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ORIGINAL ARTICLE

Relation of Serum Resistin with Body Mass Index and Lipid Profile in Hypertensive and Ischemic Heart Disease patients

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ABSTRACT

Background: Resistin, a novel hormone, got its recognition as a regulator of lipid metabolism in obese rodents. Human researches proved its role mainly in inflammation and to lesser extent in obesity.
Aim: To observe the relationship of serum resistin with body mass index (BMI) and lipid levels in hypertensives and ischemic heart disease patients as compared to normal subjects.
Methodology: Eighty participants between the ages of thirty to fifty five years were distributed in four groups including normal subjects, first time diagnosed patients of hypertension, and first time diagnosed hypertensive cases of stable angina pectoris and myocardial infarction respectively. After history and general physical examination, fasting blood samples of the participants were tested for serum resistin by using the enzyme linked immunosorbent assay technique and lipid profile with commercially available enzymatic kits. Analysis of the data was performed by SPSS version17.0.
Results: In patients of research groups, statistically raised levels (mean±SD) of BMI, and serum values of resistin, triglycerides, low-density lipoproteins (LDL) while decreased high density lipoproteins (HDL) levels were documented in comparison with healthy subjects.
Conclusions: There are significantly higher values of body mass index, blood resistin, triglycerides and LDL while lower serum HDL levels in hypertensives and patients of ischemic heart disease as compared to normal participants.
Keywords: Resistin, ischemic heart disease, lipid profile, body mass index

INTRODUCTION

Hypertension (HTN) or high blood pressure is an evolving global epidemic due to unhealthy life style, lack of exercise, intake of calorie-rich diet, alcohol consumption, smoking etc. Untreated hypertension can lead to systemic complications, morbidity and even early death[1]. Atherosclerosis is a sub-clinical chronic inflammatory disorder of vascular endothelium. It is considered as a silent killer because in decades, it can lead to progressive occlusion of blood vessels supplying different vital organs of the body especially heart, kidney and brain. Coronary or Ischemic heart disease (IHD) is due to slow atherosclerotic changes in myocardial vasculature. Depending upon the extent of ischemia and damage to myocardium, IHD can be manifested as angina pectoris (AP) or myocardial infarction (MI)[2].

For years adipose tissue is considered as a store house of fat cells and source of energy but recent advances in scientific research has proved it as a producer of metabolically active hormones such as resistin, leptin, adiponectin, adipsin, visfatin and insulin like growth factor-1 etc[3]. White adipose tissue (WAT) in lean persons is a source of triglycerides, capable of producing energy and secreting anti-inflammatory cytokines e.g. adiponectin etc.[4] On the contrary, obese persons possess adipose tissue infiltrated with pro-inflammatory cells which produce a wide range of inflammatory mediators, such as visfatin, resistin, tumor necrosis factor etc.[5] So, obesity induces a subclinical milieu of chronic systemic inflammation known as 'metabolic inflammation'[6].

Resistin is a cysteine rich polypeptide which was discovered in 2001 by Steppan and his colleagues during an experiment on obese mice. Nuclear peroxisome proliferator activated receptor γ was studied in the research as a target for the action of antidiabetic thiazolidinediones and was found to be the chief regulator of adipogenesis in these mice[7]. So, resistin was also named as 'adipose secretory factor'[8]. Human resistin is produced by inflammatory blood cells, bone marrow and in less amounts by fat cells.[9] It possesses the amino acid sequence identical to a family of proteins known as "FIZZ - found in inflammatory zone"[10].

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Circulating blood monocytes and macrophages infiltrate the intimal layer of arteries and secrete resistin. There resistin activates nuclear factor-kappa B (NFκB), transports calcium to the cell interior, activates protein kinase C as well as 1,4,5 inositol triphosphate. All these processes cause release of inflammatory mediators, leading to local as well as systemic inflammation.[11] Resistin enhances the hepatocytic production of circulating lipids and atherogenesis through intracellular pathways of SREBP1 and SREBP2 (sterol regulatory element binding proteins 1 and 2) while apoB VLDL (very low density lipoprotein) synthesis via PI3 kinase and MAP kinase[12].

In present research we tried to explore the relationship of resistin with body fat reserves and cardiovascular pathology.

