

Serum Adiponectin and Fasting Insulin Levels in Patients with Type2 Diabetics

V. C. Renju¹, K. Santha^{1*}, S. Sethupathy¹, Manju Koshy¹, G. Marichamy² and N. Sri Kumaran²

¹*Division of Biochemistry, Rajah Muthiah Medical College and Hospital, Annamalai University, Annamalai Nagar, Tamil Nadu, India.*

²*Centre of Advanced study in Marine Biology, Annamalai University, Parangipettai, Tamil Nadu, India.*

Abstract

Adiponectin is a plasma glycoprotein present in adipose tissue. Low adiponectin levels are found in subjects with obesity and type2 diabetes mellitus. In the present study we estimate the serum adiponectin, fasting insulin levels and its correlation in patients with type2 diabetics. Anthropometric, biochemical, fasting insulin, HOMA-IR, Adiponectin levels were estimated in both groups. Serum insulin and adiponectin levels were significantly decreased in patients compared to control subjects. Adiponectin levels had no significant correlation with fasting insulin and HOMA-IR in diabetic patients. In our study there is no significant correlation between adiponectin levels and insulin resistance in diabetic cases.

Key words: Type2 diabetes, mellitus, Adiponectin, HOMA-IR

INTRODUCTION

Diabetes mellitus has been widely recognized to be a fundamental and leading cause of major health issues, in particular of all the cardiovascular diseases. It affects more than 170 million individuals worldwide. There is ample evidence indicating that by 2010, a further growth will occur, mainly caused by dramatic increases in the developing countries of Africa, Asia, and South America [40]. Insulin resistance is a syndrome characterized by a diminished ability of insulin to perform its normal physiological functions. Insulin resistance is the main feature of type 2 diabetes and also a key factor for the development of metabolic syndrome [25]. Insulin resistance represents the pathophysiological hallmark of type 2 diabetes mellitus (T2DM) and is highly prevalent in the population. Approximately one-third of the general population above the age of 50 years [28] and two-thirds of all patients with CHD are insulin resistant [34]. Adiponectin is a 244 amino acid, collagen-like protein, a member of a new family of obesity related hormones, the adipocytokines which is produced solely by white adipose tissue, may be linked to both insulin resistance and endothelial dysfunction [19]. The plasma concentration of adiponectin was reported to be lower in subjects with the phenotypes of the metabolic syndrome (MetS) [24], including obesity [2, 38, 39], type 2 diabetes [10, 35], dyslipidemia [38, 21] and hypertension [14, 13]. Lower plasma concentrations of adiponectin also were associated with insulin resistance [38, 39, 35]. Adiponectin, seems to play an important role in carbohydrate and lipid metabolism and vascular biology [3]. It has been found to be a major modulator of insulin action and resistance [35]. Furthermore, it seems to have substantial anti-inflammatory properties [3]. Adiponectin is also related to lipid metabolism, particularly higher levels of HDL cholesterol and lower levels of triglycerides [10].

In humans, several cross-sectional studies showed that adiponectin correlates negatively with measures of insulin resistance and type 2 diabetes. Results from a few prospective studies suggest that a low adiponectin level is predictive of insulin resistance or diabetes in Pima Indians [20], Asian Indians [31], and Japanese subjects [5, 37]. Low concentrations of circulating adiponectin are associated with low high-density lipoprotein cholesterol (HDL-C), obesity, hypertension, and glucose intolerance, all features of the insulin resistance syndrome. On the other hand, low adiponectin levels are associated with reduced expression of nitric oxide, and increased expression of angiotensin II and cellular adhesion molecules from the endothelium [19]. Moreover, low baseline adiponectin concentration can predict the future development of insulin resistance, while elevated baseline levels have been shown to be protective against the subsequent development of type 2 diabetes [15]. In this study we tried to find out the levels of adiponectin and its correlation with insulin resistance in patients with type2 diabetes mellitus.

