ORIGINAL ARTICLE

Serum Resistin Levels in Patients of Hypertension and Coronary Artery Disease

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ABSTRACT

Background: Hypertension is a chronic disease which affects different body organs, especially heart and blood vessels leading to coronary artery disease. Resistin, secreted from inflammatory blood cells, is a cysteine rich polypeptide and is related to obesity, inflammation and atherosclerosis in humans.
Aim: To determine and compare serum resistin levels in normotensives, newly diagnosed patients of hypertension, stable angina pectoris and myocardial infarction with hypertension.
Methodology: In this comparative study, eighty subjects both male and female, within the age limit of 35 – 55 yrs were divided into four equal groups i.e. normotensives, newly diagnosed cases of hypertension, stable angina pectoris and myocardial infarction, both with hypertension. Serum resistin was determined by enzyme linked immunosorbent assay in their fasting blood samples and compared according to appropriate statistical techniques using SPSS 17.0.
Results: Serum resistin levels were significantly raised in patients of hypertension and coronary artery disease as compared to normotensives. Resistin levels were found progressively raised with increasing severity of cardiac disease.
Conclusions: The Increase in serum resistin levels in patients of hypertension and coronary artery disease may reveal a possible involvement in induction and progress of pathological changes in heart and blood vessels.
Key words: Resistin, hypertension, angina pectoris, myocardial infarction, coronary artery disease

INTRODUCTION

Hypertension is defined as the persistent elevation of blood pressure with systolic and diastolic pressures more than 140/90 mmHg respectively[1].

It is a progressive disease affecting many organs of the body especially heart, brain, kidneys and blood vessels. Influenced by various environmental factors[2], hypertension accounts for almost 4.5% of the global disease burden[3]. By year 2025, about 29% of the world adult population is predicted to be hypertensive[4]. In Pakistan, its prevalence is approximately 10% encompassing about 33% of adult population over 45 years of age[5].

Coronary artery disease, also known as ischemic heart disease, is the progressive narrowing and ultimately occlusion of coronary arteries by atherosclerotic plaques[6]. These plaques are caused by the interaction of immune mechanisms with metabolic risk factors causing initiation and propagation of atherothrombotic lesions in blood vessels[7].

This disease is becoming a global epidemic due to increased urbanization, environmental, socioeconomic and demographic changes[8]. Different studies have reported that South Asians have highest rates of ischemic heart disease[9]. In Pakistan, it is ranked as the second deadliest disease as it accounts for 11% of all deaths[10].

Angina pectoris is a common clinical syndrome which occurs due to transient ischemia of myocardium. It occurs in conditions of increased cardiac work load and oxygen demand, as the narrow atherosclerotic coronary arteries are unable to supply adequate oxygenated blood to the myocardium. Angina pectoris is classified as 'Stable' or 'Unstable' according to the presentation of the patient[11].

Myocardial Infarction is myocardial cell death due to prolonged ischemia. It can be diagnosed on the basis of ischemic symptoms, electrocardiographic abnormalities and cardiac biomarkers preferably troponin[12].

Resistin, is a 12.5-KDa polypeptide belonging to the family of "resistin-like molecules" (RELMs)[13]. Initially, discovered in rodents as adipocytokine, it was thought as a missing link between obesity, diabetes mellitus and insulin resistance[14] hence, was also named as 'adipose secretory factor'[15]. In humans, resistin is mainly secreted by bone marrow as well as monocytes and macrophages and to a lesser extent by adipocytes[16]. From macrophages its secretion is almost four times more as compared to monocytes[17].

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Resistin, under the action of certain cytokines like IL-6 and TNF-α activates nuclear transcription factor-kappa B (NF-κB) which increases the secretion of inflammatory cytokines by mobilizing intracellular calcium and activating protein kinase C as well as 1,4,5 inositol triphosphate[18]. It can upregulate various adhesion molecules and cytokines resulting in endothelial dysfunction, vascular smooth muscle cell proliferation and migration as well as activation of monocytes and macrophages transforming them into foam cells[19]. Both these structural and functional alterations of endothelium ultimately lead to vasoconstriction and contribute to the pathogenesis of hypertension. So, hypertension and atherosclerosis are considered as resistin mediated inflammatory processes[20].

MATERIALS AND METHODS

This comparative study was conducted in Department of Physiology, PGMI, Lahore, in cooperation with the Punjab Institute of Cardiology, Lahore. It was approved by the Advanced Science and Research Board of the University of Health Sciences (UHS), Lahore.