METHODS

The approval of this comparative research was obtained from Advanced Science and Research Board of the University of Health Sciences Lahore and was conducted in the Physiology department of Postgraduate Medical Institute. By using non probability convenience sampling technique, a total of eighty participants aging between thirty to fifty five years were recruited from Punjab Institute of Cardiology Lahore. The participants were organized into four groups, 20 each, with equal number of both genders. Group 1included participants with normal arterial pressure while group 2 comprised of patients diagnosed with hypertension for the first time. In group 3, stable angina pectoris patients with HTN and group 4 comprised of MI patients with HTN respectively. All these patients were new or first time diagnosed within the time frame of previous one month. Subjects excluded were obese, with acute or chronic inflammation, underlying cardiac or endocrinological disorder and smokers. Included participants were explained about the research and after taking their written consent, medical history was inquired. Examination including estimation of BMI and blood pressure was performed. Arterial pressure of participants, determined by mercury sphygmomanometer, equal to or exceeding 140/90mmHg was labeled as hypertensive[13]. BMI was estimated by using formula; BMI=Body weight (kg)/height(m2)[14]. Fasting participants were aseptically venepunctured to collect five ml of blood in a serum vial. Centrifugation was done and serum

was stored at -20°C. Estimation of resistin in serum sample was performed by using Sandwich ELISA technique while of lipid profile by enzymatic colorimetric method (precipitation method) using commercially available kits. Analysis of data was performed via 17.0 version of SPSS in which the study variables were expressed as mean±SD using one-way analysis of variance. Post-hoc was applied for comparison of the means between the groups. To study the correlation between resistin and BMI as well as serum LDL, HDL and triglyceride; Pearson's correlation coefficient was used. Statistically, *p value* less than 0.05 was considered as significant.

RESULTS

Present research included four groups of 80 participants with equal number of male and female participants. The determined levels (mean±SD) of BMI, serum resistin, LDL, HDL and triglycerides of the participants are presented in table 1 which revealed the statistically significant increase in the calculated values of BMI (p<0.001), resistin (p<0.001), LDL (p<0.001) and triglyceride (p=0.001) in hypertensives (group 2), patients of angina pectoris with HTN (group 3), and MI with HTN (group 4) as compared to normotensives (group 1). However, high density lipoprotein levels were significantly lowered in sera of study groups as compared to group 1 participants (p<0.001).

In table 2 the comparison of the above mentioned variables by Post hoc analysis expressed significant differences of BMI between groups 1 and group 2 (p=0.002), 1 and 3 (p<0.001) as well as group 1 and 4 (p<0.001). Significant difference of serum resistin (p<0.001) between group 1 and other groups such as 2, 3 and 4 was also observed. Similar comparison of serum HDL levels revealed significant difference between group 1 and 3 (p<0.001), 1 and 4 (p<0.001), 2 and 3 (p=0.014), and between 2 and 4 (p=0.001). For serum LDL, the comparison was significant among groups 1 and 3 (p=0.002), 1 and 4 (p<0.001), 2 and 3 (p=0.046), as well as groups 2 and 4 (p=0.011). Multiple comparisons of mean serum triglyceride levels between the groups revealed statistically significant differences between groups 1 and 2 (p=0.046), 1 and 3 (p=0.007), and groups 1 and 4 (p=0.001).

Pearson's coefficient was applied to observe the correlation between study variables. No significant correlation was found between serum resistin and BMI, serum HDL, LDL, and triglyceride levels in study groups (Table 3).

Table 1: Comparison of values (mean ± SD) of Age, BMI, serum resistin, HDL, LDL and triglycerides by ANOVA in groups 1, 2, 3 & 4

Parameters	Group 1	Group 2	Group 3	Group 4	p – value
Age (years)	44.75 ± 3.40	45.50 ± 5.88	48.05 ± 5.53	47.90 ± 5.24	0.101
BMI (kg/m^2)	25.08 ± 1.88	26.60 ± 1.14	27.27 ± 0.96	26.97 ± 0.95	<.001*
Resistin (ng/ml)	6.80 ± 1.01	16.73 ± 3.78	17.51 ± 8.04	21.07 ± 7.12	<.001*
HDL (mg/dl)	66.00 ± 27.37	56.80 ± 13.87	40.10 ± 12.79	34.90 ± 6.60	<.001*
LDL (mg/dl)	132.05 ± 32.71	149.75 ± 56.01	193.55 ± 49.37	202.00 ± 64.86	<.001*
Triglyceride (mg/dl)	142.65 ± 42.79	199.95 ± 84.49	214.80 ± 64.54	230.60 ± 73.39	0.001*

Group 1 = Normal participants Group 2 = Hypertensive participants Group 3 = Hypertensive participants with angina pectoris
Group 4 = Hypertensive participants with myocardial infarction * denotes statistical significance

Table 2: Comparison (Post hoc) of means of BMI, serum resistin, HDL, LDL and triglyceride values between groups 1, 2, 3 & 4

