A STUDY OF FASTING INSULIN LEVELS IN NON-OBESE INDIVIDUALS WITH ESSENTIAL HYPERTENSION AND ITS COMPLICATIONS
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ABSTRACT
BACKGROUND
An association between essential hypertension and defective insulin secretion has been identified. To study the fasting insulin levels in non-obese, non-diabetic hypertensive subjects. Although hyperinsulinemia, a surrogate of insulin resistance, may play a role in the pathogenesis of hypertension (HTN), the association between fasting insulin level and HTN development is still controversial. We examined the relation between fasting insulin and incidence of HTN in nonobese individuals. To correlate insulin levels with hypertension and its complications.

METHODS
50 patients diagnosed to have hypertension stage I and above as per jNCC - 7 report and 50 controls who are sex matched normal healthy controls. This study is conducted in Bangalore medical college Victoria hospital, Bangalore. Patients of essential hypertension of varying duration admitted to medical wards or treated at OPD department were chosen randomly for this study. All patients who are detected to have hypertension as per report of the JNC7 and are non-obese with BMI<30Kg/m2. Two or more readings separated by 2 minutes were averaged. In newly detected hypertensive patients the diagnosis is based on the average of two or more readings taken at each of two or more visits after an initial screening. Clinical examination and appropriate investigation ruled out secondary hypertension. Fasting serum insulin levels - (normal value 2.1 to 30micro units/ml) estimated by radioimmunoassay method.

RESULTS
Fasting serum insulin level was significantly (p<0.001) higher in essential hypertensive male patients than normotensive subjects. Fasting serum insulin level shows significant positive correlation with systolic blood pressure in hypertensive patients.

CONCLUSIONS
This study reveals that essential hypertension has positive and significant relationship with fasting serum insulin level.

KEYWORDS
Essential hypertension, fasting serum insulin level, systolic blood pressure.


BACKGROUND
Various factors implicated in the genesis of Essential hypertension include genetic influence, age, sex salt sensitivity, an adverse lipoprotein profile, smoking, glucose intolerance and obesity.1 Of late, hyperinsulinemia has also generated considerable interest as a potential factor. The association of hyperinsulinemia in essential hypertension was first discovered and discussed in detail at Banting lecture in 1983. Ferrannini et al and Reaven et al extensively studied the role of insulin in hypertension. Several investigators have in the past reported hyperinsulinemia in hypertensive subjects,2 The exact relationships between the two is still a matter of speculation, although two possible mechanism have been proposed the first presupposes an insulin induced rise in plasma catecholamines,2 while the second relates to promotion of renal tubular sodium reabsorption by insulin.4

History of Insulins
Langerhans identified the islets in 1860s but did not understand their function. Van Mering and Minkowski, who demonstrated in 1889 that pancreaticectomy, produced diabetes.

It was first protein sequenced (Sanger et al, 1955), the first protein synthesized by chemical techniques. (Du et al; Katsoyannis; 1964). It is the first protein synthesized as a large precursor molecule, and the first protein prepared for commercial use by recombinant DNA technology. Hypertension is a major public health problem all over the world. It has been ranked as the fourth largest mortality risk factor in the world accounting for 6% of deaths in the United States because of its high prevalence.5
The prevalence of hypertension in India is 59.9 and 69.9 per 1000 in males and females respectively in urban population and 35.5 & 35.9 per 1000 in male & females respectively in the rural population. The present study was conducted to know the association of hyperinsulinemia in a representative population treated for hypertension at Victoria hospital.

Fasting plasma insulin levels were estimated in 50 hypertensive subjects and 50 matched healthy controls by radio-immuno assay. 52% of hypertensives showed hyperinsulinemia.

Significant number of hypertensive patients who are hyperinsulinemic showed higher incidence of complications such as left ventricular hypertrophy, ischemic heart disease and cerebro vascular disease. Although most hyperinsulinemic patients exhibited an abnormal lipid profile, there was no statistical correlation between lipid values and insulin.

