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Association of Serum Leptin Levels with Essential Hypertension Independent of Obesity

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Abstract **Original Research Article**

Essential Hypertension though being one of the major global health burden, its pathophysiology is still not established well. This is because it is a complex disorder with multiple factors contributing to its evolution. Recently, hormones like Leptin secreted by adipose tissue are gaining significance in research studies linking hypertension and obesity. So we decided to find the association of serum leptin levels with essential hypertension and whether it is independent of obesity. The study included 60 essential hypertensives in the age group of 45-60years with both genders. Anthropometric measurements and blood pressure were recorded. Body mass index were calculated. Serum leptin levels were measured from collected fasting blood sample. Descriptive statistics were derived. Binary logistic regression was done. Serum leptin levels were found to be increased in hypertensives even after adjusting for obesity with p value<0.000

Keywords: Essential hypertension, Body mass index, Leptin, Obesity.

INTRODUCTION

Leptin, an adipose tissue derived peptide hormone is known to regulate food intake and energy expenditure [1]. Therefore it is assumed to play a key role in determining the weight of an individual. In addition to this, many studies have shown that leptin has a direct effect on maintaining blood pressure of an individual [2]. Leptin has both pressor and depressor effects on blood pressure. Its depressor effects are believed to be due to natriuretic effect, stimulation of endothelial nitric oxide and indirectly by increasing insulin sensitivity. Its pressor effects are due to increased sympathetic nervous system activity and due to adverse shifting of pressure-natriuresis curve [3]. Although leptin has dual and opposite roles over blood pressure regulation, in order to maintain the normal vascular tone usually the pressor effects predominate over the depressor effects. Thus when there are increased levels of leptin as in leptin resistance, it results in increased activation of the renal sympathetic system coupled with decreased natriuresis [4]. Thus hyperleptinemia is likely to produce hypertension [5]. Also leptin is found to increase the production of pro-opio melanocortin which on activation leads to synthesis of alpha melanocyte stimulating hormone. This hormone in turn activates renal sympathetic nervous system and thereby increasing blood pressure [6]. Several studies have shown the positive role of hyperleptinemia in obesity induced hypertension [7-10]. Many other studies could not support the role of leptin in obese hypertensives [11,12]. So we wanted to conduct a study to know the relationship of leptin levels to hypertension in our population and also to know whether it was independent of obesity.

MATERIALS AND METHODS

A cross-sectional study was carried out at a government tertiary care hospital in north Tamilnadu for a period of 9 months. Ethical committee clearance was obtained from the institution. Convenient sampling was made with 60 newly diagnosed essential hypertensives with both the genders (male =36, female =24) between the age groups of 45 to 60 years. They were not started on any drugs when included in the study. Patients with secondary hypertension, diabetes mellitus, cardiovascular disease, cerebrovascular disease, thyroid disorders, renal disorders, recent drug intake for other ailments were excluded from the study.

After obtaining informed consent in local language, anthropometric measurements such as weight in kilograms and height in metres were measured and body mass index were calculated as (weight in kg)/ (height in m)² for each individual. Subjects with BMI more than or equal to 25kg/ m^2 were considered as obese according to revised guidelines based on

consensus developed through discussions by a Prevention and Management of Obesity and Metabolic Syndrome group [13]. Resting Blood pressure were recorded using sphygmomanometer in lying down position after a resting period of half an hour. Systolic BP more than or equal to 140 mm of Hg and diastolic BP more than or equal to 90 mm of Hg were considered as hypertension.

After an overnight fasting of 12 hours, 5 mL of venous blood sample were collected under sterile conditions in plain tubes. Blood was withdrawn with disposable syringes from the cubital vein of the subjects. Serum was separated by centrifuging the sample at 2500 revolutions per minute. 1mL of serum of each subject was aliqouted in separate eppendorfs and stored at -20^{0}C. Serum leptin levels were measured using Human Leptin ELISA kit procured from dbc – Diagnostics Biochem Canada Inc.

Statistical analysis

All the data were entered in excel sheet and analysed using SPSS software. Simple frequency tests were calculated. Descriptive statistics of age, gender, blood pressure, body mass index, serum leptin were derived as Mean and standard deviation. Chi square test was done for comparision of variables. Logistic regression was done to determine the relation of leptin, body mass index and hypertension. It was also adjusted for obesity to know the direct association of serum leptin level and hypertension.

RESULTS

Descriptive statistics is given in Table:1. The cases had mean age of 51.8 ± 5.7 years, systolic BP of 150 ± 14 mm of Hg, diastolic BP of 96 ± 8 mm of Hg and body mass index of 25.9 ± 3.9 kg/m^2, serum leptin levels of 31.9±32.5. Binary logistic regression for leptin and body mass index showed a significant association p=0.000 as shown in Table: 2. and this data were further adjusted for obesity. Even after eliminating the influence of obesity, serum leptin levels showed a statistically significant association with essential hypertension (p=0.000).

Table-1: Descriptive statistics

	Mean	Standard deviation
Age	51.8	5.7
Systolic BP	150	14
Diastolic BP	96	8
Body mass index	25.9	3.9
Serum leptin levels	31.9	32.5

Table-2: Binary logistic regression

	B	S.E	Wald	df	Sig.	Exp(B)	95% C.I for EXP (B)	
							Lower	Upper
Leptin cate	-2.276	.626	13.223	1	.000	.103	.030	.350
Obesity	.544	.631	.744	1	.388	1.723	.500	5.932
Constant	2.629	.849	9.599	1	.002	13.859		

P value <0.05 is significant

After adjusting for infleunce of obesity , most of the hypertensives have high leptin level

DISCUSSIONS

Till date many animal studies have revealed the significant relation of high serum leptin levels with high blood pressure [14]. Human studies are less consistent with the same findings [15,16]. It is a recognized fact that serum leptin levels correlates well with obesity. As expected, this was true in our study. Serum leptin levels were found to be increased in obese hypertensives study which was in line with many other similar studies. In contrast few other studies couldn't obtain a direct positive association between serum leptin levels and blood pressure. Raised serum leptin levels in our study could be due to selective leptin resistance where the metabolic effects are blunted leading to obesity while the neural action of leptin maintaining the normal vascular tone is impaired, leading to increased pressor effects ,thereby increasing blood pressure. One other possibility could be via insulin resistance. Normally leptin is found to enhance the sensitivity of insulin and simultaneously lowering its production. Hyperleptinemia due to leptin resistance could have caused insulin resistance. Insulin resistance and hyperinsulinemia per se are linked to hypertension [17,18]. The difference between serum leptin levels among obese hypertensives and non obese hypertensives was statistically significant in our study. It was also found that even after adjusting for influence of obesity, leptin levels were significantly high in hypertensives. Thus we found that high levels of leptin had direct role in hypertension independent of obesity.

There could be several mechanisms for such a finding. Elevated serum leptin levels could be linked to increased blood pressure via adrenergic or renal mechanisms and have been highly suggested as another possible link for hypertension. Further research studies should be conducted to know the possible mechanism for our finding. The limitations of this study were small sample size. Differences in study design, ethnic and racial differences across study populations may account for the inconsistency of various other similar studies.

CONCLUSION

We conclude from our study that serum leptin levels are high in essential hypertension probably due to selective leptin resistance and this inturn needs further evaluation on a larger population. Leptin is an attractive target for extended research particulary in deriving at the pathophysiology of essential hypertension thereby a potential candidate for pharmacotherapy.

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