ORIGINAL ARTICLE

RELATIONSHIP OF SERUM RESISTIN AND LIPID PROFILE IN TYPE 2 DIABETICS

Abida Akhtar, Muniza Saeed*, Qammar Shakoor

Department of Physiology, Lahore Medical and Dental College, *Department of Physiology, Postgraduate Medical Institute, Lahore

Background: Resistin an adipocyte derived factor has cysteine-rich C-terminal domain and has emerged as controversial link between obesity and type 2 diabetes mellitus (T2DM) in different studies and leads to dyslipidemia. This study was designed to determine and compare serum resistin, LDL and HDL levels in non-obese and obese type 2 diabetics. **Methods:** It was a cross-sectional analytical study in which eighty diabetic patients were recruited and were divided into two groups non-obese and obese on the basis of body mass index (BMI) and waist circumference (WC) (BMI ≤23, WC <90 Cm in group I and BMI ≥25, WC >90 Cm in group II). Serum resistin was measured by commercially available ELISA Kit. Serum LDL and HDL levels were measured by direct quantitative measurement. **Results:** Higher serum resistin and LDL, and lower serum HDL levels were recorded in obese diabetics compared to non-obese diabetics. Significant positive correlation of serum resistin with LDL and negative correlation between serum resistin and HDL was present in all type 2 diabetics. **Conclusions:** The positive correlation of serum resistin with serum LDL and negative correlation with serum HDL suggests serum resistin to be a link between obesity and T2DM and it may be responsible for altering lipid profile.

Keywords: Type 2 diabetes mellitus, serum, resistin, obesity, BMI, HDL, LDL, dyslipidemia

Pak J Physiol 2017;13(2):3–5

INTRODUCTION

Type 2 diabetes is posing threat to economy and people of Pakistan due to high prevalence rate (7.6–11%). Strong gene and environmental interaction plus South Asian phenotype of population are main contributing factors to high prevalence of T2DM. Obesity, an environmental factor is one of the strongest predictor of T2DM.[1] Obesity is becoming overwhelming health problem in Pakistan also due to eating, living and social habits of people. Increase in body mass index (BMI) is not only associated with I-R, but is also associated with dyslipidemia.[2]

Fat accumulation in abdominal region affects both lipid and glucose metabolism.[3] Increased adipose tissue deposits are responsible for increased secretion of pro-inflammatory cytokines like tumour necrosis factor-α, interleukin-6, resistin and visfatin. Resistin expressed from adipose tissue is suspected to participate in low grade inflammation leading to insulin resistance, metabolic disorders and type 2 diabetes mellitus.[4]

Human resistin which is only partially identical with mice counterpart has controversial results. Resistin is sparsely secreted from adipocyte and is detectable more in mononuclear blood cells as it is secreted both by monocyte and macrophages.[5] Some studies[6,7] failed to demonstrate any relationship between resistin and insulin resistance, while a study[8] showed progressive increase in resistin levels from lean to obese and in diabetics. Levels of serum resistin were also higher in obese subjects as compared to lean volunteers.[9,10] Resistin acts as a pathogenic factor contributing to insulin resistance by antagonizing insulin action and also interferes with normal insulin signalling. It causes reduction in insulin receptor substrate protein-1 (IRS-1) expression and phosphorylation and the expression of IRS-1is down regulated in resistin treated cells also.[11] Upregulation of resistin is followed by down regulation of peroxisome proliferation activated receptor-γ (PPAR-γ) which is normally induced during adipogenesis, thus inhibiting adipocyte differentiation. This leads to increase in non-esterified fatty acids (NEFAs).

Increased free fatty acids contribute to insulin resistance by inhibiting glucose uptake, glycogen synthesis and increasing hepatic glucose output by gluconeogenesis. The inability of insulin-resistant fat cells to store triglycerides (TGs) is the first step in the development of dyslipidemia which is characteristic of insulin resistance. Dyslipidemia is characterised by elevation in very low density lipoprotein (VLDL), decrease in high density lipoprotein (HDL) cholesterol. Low density lipoprotein (LDL) levels increases as more are synthesised from VLDL and are smaller in size, cholesterol depleted and triglyceride enriched.[12]

This study was designed to determine and compare serum resistin, LDL and HDL levels in non-obese and obese type 2 diabetics.

MATERIAL AND METHODS

It was a cross-sectional, analytical study conducted in the Department of Physiology, Postgraduate Medical Institute (PGMI), in collaboration with Diabetic Clinic, Services Institute of Medical Sciences (SIMS), Lahore. Study population consisted of 80 diabetic patients, 40 non-obese and 40 obese. All patients were previously diagnosed non-complicated diabetics and were on oral anti-diabetics drugs. After approval of Ethical Review Board, all the participants were briefed about the nature

of study and fully informed consent was taken. Three ml of blood was withdrawn using aseptic technique and was added to gel activating vacutainers for serum extraction. Serum resistin levels were measured by ELISA kit using commercially available kit by Glory Science made in Germany. Serum LDL and HDL levels were measured by direct quantitative measurement.