The research was completed in almost one year (2013). Eighty male and female subjects between 30-55 years of age, divided equally into four groups were included in the study. Group A consisted of twenty normotensive healthy subjects while group B included newly diagnosed cases of hypertension. Group C comprised of newly diagnosed cases of stable angina pectoris with hypertension and in group D, newly diagnosed cases of myocardial infarction with hypertension were included.

Obese subjects, smokers, diabetics, patients with any acute or chronic inflammatory condition, major surgical or cardiac intervention and patients with congenital or valvular heart disease were excluded. Pregnant females were also excluded from the study.

After obtaining written informed consent from each participant, general physical and systemic examinations were conducted to rule out any underlying disease. Blood pressure was estimated by using mercury sphygmomanometer. Body mass index was calculated with the help of formula; BMI = Body weight (kg) / height (m^2)[21].

For estimation of resistin, 3 ml of fasting blood sample was drawn using aseptic technique, and placed in serum vial. Serum was obtained after centrifugation at a speed of 5000 rpm for 10 minutes and stored in aliquots at -20^{0}C till further analysis. Sandwich ELISA technique was used for quantitative estimation of serum resistin by using the kit of Creative Diagnostics, USA; with Stat Fax 303, Awareness Technology, Inc. USA. The collected data was entered and analyzed by using SPSS version 17.0.

RESULTS

Eighty age and sex matched subjects were divided in four equal groups in this study. One way ANOVA reveals significant difference ($p<0.001$) of serum resistin levels between normal subjects (6.8±1.01 ng/ml), patients of hypertension (16.73±3.78ng/ml), angina pectoris (17.51±8.04 ng/ml) and myocardial infarction with hypertension (21.07±7.12ng/ml). An increase in serum resistin levels with severity of disease was also observed (Fig. 1). Post hoc Tukey test in table 1 shows highly significant differences between groups A and B ($p<0.001$), A and C ($p<0.001$) and groups A and D ($p<0.001$), while the difference was non-significant between groups B and C ($p = 0.973$), B and D ($p=0.086$) and groups C and D ($p=0.208$).

Fig. 1: Comparison of serum resistin level (ANOVA) in groups A, B, C and D

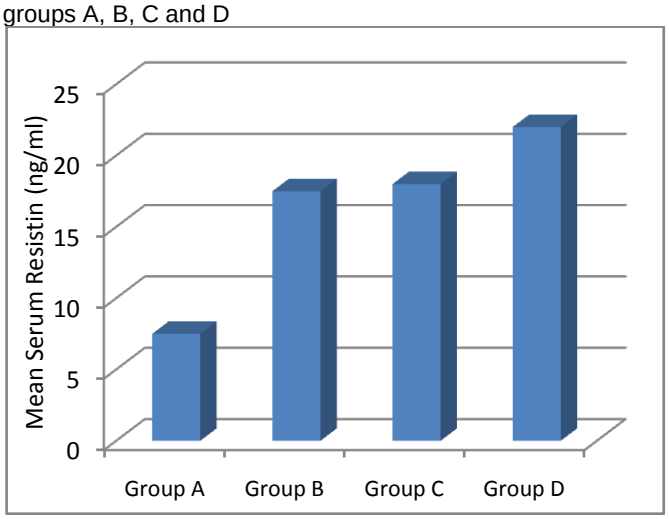

Table 1: Post hoc comparison of serum resistin level between individual study groups

(I) Group	(J) Group	Mean Difference (I-J)	p-value
A	B	-9.92	<0.001*
A	C	-10.70	<0.001*
A	D	-14.26	<0.001*
B	C	-0.77	.973
B	D	-4.34	.086
C	D	-3.56	.208

Group A = Normal subjects
Group B = Subjects with hypertension
Group C = Subjects of stable angina pectoris with hypertension
Group D = Subjects of myocardial infarction with hypertension
* = highly significant

DISCUSSION

Resistin was initially known as the main regulator of obesity and diabetes mellitus[14] but its role in causation of insulin resistance was found controversial[22]. However various human studies proved resistin as a pro-inflammatory hormone[16,19] as it causes release of cytokines from monocytes as well as macrophages and initiates intracellular inflammatory cascades leading to multiple disorders[18].

In this study, significant and progressive increase of circulating resistin levels with increasing severity of cardiac disease was observed. Several studies have also proved strong association of raised serum resistin levels with coronary heart disease[23], atherosclerosis[24], hypertension[25] as well as with increasing myocardial impairment[17].

The present study supports the role of resistin in patients of hypertension and coronary artery disease. Future endeavors in this direction, overcoming the limitations of this study, will help in better understanding of interrelationship between the triad of resistin, coronary artery disease and inflammation. Small sample size and lack of observation of association of resistin with other risk factors and confounders of coronary artery disease are the limitations of this study.

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