MATERIALS AND METHODS

Sixty Type 2 diabetic patients of both sexes aged 35-55 years with less than 5 years duration attending and on oral hypoglycemic drugs diabetic out-patient department of Rajah Muthiah Medical College Hospital, Annamalai nagar, were selected for our study. Twenty healthy, age, and sex matched subjects were selected as control. Patients on insulin, smokers, alcoholics, tobacco chewers, hypertension, and other systemic illness were excluded from this study. Institutional ethical committee of this medical college have approved the study and informed consent obtained from the patients.

Anthropometric measurement

Anthropometric data including height, weight, waist and hip circumferences, and BMI were measured using a standard technique. Body mass index (BMI) was calculated by dividing the weight in kilograms by height in meters squared. We defined BMI ≥ 23 kg/m² as overweight individuals according to the revised guideline of WHO Western Pacific Region [35].

Biochemical analysis

Fasting venous blood was collected immediately after enrolment in tubes containing EDTA. Blood samples were centrifuged at 2000×g for 10 min. Samples were analyzed for fasting blood glucose, Lipid Profile (Total Cholesterol, HDL, LDL, Triglycerides), Renal function Tests (Urea, Creatinine), HbA1c, Liver Function tests (Total protein, Albumin, Globulin, ALT, AST, ALP) by using Auto analyzer.

Hormones assay

Serum insulin levels and adiponectin levels were determined by using Enzyme immuno assay. The homeostasis model assessment for insulin resistance (HOMA-IR) was calculated as fasting Insulin (mg/dl) x Fasting glucose (mg/dl) divided by 405.

Statistical analysis

All results were shown as mean±SD. Results were evaluated using Student's t-test. Simple correlations were determined by Pearson's correlations analysis. P-value <0.05 was considered statistically significant. Statistical analysis was performed using SPSS software.

RESULTS AND DISCUSSION

Adiponectin is a relatively abundant serum hormone, which was reported to influence both lipid and glucose metabolism in the liver and in muscle tissue [7]. Adiponectin has been associated with insulin sensitivity, as circulating levels are reduced in a number of insulin-resistant conditions in humans and animals, including obesity [12, 2], type 2 diabetes [10, 11, 35, 33] and cardiovascular disease [41]. Circulating adiponectin levels have been shown to be negatively correlated with BMI [2], plasma glucose, triglyceride, and insulin levels [10]. Plasma adiponectin levels have also been reported to be reduced in obese humans, particularly those with visceral obesity, and to correlate inversely with insulin resistance [2, 29]. Prospective and longitudinal studies [20, 5, 31, 32, 6, 17] have shown that lower adiponectin levels are associated with a higher incidence of diabetes. Adiponectin, has been shown to be significantly related to the development of type 2 diabetes in Pima Indians [17]. Hypoadiponectinemia has also been demonstrated to be independently associated with the metabolic syndrome - indeed, more strongly than any other inflammatory markers [22]. Reduced plasma adiponectin levels are also commonly observed in a variety of states frequently associated with insulin resistance, such as cardiovascular disease [18, 27] and hypertension [26, 1].

In the present study the anthropometric measurement, no significant difference in age, waist hip ratio, BMI, Total protein, albumin, Globulin, Blood Urea, Creatinine,

potassium, chloride except sodium between Type 2 diabetics and control subjects (Table.1). According to Table 2 all analytes were statistically significant in patients compared to control subjects (Fasting plasma glucose, HbA1C, Insulin, Adiponectin) except Lipid Profile (Total Cholesterol, HDL, LDL, Triglycerides) and HOMA-IR. There was no correlation between adiponectin and measured parameters (Table. 3). In our case-control study we found low serum adiponectin levels and low fasting insulin. Many studies have been found that, reduced adiponectin is related to impaired insulin action in type 2 diabetics [10, 9]. We also found that adiponectin level was negatively correlated with fasting insulin levels and HOMA-IR but it was not significant. This could probably be due to the anti-hyperglycemic effect of drugs which might have improved the insulin levels.