Aims and Objectives
1. To study the fasting insulin levels in non-obese, non-diabetic Hypertensive subjects.
2. To correlate insulin levels with hypertension and its complications.

The Control Group
It included 50 persons who are non-hypertensive, non-diabetic and non-obese and who are of the same age group as the study group. Those controls with renal or other systemic diseases, which are going to affect hypertension and insulin levels, were excluded.

Control subjects underwent similar Investigation as for cases and data were analyzed.

Compare and contrast analyses of data were done through statistical methods.

Hypertension and Hyperinsulinemia
MK Bhatnagar and associates conducted a study on 100 hypertensive subjects and 25 matched healthy controls. Fasting and 2 hours post-prandial serum insulin levels were estimated by radio-immuno assay. 74 of 100 hypertensives exhibited fasting hyperinsulinemia. Post-prandial hyperinsulinemia was present in 85 hypertensives. None of the healthy controls demonstrated hyperinsulinemia.

Although, most hyper insulinemia patients exhibited an abnormal lipoprotein profile, there was no statistical correlation between lipoprotein and insulin. Abnormalities of glucose, insulin, and lipoprotein metabolism are common in patients with hypertension. These changes can also be discerned in normotensive first-degree relatives of hypertensive patients. They are not present in patients with secondary forms of hypertension, do not necessarily improve when blood pressure is lowered pharmacologically, and may even be made worse by some forms of antihypertensive treatment. These metabolic abnormalities may play a part in both the pathogenesis and the complications of hypertension in many patients.

Sympathoadrenal system is linked to the metabolic abnormalities of hypertension.2

The Shen O-C et al study results document the fact that those patients with hypertension, whether treated or untreated, are insulin resistant, hyperglycemic, and hyperinsulinemic compared to a well-matched control group.7

Study done by Reaven et al showed that approximately 50% of an unselected group of patients with hypertension were hyperinsulinemic. Insulin levels were comparable in treated and untreated patients with high blood pressure, and hyperinsulinemic patients also tended to be glucose intolerant and dyslipidaemic.8

Study conducted by Ferrannini et al concluded that the insulin resistance involves glucose but not lipid or potassium metabolism, is located in peripheral tissues but not the liver, is limited to nonoxidative pathways of intracellular glucose disposal, and is directly correlated with the severity of hypertension.9

Insulin resistance and compensatory hyperinsulinemia are primary events, and enhanced sympathetic activity and diminished adrenal medullary activity are important links between the defect in insulin action and the development of hypertension in susceptible subjects predisposed to hypertension by heredity or environmental factors.

In this study, the group of metabolic abnormalities suggests that in the treatment of hypertension, non-pharmacologic interventions that increase sensitivity to insulin, including weight reduction, low-fat diet, and increased physical activity, have a primary role. When pharmacologic treatment is required, a case can be made for drugs that improve insulin sensitivity and the attendant profile of risk factors for coronary heart disease, as well as lower blood pressure.

Bianchi, S., Bigazzi, R., et al concluded that the micro albuminuria in essential hypertension signals the presence of a selective impairment in peripheral insulin-mediated glucose uptake and an enhanced insulin secretory response to glucose. Insulin levels rather than insulin sensitivity appear to be related to urinary albumin excretion.10

Insulin resistance describes an impaired biological response to insulin11,12,13,14. In the early stages of insulin resistance there is a compensatory increase in insulin concentrations. Although hyperinsulinemia may compensate for resistance to some biological actions of insulin, it may result in over expression of actions in tissues that retain normal or minimally impaired sensitivity to insulin. In addition, high concentrations of insulin can act through receptors for insulin-like growth factor I (IGF-I).15,16,17,18

Four large prospective studies,19,20,21,22 have shown that hyperinsulinemia is a predictor of coronary artery disease (CAD).

