*Original Research Article*

# Study of Adiponectin and Lipid Profile Levels in Normotensive and Hypertensive Type 2 Diabetic Patients

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*Background:* Hypertension and type 2 diabetes mellitus (T2DM) are major health problems worldwide, associated with excess morbidity and mortality. Serum adiponectin is a biomarker that is associated with type 2 diabetes and hypertension, higher levels are protective while lower circulating levels are risk factors. *Objective:* To evaluate the adiponectin and lipid profile levels in normotensive and hypertensive type 2 diabetic patients. *Method:* A case-control study of 510 participants included three groups: (150 type 2 diabetic patients without hypertension, 210 type 2 diabetic patients with hypertension and 150 healthy control). The patients were randomly selected based on World Health Organization (WHO) guideline. *Results:* The result revealed significant increased values of adiponectin and high-density lipoprotein (HDL) and decreased serum cholesterol (TC), triglyceride (TG), low-density lipoprotein (LDL) and very low-density lipoprotein (VLDL) in control group when compared with diabetic normotensive and hypertensive patients groups (p<0.05). The current study also found that the mean of serum TC, TG, LDL and VLDL were higher and decline in serum adiponectin and high-density lipoprotein in hypertensive type 2 diabetic patients compared with non-hypertensive diabetic, although these were not significant (*P* > 0.05). Hypertensive type 2 diabetic females and males had no significantly higher serum TC, TG, LDL and VLDL and decline in serum adiponectin and HDL when compared with non-hypertensive diabetic females and males, respectively. *Conclusion:* This study demonstrated that no significant differences of adiponectin and dyslipidemia in hypertensive type 2 diabetic compared with non-hypertensive type 2 diabetic patients.

**Keywords:** Adiponectin level, lipid profile, Type-2 diabetes mellitus, Hypertension.

## INTRODUCTION

Hypertension and diabetes mellitus are common diseases that coexist with each other and constitute the most common risk factors for coronary heart diseases (CHD) [1-3]. Hypertension is well known as a common comorbidity in patients with diabetes with its prevalence ranging from 60% to 80% [4]. Hypertension in the diabetic individual markedly increases the risk and accelerates the course of cardiac disease. Diabetes mellitus has been known to be associated with lipid disorders and cardiovascular complications. Both diabetes mellitus and hypertension alter lipid and lipoprotein metabolism and increase the risk of coronary artery disease [5].

Adiponectin is a hormone act as anti-inflammatory, improving the sensitivity of insulin and endothelial function and has an anti-atherogenic effect. Decreased adiponectin concentrations correlated with increase risk of coronary diseases [6]. Type 2 diabetes mellitus and hypertension present with endothelial dysfunction and pro-inflammatory state which favoring atherosclerosis. Some authors suggest that decreased serum adiponectin concentrations are risk factors for hypertension and type 2 diabetes mellitus [3].

## MATERIAL AND METHOD

A case-control study which included 150 type 2 diabetic patients (74 males and 76 females), 210 hypertensive type 2 diabetic patients (119 males and 91 females) who attended the diabetes center at AL-Sader Medical City, Najaf, Iraq and 150 healthy control. All participants were aged 40 years and older. The patients were diagnosed by specialist physicians based on WHO guidelines. Patients with any other chronic diseases and patients suffering from type 1 diabetes mellitus were excluded from the study. Major selection criteria for diabetes was fasting plasma glucose level of 126 mg/dL or greater and for hypertension was the untreated hypertensive patients. Standard blood pressure measurements were done using mercury sphygmomanometer. A detailed history was taken and the fasting estimation of serum TC, TG, LDL and HDL levels

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were done by using standard methods. Serum adiponectin levels were analyzed by ELISA. The study protocol was approved by Kufa Medical College Ethical Committee.

### Statistical analysis

Student paired T-test and ANOVA test were done by using SPSS 20 windows software (SPSS Inc., Chicago, IL, USA). Values for the continuous variables are expressed as mean ± SD and a level of P < 0.05 was considered as statistically significant.

### RESULTS

The anthropometric and biochemical parameters of the individuals in normotensive diabetics, hypertensive diabetes and healthy control groups are shown in table 1. The results showed significantly decreased (P<0.001) in fasting serum adiponectin and HDL concentrations in normotensive type 2 diabetic and hypertensive type 2 diabetic patients groups with respect to normal control. Whereas, the TC, TG, LDL and VLDL levels were significantly increased (P<0.001) in diabetic patients without hypertension and diabetes with hypertension when compared to normal control.