Table 1: Biochemical Data of Patients and control subjects

PARAMETERS	Patients (n=60)	Control (n=20)	P VALUE
Age	46.4±6.2	41.4±5.4	0.373
Waist Hip Ratio	0.92±0.06	0.90±0.06	0.654
Body Mass Index	24.85±4.4	25.35±5.1	0.871
Serum Total protein (g/dl)	7.63±0.5	7.85±0.5	0.609
Albumin (g/dl)	4.1±0.2	4.2±0.2	0.387
Globulin (g/dl)	3.5±0.4	3.8±0.3	0.817
Blood Urea (mg/dl)	28.1±6.5	25.5±4.3	0.059
Serum Creatinine (mg/dl)	0.80±0.1	0.81±0.1	0.890
Serum Sodium (mmol/l)	136.2±2.9	138.2±1.2	0.000
Serum Potassium (mmol/l)	4.1±0.4	4.1±0.2	0.515
Serum Chloride (mmol/l)	100.3±1.9	100.14±2.7	0.211

Data are expressed as mean±SD, P<0.05 was considered statistically significant.

Table 2: Glycemic status and lipid profile of patients and control subjects.

PARAMETERS	Patients (n=60)	Control (n=20)	P VALUE
Fasting plasma glucose (mg/dl)	150.53±64.8	77.50±13.48	0.000
HbA _{1c}	8.5±0.81	6.5±0.50	0.010
Serum cholesterol (mg/dl)	165.32±32.8	181.35±25.4	0.177
Serum Triglycerides (mg/dl)	150.90±63.1	161.35±73.8	0.462
HDL cholesterol (mg/dl)	43.60±2.89	44.15±3.2	0.290
LDL cholesterol (mg/dl)	91.48±30.59	108±20.93	0.080
Serum Insulin (U/ml)	14.77±9.43	39.05±14.41	0.006
HOMA-IR	5.48±4.34	7.41±3.19	0.297
Adiponectin	6.86±4.99	11.6±14.51	0.006

Data are expressed as mean±SD, P<0.05 was considered statistically significant.

Table 3. Correlation between adiponectin & measured parameters

PARAMETERS	Correlation Coefficient (r=)	P VALUE
Fasting plasma glucose	-.055	.339
HbA ₁ C	-.065	.310
Serum cholesterol	.001	.498
Serum Triglycerides	-.041	.376
HDL cholesterol	.080	.271
LDL cholesterol	.010	.469
Serum Insulin	-.007	.480
HOMA-IR	-.076	.283

P<0.05 was considered statistically significant.

One of the recent study shows, there is an increased association between type2 diabetics and CHD with the reference values of low adiponectin and low HDL Cholesterol[16]. In our study between the groups significantly low adiponectin levels, have no significant correlation with HDL Cholesterol. Salmenniemi et al.,[30] shows that energy expenditure during hyperinsulinemia was positively associated with adiponectin levels, hypo adiponectinemia were relative to high fasting plasma glucose and triglycerides, and lower HDL cholesterol.

Hypo adiponectinemia is a primary, genetically determined defect contributing to the etiology of obesity and insulin resistance [24]. One of the cross-sectional studies suggests that in human adiponectin levels are strictly associated with the amount of centrally located fat [4]. High plasma levels of adiponectin in type2 diabetic nephropathy are positively associated with fasting insulin and HOMA-IR was demonstrated by Guo et al.,[8]. This present study concludes that type2 diabetics have low serum adiponectin levels, which is not significantly correlated with fasting insulin levels and HOMA-IR.

ACKNOWLEDGEMENT

Authors are thankful to authorities of Rajah Muthiah Medical College and Hospital, Annamalai University, Annamalainagar for providing the facilities to this work.

