RA Publications
Journal of Medical Science & Technology

Original Article **Open Access**

Association of insulin resistance and dyslipidemia in non diabetic essential hypertension

K Ramalingam*[1], M Rajesh Kumar, [2] K Santha[3], R Sethupathy[3], J N Naidu[1],
[1]Department of Biochemistry, Narayana Medical College, Andhra Pradesh, India
[2]Department of General Medicine, Narayana Medical College, Andhra Pradesh, India
[3]Department of Biochemistry. Raja Muthiah Medical College, Tamilnadu, India

Abstract

Hypertension has been reported to have greater risk for the development of cardiovascular diseases when compared to normotensive subjects. Insulin resistance was demonstrated in non diabetic hypertensive patients. Insulin resistance and hyperinsulinemia have been considered important risk factors for the development of hypertension. Dyslipidemia an elevated levels of blood lipids shown in essential hypertensive patients. The present study aimed to demonstrate the relation between insulin resistance and dyslipidemia in freshly diagnosed non diabetic hypertensive patients. 203 freshly diagnosed essential hypertension subjects were included in this study. 210 healthy, age, sex matched subjects were selected as controls. Serum Total cholesterol, HDL- cholesterol, LDL- cholesterol, Triglycerol, fasting insulin and insulin resistance were estimated in patients and control subjects and they are significantly elevated in patients than the controls. Total cholesterol is positively correlated and HDL cholesterol is negatively correlated with Insulin resistance. Our results demonstrate the presence of insulin resistance in non diabetic hypertension and its association with dyslipidemia.

Key words; Insulin resistance, dyslipidemia, hypertension, cardiovascular disease

*Corresponding Author: K. Ramalingam, Assistant Professor, Biochemistry, Narayana Medical College Hospital, Nellore, Andhra Pradesh, India. E.mail: ramaclinbio@gmail.com

Received: December 20, 2012 Accepted: January 4th 2013. Published on: January 20, 2013.

Introduction

Hypertension is reported to be the fourth contributor of premature deaths in developed countries, where as it occupies seventh place in developing countries [1]. In the year 2000, reports indicate that nearly 1 billion adults (more than a quarter of the world's population) has been suffered from hypertension and this is predicted to increase to 1.56 billion by 2025 [2]. A meta-analysis of hypertension prevalence rates in India [3-4] demonstrated a significant increase in the prevalence of hypertension which is comparable with that of USA. [5-6] The prevalence of hypertension has been higher in urban compared to rural areas. Various factors might have contributed to this rising trend attributable to several indicators of economic progress such as increased life expectancy, urbanization and its attendant lifestyle changes including increasing salt intake and the overall epidemiologic transition India is experiencing currently [4].

Hyperinsulinemia as a consequence of insulin resistance and reduced clearance could induce hypertension [7]. Insulin normally acts as a

vasodilator [8-9]. It had been shown that although insulin increased sympathetic activity, the effect was normally overridden by the direct vasodilatory effect of insulin. There may be an imbalance between the sympathetic and vascular actions of insulin in conditions such as obesity and hypertension and that result in elevated blood pressure [9]. Insulin resistance was demonstrated in non diabetic hypertensive patients [10]. Insulin resistance and hyperinsulinemia have been considered important risk factors for the development of hypertension, and there is a significant association between hypertension and insulin resistance in both obese and non obese individuals. [11] That this relationship persists even in the absence of obesity or overt glucose intolerance suggests a more fundamental relationship between hypertension and insulin resistance. However, it is not clear whether this relationship results from a direct manifestation of insulin resistance per se or to hyperinsulinemia secondary to the insulin resistance. Common characteristic features of atherogenic pattern of lipid profile are the elevation of plasma triglycerides and triglyceride rich VLDL-cholesterol, reduced HDL-cholesterol, and an increased number of small dense LDL particles. [12] The present study aimed to demonstrate the relation between insulin resistance and dyslipidemia in freshly diagnosed non diabetic hypertensive patients

Materials and Methods

The subjects were selected from those who visited for a checkup and treatment at Narayana Medical College and Superspeciality Hospital, Nellore, Andhra Pradesh, India. Two hundred and three freshly diagnosed essential hypertension subjects of age between 35-60y (SBP ≥140mmHg and/ or DBP ≥ 90mmHg) were included in this study. Two hundred and ten normotensive(SBP≤ 120mmHg and/ or DBP≤ 80mmHg) healthy, age(35-60 y), sex matched subjects were selected as controls (n=210) only patients having mild to moderate hypertension were included in this study. Patient suffering from severe essential hypertension, secondary hypertension, diabetes mellitus, known cardiac abnormalities, renal, liver, nutritional disorders and pregnant women were excluded from this study. Institutional ethical committee of this medical college have approved the study and informed consent obtained from the patients.