Table II shows Serum adiponectin and lipid profile concentrations in T2DM patients with and without hypertension groups. Serum adiponectin and HDL levels were decline, whereas, TC, TG, LDL and VLDL levels were higher in hypertensive type 2 diabetic patients compared with non-hypertensive type 2 diabetic patients, although all these differences were not significant (*P* > 0.05).

Table III shows adiponectin and lipid profile concentrations in T2DM females and males with and without hypertension. Female and male patients in the T2DM with hypertension groups had not significantly differences of adiponectin and lipid profile concentrations as compared to the patients in T2DM females and males without hypertension groups, respectively.

### DISCUSSION

Adiponectin is a cytokine produced and secreted exclusively by adipocytes, and it modulates several obesity-induced pathophysiologic processes potentially involved in the development of hypertension [7]. Adiponectin enhances peripheral tissue insulin sensitivity and promotes fatty acid oxidation [8]. In patients with obesity-related metabolic disorders, improvements in insulin sensitivity [9] and fatty acid metabolism [10] concurred with lowering of blood pressure (BP). Adiponectin also stimulates the production of nitric oxide in endothelial cells, [11] and attenuates smooth muscle cell proliferation and migration [12], which exert direct benefits on the vascular system.

Moreover, adiponectin can inhibit the production and activity of tumor necrosis factor in macrophages [13] and suppress the generation and release of reactive oxygen species. These anti-inflammatory and anti-oxidative properties may also contribute to the prevention of hypertension [14]. Despite the evidence of the excess risk associated with the coexistence of HT and T2DM, very limited information exists on the etiology for this coexistence [15]. Serum adiponectin was inversely associated with lipid levels and marker of inflammation, supporting the hypothesis that these factors potentially mediate the protective effect of adiponectin against hypertension. Prospective studies have indicated that hypoadiponectinemia is an independent risk factor for type 2 diabetes [16, 17] and coronary heart disease [18]. The relation

between adiponectin and BP or hypertension was less studied. An inverse correlation between adiponectin and Systolic BP and diastolic BP was found in cross- sectional studies of healthy individuals [19, 20]. The results of this study showed significant (p < 0.001) lowering in fasting serum adiponectin hormone concentration for  type 2 diabetic and type  2 diabetic with hypertension groups with respect to normal control. These results are in agreement with previous studies [21-24].

The mechanism responsible for the decreased adiponectin concentration in type 2 diabetes mellitus has been obscure. TNF- is one of the candidate molecules responsible for causing insulin resistance [25]. The expression and secretion of adiponectin from adipocytes were significantly reduced by TNF- in a dose and time-dependent manner via its promoter activity. The expression of adiponectin mRNA was reduced in the adipose tissue of insulin-resistant humans and rodents, where TNF- production was increased [26]. Therefore, increased TNF- might be partially responsible for the decreased adiponectin production.

The present study found that there was a significant increase (P<0.001) in serum TC, TG, LDL and VLDL in diabetic patients with or without hypertension, while HDL – cholesterol was declined significantly (P< 0.001) when compared to normal control. The dyslipidaemia that is often present in individuals with type 2 diabetes is characterized by hypertriglyceridaemia, raised LDL and a low HDL profile [27]. The overstimulation of lipogenesis at the liver due to hyperinsulinaemic conditions is thought to be a critical component of the overproduction of lipid in type 2 diabetes [28]. These observations of dyslipidaemia in with diabetes mellitus are in agreement with the finding of previous studies [29]. In diabetic, patients without hypertension were low and not significant differences in serum adiponectin levels (P> 0.05) as compared to their levels in diabetic patients with hypertension group, these findings confirmed previous observation [30].

The results also showed that there were higher and not significant differences (P< 0.05) in serum lipid profile levels in normotensive diabetic patients in comparison with hypertensive diabetic patients group, findings are consistent with many studies [29, 31. 32, 33]. The current study also revealed that adiponectin levels and lipid profiles of normotensive type 2 diabetic male and female patients were higher and not statistically different from those of hypertensive diabetic male and female patients, respectively. It may be attributable to gender differences in adiposity. In addition, it is also possible sex-specific hormones, such as estradiol and testosterone, may also explain the sex difference in the association of adiponectin with diabetes and hypertension in this study [34, 35].

