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Study of Left Ventricular Hypertrophy and their Association to Metabolic Syndrome

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Abstract: *Metabolic syndrome is wide spread among adult population in the world and which is increasing with age. This study was done to know the relation-ship of left ventricular hypertrophy to chronic hypertension in middle aged women and men of metabolic syndrome.*

Objectives under study are: *Measurement of waist circumference in subjects and controls.*

1. *Measurement of blood pressure.*
2. *Estimation of Blood glucose levels.*
3. *Estimation of Triglycerides.*
4. *Estimation of HDL Cholesterol.*

Keywords: *Cardiovascular disease, Chronic Hypertension, Left-ventricular Hypertrophy, Metabolic syndrome (MetS).*

I. Introduction

Left ventricular hypertrophy (LVH) develops in response to increased biomechanical stress due to high blood pressure (BP) which results in the increased after-load associated with elevated systemic vascular resistance. LVH can be viewed as necessary and protective up to a certain point; beyond that point, a variety of dysfunctions can result in. Large population studies have provided evidence that LVH confers increased risk for stroke, myocardial infarction, heart failure and cardiovascular death[1]. This association was found both in samples of the general population, such as the Framingham study[2,3] and the Second National Health And Nutrition Examination Survey Epidemiological Follow-up Study (NHANES-II)[4], and in groups of patients who were already suffering from a symptomatic vascular disease, e.g. the Heart Outcomes Prevention Evaluation (HOPE) study[5]. LVH has been associated with an increased risk of LV dysfunction[6].

LVH can have a concentric morphology, i.e. increased mass in the absence of dilation, or an eccentric morphology, i.e. increased mass with dilation.

Pathophysiology of Hypertension

Pathophysiology of hypertensive heart disease is a complex interplay of various hemodynamic, structural, neuroendocrine, cellular, and molecular factors. On the one hand, these factors play integral roles in the development of hypertension and its complications; on the other hand, elevated BP itself can modulate these factors. Elevated BP leads to adverse changes in cardiac structure and function in 2 ways: directly by increased afterload as Left Ventricular Hypertrophy and indirectly by associated neurohormonal and vascular changes.

Uncontrolled and prolonged elevation of BP can lead to a variety of changes in the myocardial structure, coronary vasculature, and conduction system of the heart. These changes in turn can lead to the development of left ventricular hypertrophy (LVH), coronary artery disease, various conduction system diseases. The systolic and diastolic dysfunction of the myocardium of LVH can manifest clinically as angina or myocardial infarction, cardiac arrhythmias (especially atrial fibrillation), and congestive heart failure (CHF). Thus, hypertensive heart disease is a term applied generally to heart diseases, such as LVH, coronary artery disease, cardiac arrhythmias, and CHF, those are caused by direct or indirect effects of elevated BP. Although these diseases generally develop in response to chronically elevated BP, marked and acute elevation of BP can also lead to accentuation of an underlying disease process.

LVH was originally thought to be required for the normalization of wall stress in hemodynamic overload[7]. This concept of 'adaptive hypertrophy' is now being challenged by a large number of animal experiments, consistently suggesting that any degree of LVH is detrimental for LV function and survival[1].

Echocardiography (2D-ECHO) is being used because it is much more sensitive than Electrocardiography (ECG) in recognizing early cardiac involvement. By Echocardiography, left ventricular mass is shown to progressively increase with increases in BP[8].

The pathogenesis of LVH involves a number of variables other than the pressure load, one of which is hemodynamic volume load. Devereux and colleagues[9] found a closer correlation between left ventricular stroke volume and left ventricular mass with diastolic than with systolic blood pressure. Other determinants are obesity[10], activity of sympathetic nervous system and renin-angiotensin system activity, and whole blood viscosity, presumably by way of its influence on peripheral resistance. The degree of increased muscle mass is a strong and independent risk factor for cardiac mortality over and above the extent of coronary artery disease[8.]

Of patients with hypertension, 15-20% develop LVH. The risk of LVH is increased 2-fold by associated obesity. Studies have shown a direct relationship between the level and duration of elevated BP and LVH. The LVH, defined as an increase in the mass of the left ventricle (LV), is caused by the response of myocytes to various stimuli accompanying elevated BP. Myocyte hypertrophy can occur as a compensatory response to increased afterload. Myocardial oxygen supply in hypertensive may be limited by coronary artery disease (CAD) while myocardial oxygen demand is often greater because of the increased impedance to left ventricular ejection and the frequent presence of left ventricular hypertrophy (LVH) [11]. Mechanical and neurohormonal stimuli accompanying hypertension can lead to activation of myocardial cell growth, gene expression and thus to LVH. In addition, activation of the renin-angiotensin system, through the action of angiotensin II on angiotensin I receptors, leads to growth of interstitium and cell matrix components. In summary, the development of LVH is characterized by myocyte hypertrophy and by an imbalance between the myocytes and the interstitium of the myocardial skeletal structure[11].