Lakka, H. et al conducted a study to identify the causal relationship between Hyperinsulinemia and the risk of Cardiovascular Death and Acute Coronary and cerebrovascular Events in Men. They concluded that Hyperinsulinemia had a modest association with increased cardiovascular mortality in middle-aged men. Obesity,
hypothesis, and Dyslipidemia largely explained this relationship. Hyperinsulinemia had even weaker associations with the risk of acute coronary event and stroke.\textsuperscript{23}

This study was conducted to know the effect of hyperinsulinemia on left ventricular mass.

They concluded that in nonobese subjects with high normal BP, insulin sensitivity is related to LVM independently of BP and may be an important modulator of LV growth. In addition to a reduction of arterial BP, optimal prevention of LV hypertrophy in hypertensives may require improved insulin sensitivity.\textsuperscript{24}

Grandi, A. M., et al concluded that genetic predisposition to hypertension is associated with a reduced insulin sensitivity and affects the response of the myocardium to increased insulin levels, inducing a greater impairment of diastolic function. Insulin sensitivity and genetic predisposition to hypertension seem to have no influence on LV mass.\textsuperscript{25}

Shinozaki, K., et al concluded that the higher insulin level was significantly elevated in-patients with Vasospastic Angina and obstructive coronary artery disease compared with control subjects. This indicates that hyperinsulinemia is secondary to insulin resistance, both of which are thought to play important roles as risk factors for Vasospastic Angina in the early atheromatous lesion and in the future development of occlusive lesions when chronically present.\textsuperscript{26}

McNulty, P. H., et al concluded that Acute hyperinsulinemia markedly suppresses myocardial protein degradation in-patients with cardiovascular disease who are resistant to its effects on whole-body glucose metabolism. This anti proteolytic action represents a potential mechanism by which hyperinsulinemia 7 could contribute to the development of myocardial hypertrophy in-patients with cardiovascular disease.\textsuperscript{27}

According to Costa, C. H.R.M., et al study, in nonobese hypertensive patient’s insulin resistance does not have any influence on the 24-hour blood pressure profile or on left ventricular mass index. Blood pressure levels during sleep in these patients seem to contribute to increases in left ventricular mass.\textsuperscript{28}

Regression of left ventricular hypertrophy (L VH) and decrease in Microalbuminuria independent of blood pressure changes have been shown with the angiotensin receptor blockers (ARB) valsartan\textsuperscript{29} and losartan.\textsuperscript{30}

Shinozaki, K., ET al concluded that Insulin resistance in association with compensatory hyperinsulinemia and Dyslipidemia may be an important pathogenetic factor underlying the development of athero thrombotic infarction.\textsuperscript{31}

Facchini F, Chen Y-01, et al conducted a study on normotensive individuals with a family history of hypertension to know the insulin sensitivity and plasma lipid levels. Their results indicate that normotensive individuals with a family history of hypertension are relatively insulin resistant.\textsuperscript{32,33}

Plasma very low-density lipoprotein (VLDL), Triglyceride and VLDL cholesterol were higher in those with a family history of hypertension, as was the ratio of total to high-density lipoprotein cholesterol.

Thus, normotensive individuals with a family history of high blood pressure are insulin resistant, hyperinsulinemic and dyslipidemia when compared to an attached group of healthy volunteers without a family history of hypertension.

**Insulin and Hypertension**

Insulin produces renal sodium retention and hence water retention by the proximal tubular cells.

It increases sympathetic activity. Insulins mitogenic action on smooth muscle cells results in vascular smooth muscle hypertrophy.

Insulin modifies ion transport across the cell membrane there by potentially increasing the cytosolic calcium levels of insulin sensitive vascular or renal tissues.

Insulin causes nonmodulation, i.e., salt restriction or excess will not modulate any effect on renal tubular cells or renal vascular system by angiotensin II.\textsuperscript{34}

**Clinical Characteristics**

Patients may have headaches; fatigue but these are not predictive of hypertension.