### CONCLUSION

The major findings of this study showed that plasma adiponectin and lipid profile levels were not significantly reduced in hypertensive type 2 diabetic patients when compared with normotensive type 2 diabetic patients, also plasma adiponectin and lipid profile levels were not significantly different between normotensive type 2 diabetic females and males and hypertensive type 2  diabetic females and males, respectively. The current study demonstrated that hypo-adiponectinaemia and dyslipidemia significantly existed in normotensive and hypertensive type 2 diabetic patients compared with normal control.

**Table 1.** The anthropometric and biochemical characteristics baseline of patients and control

| Variables | T2DM without hypertension (No.=150) | T2DM with hypertension (No.= 210) | Control (No.= 150) | P. value | |
| --- | --- | --- | --- | --- | --- |
| | | | | T2DM without hypertension vs. Control | T2DM with hypertension vs. Control |
| Age (y) | 47.20± 6.07 | 49.1±6.45 | 47.22±6.63 | 0.978 | 0.008 |
| BMI (kg/m$^2$) | 28.79± 4.93 | 30.77± 5.32 | 25.97± 5.03 | P<0.001 | P<0.001 |
| Systolic BP(mm Hg) | 123.44 ± 11.58 | 126.77 ± 17.15 | 118.3±4.2 | P<0.001 | P<0.001 |
| Diastolic BP( mm Hg) | 79.1± 8.75 | 81.98 ± 9.55 | 78.5±3.3 | P<0.001 | P<0.001 |
| TC (mg/dL) | 233.5 ± 35.28 | 235.44± 35.26 | 152.63±20.39 | P<0.001 | P<0.001 |
| TG (mg/dL) | 224.63± 40.52 | 229.90± 39.62 | 117.36±18.85 | P<0.001 | P<0.001 |
| HDL (mg/dL) | 48.41±6.79 | 47.45± 6.48 | 72.2± 6.01 | P<0.001 | P<0.001 |
| LDL (mg/dL) | 140.16± 37.00 | 142.00± 35.0 | 56.95± 21.82 | P<0.001 | P<0.001 |
| VLDL (mg/dL) | 44.92± 8.10 | 45.97± 7.92 | 23.47± 3.77 | P<0.001 | P<0.001 |
| Adiponectin (µg/mL) | 6.27± 2.49 | 5.48± 2.44 | 8.62± 2.85 | P<0.001 | P<0.001 |

**Table II.** Comparison between T2DM patients with and without hypertension.

| Variables | T2DM without hypertension (No.=150) | T2DM with hypertension (No.= 210) | P. value |
| --- | --- | --- | --- |
| Age (y) | 47.2± 6.07 | 49.10±6.45 | 0.005 |
| BMI (kg/m$^2$) | 28.79± 4.93 | 30.77± 5.32 | P<0.001 |
| TC (mg/dL) | 233.50 ± 35.28 | 235.44± 35.26 | 0.987 |
| TG (mg/dL) | 224.63± 40.52 | 229.9± 39.62 | 0.221 |
| HDL – C (mg/dL) | 48.41±6.79 | 47.45± 6.48 | 0.181 |
| LDL – C (mg/dL) | 140.16± 37.0 | 142.00± 35.0 | 0.968 |
| VLDL – C (mg/dL) | 44.92± 8.1 | 45.97± 7.92 | 0.22 |
| Adiponectin (µg/mL) | 6.27± 2.49 | 5.48± 2.44 | 0.442 |

**Table III.** Adiponectin and lipid profile concentrations in T2DM females and males with and without hypertension.

| Variables | T2DM females | | | T2DM males | | |
| --- | --- | --- | --- | --- | --- | --- |
| | without hypertension (No.= 75) | with hypertension (No.= 92) | P. value | without hypertension (No.= 74) | with hypertension (No.= 119) | P. value |
| Age (y) | 46.6± 5.76 | 50.02±6.8 | 0.001 | 47.91± 6.33 | 48.31±6.13 | 0.666 |
| BMI (kg/m$^2$) | 28.69± 5.2 | 30.29± 5.46 | 0.055 | 28.95± 4.66 | 31.08± 5.23 | 0.004 |
| TC (mg/dL) | 239.80± 26.94 | 240.29± 36.35 | 0.291 | 228.10± 36.48 | 233.54± 34.21 | 0.297 |
| TG (mg/dL) | 227.19± 42.63 | 228.0± 38.92 | 0.899 | 223.20± 37.41 | 230.6± 40.97 | 0.199 |
| HDL (mg/dL) | 48.14±6.88 | 48.02± 6.28 | 0.989 | 48.74±6.77 | 46.90± 6.59 | 0.066 |
| LDL  (mg/dL) | 140.51± 38.43 | 146.10± 31.0 | 0.311 | 135.07± 38.6 | 140.15± 35.89 | 0.355 |
| VLDL (mg/dL) | 45.43± 8.52 | 45.60± 7.78 | 0.899 | 44.12± 7.48 | 46.63± 8.19 | 0.199 |
| Adiponectin(µg/mL) | 7.3± 2.39 | 7.07± 2.56 | 0.355 | 5.5± 2.16 | 5.82± 2.29 | 0.388 |