REFERENCE

- Adamczak, M., Wiecek, A., Funahashi, T., Chudek, J., Kokot, F., Matsuzawa, Y., *Am. J. Hypertens.* 2003, 16, 72–75.
- Arita, Y., Kihara, S., Ouchi, N., Takahashi, M., Maeda, K., Miyagawa, J., Hotta, K., Shimomura, I., Nakamura, T., Miyaoka, K., *Biochem. Biophys. Res. Commun.* 1999, 257, 79–83.
- Chandran, M., Phillip, S.A., Ciaraldi, T., Henry, R.R., *Diabetes Care.* 2003, 26, 2442–2450.
- Cnop, M., Havel, P.J., Utzschneider, K.M., Carr, D.B., Sinha, M.K., Boyko, E.J., Retzlaff, B.M., Knopp, R.H., Brunzell, J.D., Kahn, S.E., *Diabetologia.* 2003, 46, 459–469.
- Daimon, M., Oizum, T., Saitoh, T., Kameda, W., Hirata, A., Yamaguchi, H., Ohnuma, H., Igarashi, M., Tominaga, M., Kato, T., *Diabetes Care.* 2003, 26, 2015–2020.
- Duncan, B.B., Schmidt, M.I., Pankow, J.S., Bang, H., Couper, D., Ballantyne, C.M., Hoogeveen, R.C., Heiss, G., *Diabetes.* 2004, 53, 2473–2478.
- Fruhbeck, G., Gomez-Ambrosi, J., Muruzabal, F.J., Burrell, M.A., *Am. J. Physiol. Endocrinol. Metab.* 2001, 280, E827–E847.
- Guo, L.L., Pan, Y., Jin, H., *Nephrol. Dial. Transplant.* 2009, 24, 1876–1883.
- Haque, W., Shimomura, I., Matsuzawa, Y., Garg, A., *J. Clin. Endocrinol. Metab.* 2002, 87, 2395–2398.
- Hotta, K., Funahashi, T., Arita, Y., Takahashi, M., Matsuda, M., Okamoto, Y., Iwasashi, H., Kuriyama, H., Ouchi, N., Maeda, K., *Arterioscler. Thromb. Vasc. Biol.* 2000, 20, 1595–1599.
- Hotta, K., Funahashi, T., Bodkin, N.L., Ortmeier, H.K., Arita, Y., Hansen, B.C., Matsuzawa, Y., *Diabetes.* 2001, 50, 1126–1133.
- Hu, E., Liang, P., Spiegelman, B.M., *J. Biol. Chem.* 1996, 271, 10697–10703.
- Huang, K.C., Chen, C.L., Chuang, L.M., Ho, S.R., Tai, T.Y., Yang, W.S., *J. Clin. Endocrinol. Metab.* 2003, 88, 4130–4.
- Kazumi, T., Kawaguchi, A., Sakai, K., Hirano, T., Yoshino, G., *Diabetes. Care.* 2002, 25, 971–6.
- Kim, C., Park J., Kang, E., Ahn, C., Cha, B., Lim, S., Kim, K., Lee H., *Obesity.* 2004, 14, 1164–1171.
- Koenig, W., Khuseynova, N., Baumert, J., Meisinger, C., Lowel, H., *J. Am. Coll. Cardiol.* 2006, 48, 1369–77.
- Krakoff, J., Funahashi, T., Stehouwer, C.D., Schalkwijk, C.G., Tanaka, S., Matsuzawa, Y., Kobes, S., Tataranni, P.A., Hanson, R.L., Knowler, W.C., Lindsay, R.S., *Diabetes Care.* 2003, 26, 1745–1751.
- Kumada, M., Kihara, S., Sumitsugi, S., Kawamoto, T., Matsumoto, S., Ouchi, N., Arita, Y., Okamoto, Y., Shimomura, I., Hiraoka, H., Nakamura, T., Funahashi, T., Matsuzawa, Y., *Arterioscler. Thromb. Vasc. Biol.* 2003, 23, 85–89.
- Lau, D.C., Dhillon, B., Yan, H., Szmitko, P.E., Verma, S., *Am. J. Physiol. Heart. Circ. Physiol.* 2005, 288, 2031–41.
- Lindsay, R.S., Funahashi, T., Hanson, R.L., Matsuzawa, Y., Tanaka, S., Tataranni, P.A., Knowler, W.C., Krakoff, J., *Lancet.* 2002, 360, 57–58.
- Matsubara, M., Maruoka, S., Katayose, S., *J. Clin. Endocrinol. Metab.* 2002, 87, 2764–9.