Most clinical characteristics of hypertension are transient ischemic attacks (TIA), ischemic stroke, multiple cerebral infarcts and cerebral hemorrhages, retinal hemorrhages - a frequent cause of blindness.

Coronary artery disease is a major complication of hypertension and it manifests as ischemic events such as angina, myocardial infarction and sudden death.

In contrast to coronary artery disease, hypertension also may promote the development of myocardial cellular remodeling resulting in left ventricular hypertrophy (L VH).

Both non- hemodynamic and hemodynamic factors may promote hypertrophy in hypertensive individuals. Left ventricular hypertrophy is potent and independent risk factors for myocardial infarction, congestive cardiac failure, arrhythmias and sudden death.

Hypertension also accelerates the rate of decline in renal function.

**Structure and Functions of Insulin**\textsuperscript{35}

Insulin a prohormone secreted by \textit{?}-cells of pancreas, which constitutes more than 70% of cells in the islets of Langerhans.

Insulin is a polypeptide consisting of two chains, A and B linked by 2 inter chain disulfide bridges. A Chain -21 amino acids, B-chain-30, C -peptides-31.

**Insulin Related Peptides**\textsuperscript{36}

Very closely related peptide hormones such as relaxin and the insulin like growth factors show same arrangement as insulin but remain single chain peptide hormones. This leads to varying antigenic response and hence does not interfere with the insulin assays by radioimmunological method.
Regulation of Insulin Secretion
The human pancreas secretes 40-50 units of insulin daily, which represents about 15-20% of the hormone stored in the gland.

The normal fasting insulin level is 2.1-30 u/ml.

Problems in Measuring Insulin
1. The presence of compounds, which are similar in structure such as pro insulin and its intermediates.
2. Presence of endogenous antibodies to insulin may interfere with the assay.
3. Antibodies produced in newly diagnosed and prediabetic IDDM patients.
   (a) Healthy subjects.
   (b) Patients with thyroid disease.
   (c) Antibodies produced after exogenous insulin treatment.
   (d) Antibody against proinsulin also interfere the assay.

Serum vs. plasma.
Stability of insulin.
Hemolysis.
Dimerization of insulin. Heterophilic antibodies, rheumatoid factor. Serum factors and protein concentrations.
Non linearity on dilution enzymatic degradation of standard insulin.
Aggregation of insulin. Absorption of insulin on to glass and plastic surfaces.

Physiological Factors Affecting Insulin Assays
Peripheral blood concentration of insulin does not correlate with rates of secretion.
Liver metabolizes insulin.
Renal (proximal tubular) insulinase degrades insulin.
Insulin is filtered through glomerulus, reabsorbed and degraded in pET and less than <1% excreted in urine. Insulin is also found in cerebral spinal fluid and saliva.
Plasma insulin concentration varies with age, exercise and body weight. The secretion of insulin is pulsatile and half-life is approximately 13 min. Insulin levels increase in liver disease, renal disease and hyperthyroidism. A point mutation affecting the structure of the molecules, which reduces clearance, is a rare cause for increased insulin level.

METHODS
Source of Data
This study is conducted in Bangalore Medical College Victoria hospital, Bangalore. Patients of essential hypertension of varying duration admitted to medical wards or treated at OPD department were chosen randomly for this study.

All patients who are detected to have hypertension as per report of the JNC7 and are non-obese with BMI<30Kg/m².

Two or more readings separated by 2 minutes were averaged. In newly detected hypertensive patients the diagnosis is based on the average of two or more readings taken at each of two or more visits after an initial screening. Clinical examination and appropriate investigation ruled out secondary hypertension.

Method of Collection of Data
Sample Size
50 patients diagnosed to have hypertension stage I and above as per mc - 7 report and 50 controls who are sex matched normal healthy controls.

Exclusion Criteria
Diabetic mellitus and impaired glucose tolerance.
- Alcoholics.
- Smokers.
- Renal disease.
- Liver disease.
- Familial hypercholesterolemia.