## ACKNOWLEDGEMENTS

## REFERENCES

1. Tchaicaya A, Braun M, Lorenz N, Delagardelle C, Beissd J. Social inequality in awareness of cardiovascular risk factors in patients undergoing coronary angiography. Eur J prev cardiol, 2013; Vol (20), 5:872-879.

2. Gregory L, Bryan K, Derida c Y, David R, Bruce J, Psaty J, Rotter D, Siscovick S, Ian H B. Glucose insulin and incident hypertension in the multiethnic study of atherosclerosis; American journal of epidemiology; 2010, 172(10)1144-1154.

3. Rubio G A, Cabrera M J, Vargas R H, Maceda S A, Lozano N J, Escalante A B. Correlation between Levels of circulating adipokines and adiponectin/resistin index with carotid intima-media thickness in hypertensive type 2 Diabetic Patients. Cardiology 2013; 125:150-153.

4. Basevi V, Dimario S, Morciano C, Nonino F, Magrini N. American diabete Association standard of medical care in diabetes; 2011, 34 (suppl. 1): S 11- S 61. 34 (5).

5. Godkar D. Text book of medical laboratory technology; ed. 2 Bahlani Publishing house; 2003, S: 176-233.

6. Li Z Y, Wang P, Miao CY. Adipokines in inflammation, insulin resistance and cardiovascular disease. Clin Exp Pharmacol Physiol 2011; 38:888-896.

7. Matsuzawa Y, Funahashi T, Kihara S, Shimomura I. Adiponectin and metabolic syndrome. Arterio- scler Thromb Vasc Biol 2004; 24:29 –33.

8. Yamauchi T, Kamon J, Minokoshi Y, Ito Y, Waki H, Uchida S, et al. Adiponectin stimulates glucose utilization and fatty-acid oxidation by activating amp-activated protein kinase. Nat Med 2002; 8:1288–95.

9. Ikeda T, Gomi T, Hirawa N, Sakurai J, Yoshikawa N. Improvement of insulin sensitivity contributes to blood pressure reduction after weight loss in hypertensive subjects with obesity. Hypertension 1996; 27:1180–6.

10. Ferrier KE, Muhlmann MH, Baguet JP, Cameron JD, Jennings GL, Dart AM, Kingwell BA. Intensive cholesterol reduction lowers blood pressure and large artery stiffness in isolated systolic hypertension. J Am Coll Cardiol 2002; 39:1020 –5.

11. Chen H, Montagnani M, Funahashi T, Shimomura I, Quon M J. Adiponectin stimulates production of nitric oxide in vascular endothelial cells. J Biol Chem 2003; 278:45021– 6.

12. Matsuda M, Shimomura I, Sata M, Arita Y, Nishida M, Maeda N, et al. Role of adiponectin in preventing vascular stenosis. The missing link of adipo-vascular axis. J Biol Chem. 2002; 277: 37487–91.

13. Yokota T, Oritani K, Takahashi I, Ishikawa J, Matsuyama A, Ouchi N, et al. Adiponectin, a new member of the family of soluble defense collagens, negatively regulates the growth of myelomonocytic progenitors and the functions of macrophages. Blood 2000; 96:1723–32.

14. Motoshima H, Wu X, Mahadev K, Goldstein BJ. Adiponectin suppresses proliferation and superoxide generation and enhances eNOS activity in endothelial cells treated with oxidized LDL. Biochem Biophys Res Commun 2004; 315: 264 –71.

15. Savoia C, Schiffrin EL. Vascular inflammation in hypertension and diabetes: molecular mechanisms and therapeutic interventions. Clin Sci (Lond). 2007; 112:375–384.

16. Spranger J, Kroke A, Mohlig M, Bergmann MM, Ristow M, Boeing H, Pfeiffer AF. Adiponectin and protection against type 2 diabetes mellitus. Lancet 2003; 361:226–8.

17. Lindsay RS, Funahashi T, Hanson RL, Matsuzawa Y, Tanaka S, Tataranni PA, et al. Adiponectin and development of type 2 diabetes in the Pima Indian population. Lancet 2002; 360:57– 8.