RESULTS

Study consisted of two groups, group I (non-obese diabetics) and group II (obese diabetics) each group consisting of 40 patients. Test of normality 'Shapiro-Wilk' test was applied. Data was non-normally distributed ($p \leq 0.05$ for all the biomarkers). As data was non-normally distributed, non-parametric test 'Mann Whitney U-test' was applied. Median (IQR) serum resistin in non-obese group I was 3.50 ηg/ml (3.00–5.00) and in obese group II was 24.00 ηg/ml (17.62–29.00). Median (IQR) levels of serum LDL in group I was 110.50 mg/dl (85.25–123.00) and in group II was 195.5 mg/dl (172.25–220.00). Median (IQR) serum HDL levels of group I was 53.50 mg/dl (46.50–60.50) and of group II was 27.50 mg/dl (24.00–31.00) (Table-1).

Table-1: Comparison of serum resistin, LDL and HDL levels between group I and II by using Mann-Whitney U test

Parameters	Group I	Group II	*p*
Serum resistin (ηg/ml)	3.50 (3.00–5.00)	24.00 (17.62–29.00)	0.000*
Serum LDL (mg/dl)	110.50 (85.25–123.00)	195.50 (172.25–220.00)	0.000*
Serum HDL (mg/dl)	53.50 (46.50–60.50)	27. 50 (24.00–31.00)	0.000*

Values are given as median (IQR), *Significant

Significant positive correlation was observed between serum resistin and LDL in type 2 diabetics (rho=0.731, p=0.000) (Figure-1), and significant negative correlation was observed between serum resistin and HDL (rho= -7.771, p=0.000) (Figure-2), in type 2 diabetics on application of Spearman's correlation.

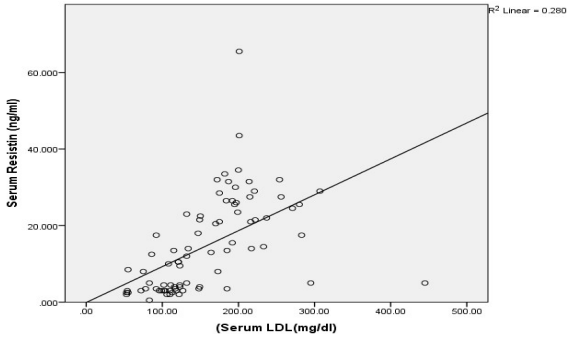

Figure-1: Scatter plot showing significant positive correlation between serum resistin and LDL in type 2 diabetics (group I and II) using Spearman's correlation coefficient (p=0.000).

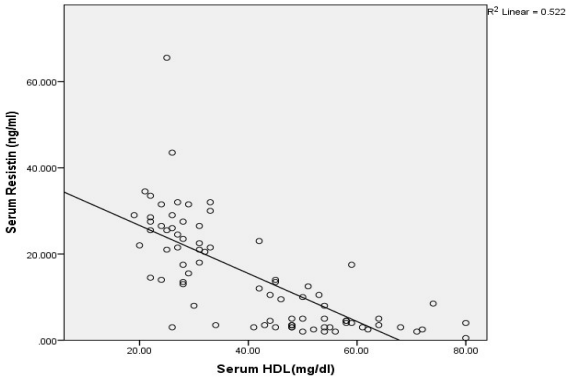

Figure-2: Scatter plot showing significant negative correlation between serum resistin and HDL in type 2 diabetics (group I and II) using Spearman's correlation coefficient (p=0.000).

DISCUSSION

Serum resistin levels were higher in obese as compared to non-obese diabetics. These results were comparable with other studies.[13,14] Higher serum resistin levels attributed by obesity and chronic inflammation were determinant of type 2 diabetes and cardiovascular diseases. Serum resistin interferes with insulin signalling as it decreases phosphorylation of insulin receptor substrate 1 (IRS-1) and inhibits activation of phosphatidyl inositol 3-kinase which is essential for insulin action.[11]

Serum LDL levels were significantly higher in group 2 which was in consistence with a previous study[15], while serum HDL levels were significantly lower in group II as compared to group I, as previously depicted by Al-Sari[16]. The HDL particles when present in normal ratio are responsible for removal of cholesterol from cells, including cholesterol in atherosclerotic plaques and carry them to liver.