Parameter	Group 1 vs Group 2	Group 1 vs Group 3	Group 1 vs Group 4	Group 2 vs Group 3	Group 2 vs Group 4	Group 3 vs Group 4
BMI	.002*	<.001*	<.001*	.359	.803	.879
Serum Resistin	<.001*	<.001*	<.001*	.973	.086	.208
HDL (mg/dl)	.322	<.001*	<.001*	.014*	.001*	.767
LDL (mg/dl)	.706	.002*	<.001*	.046*	.011*	.956
Triglyceride(mg/dl)	.046*	.007**	.001**	.901	.488	.883

* denotes statistical significance

Table 3: Correlation (Pearson's coefficient) between serum resistin and BMI, HDL, LDL and triglyceride values in groups 1, 2, 3 & 4

Parameters	Group 1		Group 2		Group 3		Group 4	
	r	*p*	*r*	*p*	*r*	*p*	*r*	*p*
Resistin and BMI	0.405	0.077	-0.308	0.186	-0.004	0.987	0.430	0.058
Resistin and HDL	-0.088	0.713	-0.049	0.837	-0.049	0.838	-0.030	0.899
Resistin and LDL	0.044	0.852	0.121	0.612	0.139	0.560	-0.330	0.156
Resistin and Triglyceride	0.421	0.065	0.120	0.613	0.097	0.683	0.319	0.170

DISCUSSION

Resistin is a well-known cytokine mainly released from inflammatory blood cells in humans but its secretion from adipocytes is also documented. It is not only thought to play a considerable role in inflammatory and autoimmune disorders but also in neurodegenerative disorders[15].

In the current research, serum resistin values were observed to possess an increasing trend with increasing pathogenesis of vasculature and myocardium. Several researchers explored the association of circulating resistin levels with myocardial disease. Resistin is found to be involved in vascular remodeling and altered renin angiotensin pathway leading to hypertension[16]. Another research aimed to explore the role of resistin in patients of peripheral arterial disease revealed that through various intracellular signaling pathways, resistin causes endothelial dysfunction of major arteries and leads to adverse cardiac events and mortality of the patients[17].

Initially discovered as an adipokine, resistin is linked to obesity also. In the present study, although obese persons were excluded from the study but still BMI of the diseased subjects was significantly higher as compared to normal subjects. Moreover the estimated serum values of LDL and triglyceride levels were found to be notably increased but serum HDL was decreased hypertensive and ischemic heart disease patients in comparison with normal ones. Similar association of resistin with increased BMI was observed in another study, in which blood resistin and triglyceride were correlated positively while negative correlation with HDL levels in obese hypertensives as compared to non obese one.[19] Parallel observations were also gathered from peripheral arterial diseased hypertensive patients in whom significant positive association of resistin with waist circumference and serum LDL was documented[20].

The available evidence suggests that resistin mediates the increased production of lipoproteins especially of low density as well as triglycerides from the liver.[21] In a research including Pakistani young obese individuals, serum resistin levels were observed to be significantly associated with metabolic indicators such as BMI, blood pressure, fasting blood sugar and lipid profile.[23] Another research illustrated the pathological connection of resistin with abnormal lipid profile even in healthy persons by exhibiting its positive correlation with LDL and triglycerides in healthy blood relatives of diabetic patients[22].

Although there is abundance of favoring data, but still contradicting results are also available. In a research on obese patients of IHD, no relationship between serum resistin and cardiac disease was established which was justified on the basis of small sample size.[23] Qi and colleagues also came across with differed results in middle and old aged Chinese population when they researched the relationship of resistin with markers of inflammation and serum fibrinolysins. They didn't find any connection between BMI and resistin values. It was found that low expression of resistin from human adipocytes was insufficient to raise its serum levels as compared to its secretion from inflammatory cells which contributed a major share[24].

In another study conducted on diabetic and non diabetic subjects, contrary results were obtained. Serum resistin levels were inversely correlated with serum LDL while positively correlated with HDL levels in both groups. The proposed justification given was that may be macrophagic resistin secretion is inhibited by raised serum LDL levels due to some competitive mechanisms between the two[25].

The present research had insufficient sample size to prove any cause and effect relationship between serum resistin, BMI, lipid profile and cardiovascular disease. However large scale studies targeting the intracellular signaling mechanisms of resistin will help in the identification of association of this molecule with body lipid stores and their homeostasis.

CONCLUSIONS

Serum resistin was found raised with increasing BMI in hypertensive patients and of ischemic heart disease as compared to normal ones. Serum LDL and triglyceride levels were found increased while serum HDL levels were decreased with increased severity of the disease. Although serum resistin and other variables of the study were not correlated but it is assumed that there might be some common mechanism which links resistin with the abnormality of lipid metabolism in cardiovascular disorders.

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