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Leptin in prehypertension and essential hypertension and it's association with obesity

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Abstract
Hypertension may be defined as sustained elevation of systemic arterial pressure above 140/90mm of Hg. It is the level of pressure at which institution of therapy reduces related morbidity and mortality. Leptin is a 167 amino acid hormone**,** produced by adipose tissue that helps to control energy balance by inhibiting hunger. It also plays role in other physiological processes like sympathetic nerve system activation, renal hemodynamics, blood vessel tone and blood pressure. The present study was designed to evaluating the clinical significance of serum leptin levels in pre-hypertension and essential hypertension affected individuals.
Samples were collected from newly diagnosed 100 cases of prehypertension and 100 cases of essential hypertension.
These groups were further subdivided into obese and non-obese based on waist circumference (WC) values. Leptin levels were quantitatively measured by ELISA assay. Statistical analysis was done by t- test.
The present study revealed a significant increase in serum leptin levels in prehypertension when compared with essential hypertension. Elevated levels of leptin were observed in obese than in non-obese in both groups.

Keywords: leptin, pre hypertension, essential hypertension, obesity

Introduction
Hypertension may be defined as sustained elevation of systemic arterial pressure above 140/90mm of Hg. It is the level of pressure at which institution of therapy reduces related morbidity and mortality **[1]**. Hypertension usually does not cause symptoms initially, but sustained hypertension over time is a major risk factor for hypertensive heart disease, coronary artery disease, stroke, aortic aneurysm, peripheral artery disease, and chronic kidney disease. Over one billion individuals affected by hypertension worldwide and estimated to reach upto 1.56 billion by the year 2025. **[2]**According to JNC 8 hypertension is classified into primary or essential hypertension and secondary hypertension. Over 90% of patients with high blood pressure have essential Hypertension. Prehypertension is not considered a disease, but identifies those who are likely to progress to stage 1 or stage 2 HTN in the future. Activation of sympathetic nervous system is considered to have crucial function in the pathogenesis of hypertension among obese individuals.**[3,4]**
Obesity is defined as increased mass of adipose tissue and confers a higher risk of arterial blood pressure (BP) elevation or hypertension. Obesity-related hypertension may be secondary to insulin resistance and/or hyperinsulinemia [5, 6, 7, 8]. Several lines of evidence have also suggested that increased sympathetic nerve activity may contribute to the development of obesity-related hypertension. **[9, 10]**
Leptin is a 167 amino acid hormone discovered in 1994 that is almost exclusively produced by adipose tissue and possibly secreted by a constitutive mechanism. The effects of this peptide are mediated by receptors (Ob-R), most of them located in the hypothalamus, belonging to the class l cytokine receptor family. As of yet, 6 leptin receptor isoforms are known [11].
Leptin, has recently been postulated as one of the possible causes of sympathetic activation in obesity since it acts in the hypothalamus by stimulating sympathetic nervous system (SNS) centrally, causes general vasoconstriction and excess renal sodium absorption. Thus, leptin centrally increases blood pressure and heart rate. Therefore, it is possible that obesity-related hypertension is caused in part by leptin-dependent sympathoactivation [12]. Obese subjects exhibit hyperleptinemia from increased adipocyte mass, but remain obese, suggesting some degree of leptin resistance.[13,14] In addition to increased sympathetic activity in hyperleptinemia, other mechanisms may also contribute to the development of obesity-related hypertension. Leptin has been shown to increase the generation of reactive oxygen species (ROS) in endothelial cells and to stimulate secretion of pro inflammatory cytokines such as TNF-α and IL-6, both of which are promoters of hypertension and atherosclerosis [14].

Materials and Methods
Samples were collected from newly diagnosed 100 cases of prehypertension and 100 cases of essential hypertension. Above mentioned groups are further subdivided into obese and non-obese based on waist circumference (WC) values. Patients required for the study were recruited from the department of General Medicine, Mamata General Hospital, Khammam after obtaining written informed consent. The permission has taken from the institution ethical committee prior to conduction of this study. 5ml of venous blood was collected from anticubital vein and allow the blood to clot in a serum separator tube (about 4 hours) at room temperature. The separated serum was stored at -20^{0}C until the procedure is done. Leptin levels were quantitatively measured by ELISA method. Statistical analysis was done by t- test.

Results

The present study revealed a significant increase in serum leptin levels in essential hypertension when compared with prehypertension. Elevated levels of leptin are observed in obese than in non-obese in both groups.

Table 1: serum leptin levels Between Pre HTN and HTN groups.

	MEAN±SD(ng/ml)		p-value
Leptin	Pre HTN	HTN	= 0.0006
	6.80±6.88	10.02±11.27	

Table 2: serum leptin levels Between obese and non-obese sub groups of pre HTN and HTN groups.

Groups	MEAN±SD(ng/ml)		P-value
	OBESE	NONOBESE	
Prehypertension	17.92±3.91	2.99±1.15	< 0.0001
Essential hypertension	26.93±8.93	3.93±1.88	< 0.0001

Discussion

(Al-Hazimi and Syiamic. *et al*., 2004**)** [15] reported in their study higher leptin levels in obese hypertensives compared with obese normotensive individuals. Although they haven't mentioned the relationship between leptin and high blood pressure in humans directly [15]

Many clinical studies have also shown elevated plasma leptin in patients with essential hypertension (Uckaya *et al* 1999; Adamczak *et al* 2000; Takizawa *et al* 2001; Barba *et al* 2003; Canatan *et al* 2004) [16, 17, 18, 19, 20].

(Kunz *et al* 2000; Golan *et al* 2002; Itoh *et al* 2002) observed Serum leptin levels were elevated in obesity due to increase amount of adipose tissue which is the main source of the hormone and possibly secondary to some degree of central resistance to its action [21, 22, 23].

A number of studies have found leptin to be positively correlated with systolic and diastolic blood pressure in both obese and non-obese individuals (Al-Hazimi and Syiamic 2004; Canatan *et al* 2004a; Schutte *et al* 2005) [15, 20, 24].

(Kunz *et al* 2000) also mentioned that serum leptin levels were strong predictors of elevated blood pressure in obese women for early diagnosis and treatment [21].

The present study has shown significantly elevated serum leptin levels in obese hypertensives than non-obese hypertensives in both pre hypertension and essential hypertension.

There were no studies examining the serum leptin levels in patients with pre hypertension in comparison with essential hypertension. In present study found significantly increased leptin levels in essential hypertension when compared to pre hypertension. Hopefully this data will be helpful for the future researches in the same field for the purpose of comparison and as well as in clinical practice.

Conclusion

As observed in present study evaluation of leptin levels may be useful in case of pre hypertension and essential hypertension and obese subjects. Data generated by this study is helpful for clinicians for proper management of above cases in reducing morbidity and mortality. Further researches are needed with large size population with different geographic origin for providing better treatment.

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