A detailed enquiry of name, age, sex and address of the patients with telephone number were taken. History of present illness, past illness like OM, IHD, hypertension, and tuberculosis are noted. Treatment history of hypertension noted. History related to complication of hypertension is noted. Personnel history including occupation, type of diet consuming, disturbances of bowel or bladder or sleep patterns, habits like cigarette smoking, number per day, duration of smoking, alcohol consumption, type of alcohol, amount per day, duration, are noted.

Family hlo including history of hypertension, DM, IHD or their complications in the family are noted. Each patient is subjected to detailed general physical examination and vital signs are noted. Each patient is subjected to detailed systemic examination; including respiratory system, cardiovascular system, GIT system, central nervous system, and renal system.

Standard 12 head ECG is recorded in all patients to find out any abnormality such as Left ventricular hypertrophy. Chest X-ray to detect any cardiomegaly or complications of hypertension. Echocardiography had done to rule out any regional wall motion abnormality.

USG of abdomen is done to rule out renal pathology. Fundoscopic examination is done to look for any hypertensive changes in the Fundus.

Hematological Investigation Including
Hemoglobin concentration, total count, differential count, erythrocyte, sedimentation rate are noted. Urine is analyzed for the presence of albumin, sugar and microscopic appearance.

Biochemical investigations are undertaken to know fasting, blood sugar, postprandial.

Blood sugar, blood urea nitrogen, and serum creatinine to know the renal function.

Fasting serum insulin levels (normal value 2.1 to 30~ml) estimated by radioimmunoassay method.

The Control Group
It included 50 persons who are non-hypertensive, non-diabetic and non-obese and who are of the same age group as the study group. Those controls with renal or other systemic diseases, which are going to affect hypertension and insulin levels, were excluded.
Control subjects underwent similar investigation as for cases and data were analyzed. Compare and contrast analyses of data were done through statistical methods.

**Statistical Methods**

Student t test has been used to find the significance of lipid parameters and insulin levels between controls and cases. The Mann Whitney U test has been used to find the significance of mean levels of insulin levels between complicated and uncomplicated cases. Chi square and fisher exact test have been used to find the proportion of patients with elevated insulin levels between absence and presence of risk factors. The effect size (d) due to Cohen d has been computed to find the effect of hypertension on insulin levels.

<table>
<thead>
<tr>
<th>d</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>d&lt;0.20</td>
<td>No effect.</td>
</tr>
<tr>
<td>0.20&lt;d&lt;0.50</td>
<td>Mild effect.</td>
</tr>
<tr>
<td>0.50&lt;d&lt;0.80</td>
<td>Moderate effect.</td>
</tr>
<tr>
<td>d&gt;0.80</td>
<td>Large effect.</td>
</tr>
</tbody>
</table>

**Statistical Software**

The statistical software namely spss 11.0 and systat 8.0 were used for the analysis of the data and Microsoft word and excel have been used to generate graphs, tables etc.,
- p>0.05 No significance.
- 0.50<p<0.10 Trend but NS.
- 0.10<p<0.05 Trend and near significance.
- <p<0.05 Significant.
- p<0.01 highly significant.

**Study Design**

A case control study consisting of 50 hypertensive and 50 normal subjects is undertaken to investigate the relationship between the lipid profiles and insulin levels.

**RESULTS**

### Age in Years

<table>
<thead>
<tr>
<th>Age in Years</th>
<th>Cases (N=50)</th>
<th>Controls (N=50)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>21-30</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>31-40</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>41-50</td>
<td>6</td>
<td>12</td>
</tr>
<tr>
<td>51-60</td>
<td>18</td>
<td>36</td>
</tr>
<tr>
<td>61-70</td>
<td>13</td>
<td>26</td>
</tr>
<tr>
<td>71-80</td>
<td>7</td>
<td>14</td>
</tr>
<tr>
<td>&gt;80</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>57.72 ± 12.88</td>
<td>56.12 ± 12.56</td>
</tr>
<tr>
<td>Inference</td>
<td>Samples are age matched with P=0.531</td>
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</tr>
</tbody>
</table>