Beside this, it has anti-inflammmatory and anti-oxidant properties so inhibits oxidation of LDL cholesterol and expression of cellular adhesion molecules and monocyte recruitment.[17] Serum resistin was positively correlated with serum LDL, while it was negatively correlated with serum HDL. These results were in concordance with the studies carried out previously[15,4] and depicts worsening of lipid profile with progressive increase in resistin level. High LDL and low HDL cholesterol are responsible for intima-media thickness and coronary heart diseases in type 2 diabetics.[17]

CONCLUSION

Present study supports the role of resistin in obese diabetics. Raised resistin levels also alters lipid profile increasing level of serum LDL and decreasing serum HDL which over a period of time results in complications of diabetes.

REFRENCES

1. Hakeem R, Fawwad A. Diabetes in Pakistan: Epidemiology, determinants and prevention. J Diabetology 2010;3:4.
2. Humayun A, Sher Shah A, Alam S, Hussein H. Relationship of body mass index and dyslipidemia in different age groups of male and female population of Peshawar. J Ayub Med Coll Abbottabad 2009;21(2):141–4.
3. Gastaldelli A, Cusi K, Petiti M, Hardies J, Miyazaki Y, Berria R, *et al*. Relationship between hepatic/visceral fat and hepatic insulin resistance in nondiabetic and type 2 diabetic subjects. Gastroenterology 2007;133:496–506.
4. Dong-Feng L, Han-dong Y, Bo Y, Tian-jun T, Xin-wen M, Yi L, *et al*. Relationship of the serum resistin level, lipid level, obesity and insulin resistance in patients with metabolic syndrome. J Chinese Clin Med 2007;8(2):1–6.
5. Benerjee RR, Lazar MA. Resistin: molecular history and prognosis. J Mol Med (Berl) 2003;81(4):218–26.
6. Lee JH, Chan JL, Yiannakouris N, Kontogianni M, Estrada E, Seip R, *et al*. Circulating resistin levels are not associated with obesity or insulin resistance in humans and are not regulated by fasting or leptin administration: Cross-sectional and interventional study in normal, insulin resistant and diabetic subjects. J Clin Endocrinol Metabol 2003;88(10):4848–56.
7. Mohammadzadeh G, Zarghami N, Mobaseri M. Serum resistin concentration in obese diabetic patients: any possible relation to insulin resistance indices? Int J Endocrinol Metab 2008;4(6):183–93.
8. Al-Harithy RN, Al-Ghamdi S. Serum resistin, adiposity and insulin resistance in Saudi women with type 2 diabetes mellitus. Ann Saudi Med 2005;25(4):283–7.
9. DeLuis DA, Sagrado MG, Conde R, Aller R, Izaola O. Resistin levels and inflammatory markers in patients with morbid obesity. Nutr Hosp 2010;25(4):630–4.
10. Azuma K, Katsukawa F, Oguchi S, Murata M, Yamazaki H, Shimada A, *et al*. Correlation between serum resistin level and adiposity in obese individuals. Obes Res 2003;11(8):997–1001.
11. Satoh H, Nguyen MT, Miles PD, Immamura T, Usui I, Olefsky JM. Adenovirus-mediated chronic hyper resistinemia leads to *in vivo* insulin resistance in normal rats. J Clin Investig 2004;114: 224–31.
12. Zhang J, Qin Y, Zheng X, Qiu J, Gong L, Mao H, *et al*. The relationship between human serum resistin level and body fat content, plasma glucose as well as blood pressure. Zonghua Yi Xue Za Zhi 2002;82(23):1609–12.
13. Chen BH, Yiging S, Ding EL, Robert LK, Manson JE, Rifai N, *et al*. Circulating levels of resistin and risk of type 2 diabetics in men and women: Results from two prospective cohorts. Diabetes Care 2009;32(2):329–34.
14. DeLuis DA, Sagrado MG, Conde R, Aller R, Izaola O. Resistin levels and inflammatory markers in patients with morbid obesity. Nutr Hosp 2010;25(4):630–4
15. Al-Daghri N, Chetty R, McTernan PG, Al-Rubean K, Al-Attas O, Jones AF, *et al*. Serum resistin is associated with C-reactive protein and LDL cholesterol in type 2 diabetes and coronary artery disease in a Saudi population. Cardiovasc Diabetol 2005;4:1–10.
16. Al-Sari IE, Al-quobaili FA, Kabalan YM. Serum resistin levels in Syrian obese patients with diabetes mellitus type II. Saudi Med J 2007;28(12):1890–4.
17. Bitzur R, Cohen H, Kamari Y, Shaish A, Harats D. Triglycerides and HDL cholesterol: Stars or second leads in diabetes? Diabetes Care 2009;32(2):373–7.

Address for Correspondence:

Dr Abida Akhtar, Department of Physiology, Lahore Medial and Dental College, Lahore, Pakistan. **Cell:** +92-323-5116041
Email: abidamaroof@yahoo.com

Received: 28 Feb 2017 Reviewed: 11 Apr 2017 Accepted: 27 Apr 2017