- Matsushita, K., Yatsuya, H., Tamakoshi, K., Wada, K., Otsuka, R., Takefuji, S., Sugiura, K., Kondo, T., Murohara, T., Toyoshima, H., *Arteriosclerosis. Thrombosis. and Vascular Biology.* 2006, 26, 871–876.
- Matsuzawa, Y., Funahashi, T., Kihara, S., Shimomura, I., *Arterioscler. Thromb. Vasc. Biol.* 2004, 24, 29–33.
- Menzaghi, C., Ercolino, T., Paola, R.D., Berg, A.H., Warram, J.H., Scherer, P.E., Trischitta, V., Doria, A., *diabetes.* 51.7.2306–2312.
- Olatumbosun, S., Samuel, D., "Insulin Resistance." *eMedicine*, 2008, 3.
- Ouchi, N., Ohishi, M., Kihara, S., Funahashi, T., Nakamura, T., Nagaretani, H., Kumada, M., Ohashi, K., Okamoto, Y., Nishizawa, H., Kishida, K., Maeda, N., Nagasawa, A., Kobayashi, H., Hiraoka, H., Komai, N., Kaibe, M., Rakugi, H., Ogihara, T., Matsuzawa, Y., *Hypertension.* 2003, 42, 231–234.
- Pischon, T., Girman, C.J., Hotamisligil, G.S., Rifai, N., Hu, F.B., Rimm, E.B., *JAMA.* 2004, 291, 1730–1737.
- Rathmann, W., Haaster, B., Icks, A., Lowel, H., Meisinger, C., Holle, R., Giani, G., *Diabetologia.* 2003, 46, 182–189.
- Ryo, M., Nakamura, T., Kihara, S., Kumada, M., Shibazaki, S., Takahashi, M., Nagai, M., Matsuzawa, Y., Funahashi, T., *Circ. J.* 2004, 68, 975–981.
- Salmenniemi, U., Zacharova, J., Ruotsalainen, E., Vauhkonen, I., Pihlajamäki, J., Kainulainen, S., Punnonen, K., Laakso, M., *J. C. E. & M.* 2005, 90, 4216–4223.
- Snehalatha, C., Mukesh, B., Simon, M., Viswanathan, V., Haffner, S.M., Ramachandran, A., *Diabetes Care.* 2003, 26, 3226–3229.
- Spranger, J., Kroke, A., Mohlig, M., *Lancet.* 2003, 361, 226–228.
- Statnick, M.A., Beavers, L.S., Conner, L.J., Corominola, H., Johnson, D., Hammond, C.D., Rafaeloff-Phail, R., Seng, T., Suter, T.M., Sluka, J.P., *Int. J. Exp. Diabetes. Res.* 2000, 1, 81–88.
- Taubert, G., Winkelmann, B.R., Schleiffer, T., Marz, W., Winkler, R., Gok, R., Klein, B., Schneider, S., Boehm, B.O., *Am. Heart. J.* 2003, 145, 285–91.
- Weyer, C., Funahashi, T., Tanaka, S., Hotta, K., Matsuzawa, Y., Pratley, R.E., Tataranni, P.A., *J. Clin. Endocrinol. Metab.* 2001, 86, 1930–1935.
- World Health Organization. *Definition, Diagnosis and Classification of Diabetes Mellitus and its Complications.* Report of a WHO Consultation. WHO/NCD/NCS/99.2. Geneva: WHO, 1999.
- Yamamoto, Y., Hirose, H., Saito, I., Nishikai, K., Saruta, J., *J. Clin. Endocrinol. Metab.* 2004, 89, 87–90.

- [38] Yang, W.S., Lee, W.J., Funahashi, T., Tanaka, S., Matsuzawa, Y., Chao, C.L., Chen C.L., Tai, T.Y., Chuang, L.M. *J. Clin. Endocrinol.Metab.* 2001, *86*, 3815–9.
- [39] Yang, W.S., Lee, W.J., Funahashi, T., Tanaka, S., Matsuzawa, Y., Chao, C.L., Chen C.L., Tai T.Y., Chuang L.M. *Obes. Res.* 2002, *10*, 1104–10.
- [40] Zimmet, P, Alberti, K.G., Shaw, J. *Nature.* 2001, *414*, 782-787.
- [41] Zoccali, C., Mallamaci, F., Tripepi, G., Benedetto, F.A., Cutrupi, S., Parlongo, S., Malatino, L.S., Bonanno, G., Seminara, G., Rapisarda, F., *J. Am. Soc. Nephrol.* 2002, *13*, 134–141.