**Sex**

<table>
<thead>
<tr>
<th>Sex</th>
<th>Cases (n=50)</th>
<th>Controls (n=50)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>Male</td>
<td>32</td>
<td>64.0</td>
</tr>
<tr>
<td>Female</td>
<td>18</td>
<td>36.0</td>
</tr>
<tr>
<td>Inference</td>
<td>Samples are sex matched with p&gt;0.05</td>
<td></td>
</tr>
</tbody>
</table>

**Lipid Profiles and Insulin Levels**

<table>
<thead>
<tr>
<th></th>
<th>Cases (Mean±SD)</th>
<th>Controls (Mean±SD)</th>
<th>Student t</th>
<th>Effect Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol</td>
<td>202.86±46.56</td>
<td>139.04±20.51</td>
<td>p&lt;0.01 **</td>
<td>1.76</td>
</tr>
<tr>
<td>HDL</td>
<td>35.33±7.22</td>
<td>48.32±8.02</td>
<td>p&lt;0.001 **</td>
<td>1.69</td>
</tr>
<tr>
<td>LDL</td>
<td>136.20±39.92</td>
<td>101.80±33.03</td>
<td>p&lt;0.01 **</td>
<td>3.40</td>
</tr>
<tr>
<td>VLDL</td>
<td>34.43±18.49</td>
<td>29.72±18.57</td>
<td>0.209</td>
<td>0.25</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>73.45±87.81</td>
<td>91.10±44.13</td>
<td>p&lt;0.01 **</td>
<td>1.18</td>
</tr>
</tbody>
</table>

**DISCUSSION**

Hyperinsulinemia occurs more frequently in hypertensives than it was thought earlier.

Hypertension and its complications such as ischemic heart disease, left ventricular hypertrophy, retinopathy, cerebrovascular diseases are associated with hyperinsulinemia. Several studies have concluded such an association that hyperinsulinemia could be an etiological factor for the pathogenesis of hypertension and its complications. The present study is conducted to know the role of insulin in hypertension, effect of duration and intensity of hypertension on insulin levels. The present study also highlights the insulin variation in hypertension and its complications. In Indian scenario, few studies have been reported in the above context. Hence the study was conducted to establish the association between insulin and hypertension. In the present study, 50 hypertensive cases were selected; some of them are already receiving treatment for hypertension and its complications. These cases were selected based on inclusion criteria and exclusion criteria. Similarly, normal age and sex matched healthy controls were selected and they were also 50 in number. They underwent
Out of 50 patients, the majority of hypertensives were in the age group of 51-60 years (36%). Mean age was 21 years and maximum age was 85 years. When compared to other studies particularly M.K Bhatnagar, Siddarth et al the mean age was higher in the present study.

Out of 50 patients, 32 were male (64%) and 18 were female (36%). Similar patterns of sex distribution were seen in the other studies. Hypertension and insulin values. In the present study, Out of 50 patients, hyperinsulinemia were seen in 26 patients (52%), remaining 18 had normal insulin levels, and 8 were hypoinsulinemic. The mean insulin level was 70.58. The cut of insulin level was 2-32 IU/ml. Out of 18 normal insulin hypertensives 10 had high normal values insulin. Their mean Insulin level was 31.12IU/ml. Study conducted by M.K Bhatnagar, New Delhi, showed 74% of the hypertensive cases showed hyperinsulinemia. The mean insulin level was 45.99. Reaven et al study showed 41% were hyperinsulinemic, mean insulin was 66.83. I. Ferrani et al study Insulin resistance and hypertension", >80% hypertensive cases were found to have hyperinsulinemia. Harper R. Ennas C.N 92.36IU/ml. Hypertensive cases with a normal ECHO and hypertension, the difference was not statistically significant. Therefore, the present study indicates that the hyperinsulinemia seen in hypertensive subjects are not sex dependent. The mean insulin level in both male and female control was in the normal range and the difference was not significant. Hyperinsulinemia and lipid abnormalities.

