabetes, and the metabolic syndrome: lessons from human genetic studies. *Expert Rev Mol Med* 2006; 8:1-12.
10. Steven P Marso, Sameer K Mehta, Andrew Frutkin, John A House, Justin R McCrary, Krishnaji R Kulkarni. Low Adiponectin Levels Are Associated With Atherogenic Dyslipidemia and Lipid-Rich Plaque in Nondiabetic Coronary Arteries. *Diabetes Care* 2008;31:989-94.
 11. Spranger J, Kroke A, Mohlig M, Bergmann MM, Ristow M, Boeing H, Pfeiffer AF. Adiponectin and protection against type 2 diabetes mellitus. *Lancet* 2003;361:226-228.
 12. Pitch on T, Girman CJ, Hotamisligil GS, Rifai N, Hu FB, Rimm EB. Plasma adiponectin levels and risk of myocardial infarction in men. *JAMA* 2004; 291:1730-1737.
 13. Lindsay RS, Resnick HE, Zhu J, Tun ML, Howard BV, Zhang Y, Yeh J, Best LG. Adiponectin and coronary heart disease: the Strong Heart Study. *Arterioscler Thromb Vasc Biol* 2005;25:e15-e16.
 14. Lawlor DA, Davey Smith G, Ebrahim S, Thompson C, Sattar N. Plasma adiponectin levels are associated with insulin resistance but do not predict future risk of coronary heart disease in women. *J Clin Endocrinol Metab* 2005; 90:5677-5683.
 15. Sattar N, Wannamethee G, Sarwar N, Tchernova J, Cherry L, Wallace AM, Danesh J, Whincup PH. Adiponectin and coronary heart disease: a prospective study and meta-analysis. *Circulation* 2006; 114:623-629.
 16. Laughlin GA, Barrett-Connor E, May S, Langenberg C: Association of adiponectin with coronary heart disease and mortality: the Rancho Bernardo study. *Am J Epidemiol* 2007; 165:164-174.
 17. Hotta K, Funahashi T, Arita Y, Takahashi M, Matsuda M, Okamoto Y, Iwahashi H, et.al. Plasma concentrations of a novel, adipose-specific protein, adiponectin, in type 2 diabetic patients. *Arterioscler Thromb Vasc Biol* 2000; 20:1595-1599.
 18. Von Eynatten M, Schneider JG, Humpert PM, Kreuzer J, Kuecherer H, Katus HA, Nawroth PP, Dugi KA: Serum adiponectin levels are an independent predictor of the extent of coronary artery disease in men. *J Am Coll Cardiol* 2006;47:2124-2126.
 19. Wannamethee SG, Whincup PH, Lennon L, Sattar N: Circulating adiponectin levels and mortality in elderly men with and without cardiovascular disease and heart failure. *Arch Intern Med* 2007;167:1510-1517.
 20. Cavusoglu E, Ruwende C, Chopra V, Yanamadala S, Eng C, Clark LT, Pinsky DJ, Marmur JD. Adiponectin is an independent predictor of all-cause mortality, cardiac mortality, and myocardial infarction in patients presenting with chest pain. *Eur Heart J* 2006;27:2300-2309.
 21. Menon V, Li L, Wang X, Greene T, Balakrishnan V, Madero M, Pereira AA, Beck GJ, Kusek JW, Collins AJ, Levey AS, Sarnak MJ: Adiponectin and mortality in patients with chronic kidney disease. *J Am Soc Nephrol* 2006; 17:2599-2606.
 22. Gesta S, Tseng YH, Kahn CR. Developmental origin of fat: tracking obesity to its source. *Cell* 2007;131:242-56.
 23. Rajeev Ahirwar, Prakash Ranjan Mondal. Prevalence of obesity in India: A systematic review. *Diabetes Metab Syndr* 2019;13:318-321.
 24. Rodriguez A, Ezquerro S, Mendez-Gimenez L, Becerril S, Fruhbeck G. Revisiting the adipocyte: a model for integration of cytokine signaling in the regulation of energy metabolism. *Am J Physiol Endocrinol Metab* 2015;309:E691-714.
 25. Bonsoni-Lopes A, Alonso-Vale MI. Lipolysis and lipases in white adipose tissue - An update. *Arch Endocrinol Metab* 2015;59:335-42.
 26. Krause BR, Hartman AD. Adipose tissue and cholesterol metabolism. *J Lipid Res.* 1984;25:97-110.
 27. Zhang Y, Mcgillcuddy FC, Hinkle CC, Oneill SM, Glick JM, Rothblat GH, Reilly MP. Adipocyte modulation of high-density lipoprotein cholesterol. *Circulation.* 2010;121:1347-55.
 28. Peyrot M, Barnett AH, Meneghini L F, & Schumm-Draeger, P. M. Insulin adherence behaviors and barriers in the multinational Global Attitudes of Patients and Physicians in Insulin Therapy study. *Diabetic Medicine* 2012; 29: 682-689.
 29. Turner RC, Millns H., Neil H. A. W, et.al. Risk factors for coronary artery disease in non-insulin-dependent diabetes mellitus: United Kingdom prospective diabetes study (UKPDS: British Medical Journal 1998;316: 823-828.
 30. Verggès, B. New insight into the pathophysiology of lipid abnormalities in type 2 diabetes. *Diabetes and Metabolism* 2005; 31: 429-439.
 31. Rangaswamy S, Penn MS, Saidel GM, Chisolm GM: Exogenous oxidized low-density lipoprotein injures and alters the barrier function of endothelium in rats in vivo. *Circ Res* 1997; 80:37-44.
 32. Ouchi N, Kihara S, Arita Y, Nishida M, Matsuyama A, Okamoto Y, Ishigami M, et.al. Adipocyte-derived plasma protein, adiponectin, suppresses lipid accumulation, and class A scavenger receptor expression in human monocyte-derived macrophages. *Circulation* 2001;103:1057-1063.

Source of Support: Nil; **Conflict of Interest:** None

Submitted: 22-09-2020; **Accepted:** 09-10-2020; **Published:** 20-11-2020