18. Pischon T, Girman CJ, Hotamisligil G S, Rifai N, Hu F B, Rimm E B. Plasma adiponectin levels and risk of myocardial infarction in men. JAMA 2004; 291:1730–7.

19. Huang KC, Chen C L, Chuang L M, Ho S R, Tai T Y, Yang W S. Plasma adiponectin levels and blood pressures in nondiabetic adolescent females. J Clin Endocrinol Metab 2003; 88:4130–4.

20. Yamamoto Y, Hirose H, Saito I, Tomita M, Taniyama M, Matsubara K, et al. Correlation of the adipocyte-derived protein adiponectin with insulin resistance index and serum high-density lipoprotein-cholesterol, independent of body mass index, in the Japanese population. Clin Sci 2002; 103:137– 42.

21. Durrani S, Shah J, Khan M A, Jan M R, Rahman U. Relationship of hypoadiponectinemia with glycemic status and lipid profile in type 2 diabetic women with and without coronary heart disease. Biomedica, Oct. – Dec. 2014, Vol. 30, Issue 4, Bio-8. Doc P. 289 – 293.

22. Sadaf D, Jasmin S, Mudassir A K, Muhammad R J. Hypoadiponectinemia and dyslipidemia in relation to glycemic status in type 2 diabetic and coronary heart disease. KMUJ 2014, Vol. 6 No. 4.

23. Ashraf N K, Nabeel E W. Evaluation of Adiponectinin Patients with Type 2 Diabetes Mellitus in Erbil City. Inter- national Journal of Science and Research (IJSR), April 2016, Volume 5 Issue 4.

24. Chen MP, Chung FM, Chang DM, et al. Elevated plasma level of Visfatin/pre-B cell colony-enhancing factor in patients with type 2 diabetes mellitus. J Clin. Endocrinol. Metab., (2005): 90(6):3665-72

25. Hotamisligil GS, Arner P, Caro JF, et al. Increased adipose tissue expression of tumor necrosis factor-alpha in human obesity and insulin resistance. J. Clin. Invest., (1995):95:2409–2415.

26. Statnick MA, Beavers LS, Conner LJ, et al. (2000) Decreased expression of apM-1 in omental and subcutaneous adipose tissue of humans with type 2 diabetes. Int J Exp Diabetes Res., 1:81–88.

27. Krauss RM. Lipids and lipoproteins in patients with type 2 diabetes. Diabetes Care. 2004; 27:1496-504.

28. Adeli K, Taghibiglou C, Van Iderstine SC, Lewis GF. Mechanisms of hepatic very low-density lipoprotein overproduction in insulin resistance. Trends in Cardiovascular Medicine. 2001; 11:170-6.

29. Dena A. Hashim. Serum Lipid Profiles in Hypertensive Diabetes Mellitus Type 2 Patients. Journal of Al-Nahrain University. 2015; Vol.18 (1), pp.130-135.

30. Rubio G A, Vargas R H, Suárez C J, Lozano N J. Levels of Adipocytokines in Patients with Diabetes Type 2, Normotense and Hypertense. Med Int Mex 2014; 30:146-151.

31. Anne S A, Theis P S, Ronan M G, Kira D S, Bo F R, Bente K P, Kirsten M. Type 2 diabetes mellitus is associated with impaired cytokine response and adhesion molecule expression in human endotoxemia. Intensive Care Med. 2010.

32. Lorenzo G, Dalip R, Errol Y S, Eric C K, Donovan M, Martorell E. Lipid Profile of Type 2 Diabetic and Hypertensive Patients in the Jamaican Population. Journal of Laboratory Physicians; Jan-Jun 2010; Vol-2, Issue-1.

33. Qasim M T, Mahdi M R, The FTO Gene Polymorphism (Rs9939609) as Predictor for Hypertension in Iraqi Type 2 Diabetic Patients. Indian journal of applied research. 2016.Vol : 6, Issue: 6.

34. Combs TP, Berg AH, Rajala MW, Klebanov S, Iyengar P, Jimenez C J, et al. Sexual differentiation, pregnancy, calorie restriction and aging affect the adipocyte-specific secretory protein adiponectin. Diabetes. 2003; 52:268–76.

35. Xu A, Chen KW, Hoo RL, Wang Y, Tan KCB, Zhang J, et al. Testosterone selectively reduces the high molecular weight form of adiponectin by inhibiting its secretion from adipocytes. J Biol Chem. 2005; 280:18073–80.