Demographic data: Study subjects age, BMI, waist /hip ratio were recorded. Blood pressure was measured using mercury sphygmomanometer with the patient in the sitting position, legs and crossed. After 5 min of rest in the sitting position, BP was measured on both arms and the higher of the two was taken in to consideration with the systolic and diastolic pressure were in different categories, the higher of the two was used in the classification. They were classified as normotensive and hypertensive as per the recommendation of the JNC7 report.

Biochemical analysis**:** Fasting venous blood was collected immediately after enrollment in tubes containing EDTA. Blood samples were centrifuged at 2000×g for 10 min. serum samples were stored in a freezer at -20℃ for futher biochemical analysis. Samples were analyzed for fasting Glucose, Serum Creatinine, Total cholesterol, HDL- cholesterol, LDL- cholesterol, Triglycerol, analyzed by using Humaster 300(GmBh) Autoanalyser.

Analysis of serum Insulin: Serum Insulin level was determined by using Chemiluminescence immunoassay (Beckmann coulter, USA). The homeostatic model assessment (HOMA) index was used to estimate insulin resistance, and calculated as fasting serum insulin (μU/mL)× fasting serum glucose (mM /22.5). [13]

Statistical analysis: All results are shown as mean ± SD. The statistical significance of between-group differences was evaluated using Student's t-test. Simple correlations were determined by Pearson's correlation analysis. P-value of <0.05 was selected as the point of minimal statistical significance.

Results

Clinical parameters of patients and controls were reported in Table-1 .Body mass Index, Waist/Hip ratio, Systolic Blood pressure (SBP), Diastolic Blood Pressure (DBP) shows statistically significant between patients and controls (p=0.0001). Whereas age and waist hip ratio were not statistically significant.

Variables	Patients (n=208)	Controls (n=221)
Age	46.65±5.6	45.5±5
BMI (Kg/m2)	27.7±1.71*	22.84±2.2
W/H ratio	1.19±0.04*	0.97±0.09
SBP (mmHg)	147.95±9.8*	117.75±4.1
DBP (mmHg)	92.4±12.5*	78.5±3.5

Table-1: Demographic data of the patients and control subjects

*(p=0.0001): p- value <0.05 was considered statistically significant)

In Biochemical parameters except Blood glucose and serum creatinine all analytes were statistically significant in patients when compare to control subjects (p=0.0001) Total Cholesterol, LDL-Cholesterol, Triglycerides, Fasting insulin, HOMA-IR, were significantly increased in hypertensive patients when compared to controls (p=0.001) as shown in the table-2.

Variables	Patients (n=208)	Controls(n=221)
Fasting blood glucose (mg/dl)	91.03±11.1	83.38±7.88
Serum Creatinine (mg/dl)	1.01±0.17	0.91±0.18
Total Cholesterol (mg/dl)	201.8±22.8*	167.68±37
HDL-Cholesterol (mg/dl)	40.87±7.4*	45.45±3.2
LDL-Cholesterol (mg/dl)	127.8±25.3*	102.63±12.9
Triglycerides (mg/dl)	160.6±25*	136.2±25.3
Fasting insulin (µ IU/ml)	24.41±15*	5.5±1.4
HOMA-IR	4.5±2.5*	2.1±0.4

Table-2: Biochemical data of patients and control subjects

(*p -value <0.05 was considered statistically significant)

Univariate analysis showed that HOMA-IR were significantly positively correlated with total cholesterol (r = 0.14, p = 0.001), further, HOMA-IR were found to have a significant negative correlation with HDL and (r = - 0.055, p = 0.001) table-3.

Variables	r = value	P = value
HOMA-IR Vs		
Total Cholesterol	0.141	<0.001
HDL-Cholesterol	- 0.055	<0.001
Systolic blood pressure Vs		
Triglycerides	0.39	<0.001
HDL-Cholesterol	- 0.48	<0.001