Hypertensive subjects are known to have lipid abnormalities.

In the present study Pearson -correlation coefficient is used to correlate insulin levels to lipid profiles. Hypertensive cases showed an increased LDL, total cholesterol, TGL levels. HDL levels were low and the above values were statistically significant in Comparison with controls. There was a negative trend for HDL levels with respect to insulin levels. The distribution of HDL was sparse and widely distributed when compared to controls whose HDL was closely dispersed around the baseline value. There was a direct relationship between elevated LDL values and insulin levels in cases 0.17 vs controls -0.1412. However, insulin values were not statistically raised when other lipid profiles were compared.

Sallomen and Lakka et al 1998, observed that 52% had Dyslipidemia and in that hypertriglyceridemia was increased and HDL was decreased significantly.

The Kuopio Ishaemic heart disease risk factor study 1990, observed that hyperinsulinemia was associated with increased triglycerides and decreased HDL levels. In Israeli -Jewish population study, majority of hypertensive subjects was found to have hypertriglyceridemia.

**Hypertension - Hyperinsulinemia -Cardiovascular Problems.**

In the present study hypertensive cases were analyzed based on ECG and ECHO. 15 cases had left ventricular hypertrophy. 9 cases had ischemic heart disease.

8 cases had other features such as conduction abnormalities, AF, ectopics etc., 18 were having normal ECG. Hypertensive cases with abnormal ECG - 32 in number and their mean insulin level was 78.28 IU/ml were compared with hypertensive cases with normal ECG 18 in number and their mean insulin level was 58.02 IU/ml and results were analyzed.

Even though the mean insulin levels were increased in both the groups especially in hypertensives with abnormal ECG, the difference was not statistically significant.

However 15 out of 50 hypertensive cases with left ventricular hypertrophy

Shown their mean insulin levels 93.07 IU/ml were compared with hypertensives normal ECG 18 in number. The mean insulin value was 58.02 IU/ml, there was a statistical significance. Therefore, the present study indicates that the hyperinsulinemia is a direct cause of Left ventricular hypertrophy.

Hypertensive cases with abnormal Echocardiography were estimated for mean insulin level. The mean level was 92.36IU/ml. Hypertensive cases with a normal ECHO and their mean insulin level was 28.29IU/ml. The above groups were compared. There was a statistical significance in the
results indicating abnormal ECHO is due to a direct cause effect of hyperinsulinemia. This also explains that ECHO is a more sensitive than ECG in knowing the effect of hyperinsulinemia on heart. These above results were in concordance with other studies such as, Sheu WH, Jeng CY, Young MS, Le WJ, Chen Yp5 studies "Coronary artery Disease risk predicted by insulin resistance, plasma lipids, and hypertension in people without diabetes." Study included 96 patients without diabetes but with angiographically documented CAD and 96 age-, sex-, and body mass index-matched healthy control subjects. Patients with CAD had significantly higher values of fasting glucose, glucose and insulin responses to oral glucose tolerance test, total cholesterol, low- density lipoprotein (LDL) cholesterol, and Triglyceride and decreased high-density lipoprotein (HDL) cholesterol concentrations compared with those of healthy people (P <0.02-0.001). Study concluded that 36% of total risk for development of CAD in persons without diabetes.

In Jean-Pierre Despres study, "Hyperinsulinemia as an Independent Risk Factor for Ischemic Heart Disease" study 462103 men who were 45 to 76 years of age and who did not have ischemic heart disease. A first ischemic event (angina pectoris, acute myocardial infarction or death from coronary heart disease) occurred in 114 men (case patients). Fasting insulin concentrations at base line were 18 percent higher in the case patients than in the controls (p=0.001).