Table 3:- Significant correlation in the patients group

Discussion

Patients with hypertension have been reported to have greater risk for the development of cardiovascular diseases when compared to normotensive subjects. However, evidences in the literature are controversial on the association of hypertension with the development of CVD. Several reports have documented an increased risk of CVD among hypertensive subjects while others have suggested that hypertension increases the risk of CVD only modestly or that this risk increases only when hypertension is associated with additional risk factors . Lipids and blood pressure have been associated in several cross-sectional studies. Gaziano *et al.*, (1999) also noted a potential interaction between elevated cholesterol and hypertension in the development of myocardial infarction that suggested a direct relationship rather than the effect of two independent predictors. Rubin O *et al.*, (2006) demonstrated that dyslipidemia might lead to the subsequent development of hypertension and plasma lipids might be useful in the identification of men at risk for hypertension. Numerous cross-sectional studies have shown a close association between insulin resistance and hypertension [14]. Although animal and human studies have suggested that activation of the sympathetic nervous system is associated with insulin resistance-related hypertension [15] the detailed mechanism(s) are not yet clear. There have been several longitudinal studies in Caucasians on the impact of hyperinsulinemia or insulin resistance in predicting the future development of hypertension in non-diabetic, impaired glucose tolerance (IGT) , and type-2 diabetic subjects. [16] Our results revealed the presence of insulin resistance in essential hypertension. In the atherosclerotic cascade, it is well documented that reduced HDL cholesterol levels are associated with an increased risk of coronary heart disease. [17] HDL particles seem to have a cardio protective role as they have direct antioxidative and anti-inflammatory effect and the promotion of cellular cholesterol efflux. In the present study, the HDL levels were significantly decreased in hypertensive subjects when compared with control subjects.In the present study Insulin resistance was positively correlated with Total cholesterol and negatively correlated with HDL-cholesterol which demonstrates the role of insulin resistance in the progression of dyslipidemia which is an important risk factor for atherosclerosis.

Conclusion

Our study demonstrates the presence of insulin resistance in non diabetic hypertension and its association with dyslipidemia. Screening of insulin resistance may useful in non diabetic hypertensive patients to prevent the dyslipidemia a crucial risk factor for atherosclerosis.

References

1. Deepa R, Shanthirani CS, Pradeepa R, Mohan V. Is the 'rule of halves' in hypertension still valid? Evidence from the Chennai Urban Population Study. *J. Assoc. Physicians. India*. 2003;51:153-157.
2. Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J. Global burden of hypertension: analysis of worldwide data. *Lancet.* 2005;365: 217-223.
3. Gupta R. Meta-analysis of prevalence of hypertension in India. *Indian Heart. J*.1997;49: 43-48.
4. Gupta R. Trends in hypertension epidemiology in India. *J. Hum. Hypertens.* 2004;18: 73-78.
5. Expert Group. The Fifth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Arch. Intern. Med.* 1993;153: 154-86.
6. Whelton PK. Epidemiology of hypertension. *Lancet*. 344: 1994:101-6.
7. GianLuca Colussi, MD Cristiana Catena, MD, PHD, Roberta Lapenna, MD, Elisa Nadalini, MD, Alessandra Chiuch, MD andLeonardo A. SechiInsulin Resistance and Hyperinsulinemia Are Related to Plasma Aldosterone Levels in Hypertensive, doi: 10.2337/dc07-1344*Diabetes Care* October 2007vol. 30 no. 10 e107
8. Anderson EA, Mark AL. The vasodilator action of insulin implications for the insulin hypothesis of hypertension. *Hypertension.* 1993;21:136-141.
9. Baron AD, Brechtel-Hook G, Johnson A, Hardin D. Skeletal muscle blood flow: A possible link between insulin resistance and blood pressure. *Hypertension* 1993;11:129-35.
10. Esteghamati A, Gouya MM, Abbasi M et al. Prevalence of diabetes and impaired fasting glucose in the adult population of Iran: National Survey of Risk Factors for Non-Communicable Diseases of Iran. *Diabetes Care*. 2008;31: 96–98
11. Modan M, Halkin H, Almog S, Lusky A, Eshkol A, Shefi M, Shitrit A, Fuchs Z. Hyperinsulinemia. A link between hypertension obesity and glucose intolerance. *J. Clin. Invest.* 1985;75(3): 809–817.
12. A.R. Sharrett, C.M. Ballantyne, S.A. Coady, G. Heiss, P.D. Sorlie, D. Catellier and W. Patsch; Coronary Heart Disease Prediction From Lipoprotein Cholesterol Levels, Triglycerides, Lipoprotein(a), Apolipoproteins A-I and B, and HDL Density Subfractions : The Atherosclerosis Risk in Communities (ARIC) Study; *Circulation.* 2001;104:1108-1113.
13. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and β-cell function from fasting plasma glucose and insulin concentraton in man. *Diabetologia.* 1985;28:412-419.
14. Kaplan NM. The deadly quartet: upper-body obesity, glucose intolerance, hypertriglyceridemia and hypertension. *Arch. Intern. Med.* 1989;149: 1514–1520.
15. Kassab S, Kato T, Wilkins FC, Chen R, Hall JE, Granger JP. Renal denervation attenuates the sodium retention and hypertension associated with obesity. *Hypertension*. 1995;25: 893–895.
16. Bonora E, Kiechl S, Willeit J, Oberhollenzer F, Egger G, Targher G, et al. Prevalence of insulin resistance in metabolic disorders: the Bruneck study. *Diabetes*. 1998;47: 1643-1647.
17. Gordon DJ, Probstfield JL, Garrison RJ, et al. High-density lipoprotein cholesterol and cardiovascular disease. Four prospective American studies. *Circulation*. 1989;79: 8–15.