Logistic-regression analysis showed that the insulin concentration remained associated with ischemic heart disease (odds ratio for ischemic heart disease with each increase of 1 SD in the insulin concentration, 1.7; 95 percent confidence interval, 1.3 to 2.4) after adjustment for systolic blood pressure, use of medications, and family history of ischemic heart disease.

Further adjustment by multivariate analysis for plasma triglyceride, Apolipoprotein B, low-density lipoprotein. Cholesterol, and high-density lipoprotein Cholesterol concentrations did not significantly diminish the association between the Insulin concentration and the risk of ischemic heart disease (odds ratio, 1.6; 95 Percent confidence interval, 1.1 to 2.3).

They concluded that high fasting insulin concentrations appear to be an independent predictor of ischemic heart disease in men. In the present study, Hypertensive cases were further divided by hypertensive with cardiovascular complications and without complications. Out of 50 cases 30 were having cardiovascular complications either in the form of IHD, Angina, left Ventricular hypertrophy, arrhythmia, and conduction abnormalities. Out of 30-18 had hyperinsulinemia, 12 had normal insulin levels. Out of 12 normal insulin - 6 were in the high normal insulin values. The results were compared; there was no statistical Significance between the two groups. This result reveals that hyperinsulinemia is directly related to left ventricular hypertrophy and not to other complications.

Similarly, the hypertensives with all complications such as both cardiovascular and cerebrovascular involvement i.e., 34 out of 50 were compared to hypertensive cases without complications i. e 16 out of 50 cases. The mean insulin in the first group was 88.87 IU/ml and 31.76 in the second group. Insulin levels were significantly raised in complicated cases compared to uncomplicated cases (p =0.0019).

This implies that hyperinsulinemia is directly related to complications seen in hypertensive subjects. There are many studies, which give concordant results as Observed in the present study such as, Phillips- RA et al, concluded that out of 64 nonobese, non-hypertensive subjects >32% had left ventricular hypertrophy. Their mean insulin level was72.80 IU/ml suggesting hyperinsulinemia is a risk factor for left ventricular hypertrophy.

The study conducted by Me Nutty P.H. et al, where >46% hypertensive hyperinsulinemic were showing left ventricular hypertrophy. The present study doesn’t give statistically significant values for ischemic heart disease.

However many studies such as Shnozaki K et al, Me. Lakka et al showed a causal relationship between hyperinsulinemia and risk of cardiovascular death. However the above studies included diabetes also. The above studies also reveal weaker association for acute coronary events and cerebrovascular events in men who are hypertensive and hyperinsulinemic.

CONCLUSIONS
Hypertensive subjects will invariably have hyperinsulinemia which widely fluctuates based on duration of hypertension, age of onset of hypertension, and associated complications. Hyperinsulinemia seen in hypertension do not vary with sex and antihypertensive medications. Hyperinsulinemia seen in hypertension do not vary among different races. However blacks are known to have higher complications and hyperinsulinemia. Hyperinsulinemia is directly related to left ventricular hypertrophy and increases the chances of ischemic heart disease.

Hypertensives who are hyperinsulinemic will have increased risk of developing hypertension-related complications. Hyperinsulinemia in hypertensives is known to cause lipid abnormalities.

The Echocardiography is more sensitive than ECG to diagnose left ventricular hypertrophy. The complications such as left ventricular hypertrophy, IHD, cerebrovascular disease, retinopathy are directly related to hyperinsulinemia.

Summary
An association between hyperinsulinemia and hypertension has been suggested by many studies. To assess whether this association is independent of the presence of other hyperinsulinemic states, such as obesity and glucose intolerance, this study was conducted.

Fasting plasma insulin levels were estimated in 50 hypertensive subjects and 50 matched healthy controls by radio - immuno assay. 52% of hypertensives showed hyperinsulinemia.

Significant number of hypertensive patients who are hyperinsulinemic showed higher incidence of complications such as left ventricular hypertrophy, ischemic heart disease and cerebrovascular disease. Although most
REFERENCES