The Cardiovascular disease (CVD), particularly coronary heart disease (CHD), remains a major health concern in the world. Many cohort studies have demonstrated that hypertension is a strong risk factor for total mortality and cardiovascular disease (CVD)[12-16] in both developing and developed countries[13,17,18]. Although the association of cardiovascular risk with elevated blood pressure is well accepted[12-15, 17], only a few studies have addressed the absolute and relative risks of CVD for the population with blood pressure values in the high-normal range. The Framingham Heart Study revealed an association of high-normal blood pressure with increased risk of CVD[19].

Association of LVH to MetS

The Metabolic Syndrome (MetS) refers to a constellation of interrelated cardiac risk factors that appear to directly promote development of atherosclerotic cardiovascular disease (ASCVD) [20-23]. It receives widespread attention as obesity becomes a crisis of epidemic proportions in the world. This syndrome occurs in approximately one fourth of all adults in US[24] and the rest of the world.

In the current study, the association of Left Ventricular Hypertrophy (LVH) and characteristic risk factors of MetS were studied. Risk factors like central obesity and insulin resistance are the common underlying denominators of MetS, and are thought to manifest as several metabolic conditions, including elevated blood pressure, LVH (a physical consequence of chronic hypertention), atherogenic dyslipidemia, elevated plasma glucose, pro-inflammatory state and pro-thrombotic state [20-23.25]. These metabolic risk factors are believed to have a direct effect on atherosclerotic disease.

Dyslipidemia

The dyslipidemia found in individuals who have the MetS consists of an aggregate of lipoprotein abnormalities that include: high serum triglycerides, high LDL-Cholesterol (LDL-C) and low HDL-cholesterol (HDL-C), and increased number of small dense Low-Density Lipoprotein (LDL) particles and small High Density Lipoprotein (HDL) particles. All of these abnormalities are independently atherogenic [21, 26–28].

Hyperglycemia

Metabolic abnormalities observed in MetS, including hyperglycemia, insulin resistance, and dyslipidemia, alter normal arterial function and render arteries susceptible to atherosclerosis[25]. The postulated mechanisms for this include: endothelial dysfunction with decreased bioavailability of nitric oxide[29, 30], inflammation and proliferation of smooth muscle cells[31, 32], platelet dysfunction[33], and a decrease in endogenous anticoagulation associated with increased tissue factor and plasma coagulation factors[34, 35].

II. Materials and Methods

Control Group (Without Central Obesity):

Men and women who were selected of age between 40 and 60 years, who are physically healthy without hypertension or any clinical abnormality.

Test Group (With Central Obesity):

Men and women who were selected were not known diabetics of age between 40 and 60 years, who were hypertensive with increased waist circumference (Men ≥ 90 cm; women ≥ 80 cm).

1. Physical Parameters:

a) Blood Pressure, Systolic (SBP) & Diastolic (DBP) were measured using mercury sphygmomanometer
b) Waist Circumference (WC) measured using Tailor's measuring tape.
c) Left Ventricular Mass was measured using MYLAB - 2 Dimensional Echo-cardiograph

2. Chemical Parameters:

Blood sample was taken from each individual of control and test groups after 10-12 hrs. overnight fasting state for the measurements of following parameters;

a) Fasting Plasma Glucose (FPG)
b) Lipid profile:
1. Total Triglycerides, (TTG)
2. Total Cholesterol, (TCH)
3. Total HDL Cholesterol (HDLC)

All chemical parameters are done on VITROS DT 60 II module.

III. Results

Measurement of Waist Circumference (WC), Blood Pressure (BP), Fasting Plasma Glucose (FPG), Total Triglycerides (TTG), and High Density Lipoprotein Cholesterol (HDLC) are helpful in identifying cases of Metabolic Syndrome. Measurement of Left Ventricular Mass in grams is also made to assess chronic nature of hypertension. Male individuals with waist circumference above 90 cm and female individuals with waist circumference above 80 cm were considered as having central obesity, as per IDF criteria.

In this study control group was selected with normal waist circumference between ages of 40 – 60 years. The test group of central obesity was selected with increased waist circumference. The results of Waist Circumference (WC) in men control group (22) of Table-1, the average is 90.59 cms with S.D. of ±6 compared to the results of WC in men test group (22) of Table-2, the average is 99 cms with S.D. of ±6.04. The increase in WC in males is highly significant ($p < 0.001$). Whereas the results of WC in women control group (15) of Table-3, the average is 88.2 cms with S.D. of ±5.66 compared to the results of WC in women test group (15) of Table-4 the average is 99 cms with S.D. of ±4.72. The increase in WC in female is highly significant ($p < 0.001$).

The results of Systolic Blood Pressure (SBP) in men control group, the average is 120.82 mmHg with S.D. of ±6.43 compared to the results of SBP in men test group, and the average is 140.45 mmHg with S.D. of ±12.53. The increase in SBP in males is highly significant ($p < 0.001$) and the results of Diastolic Blood Pressure (DBP) in men control group, the average is 79.09 mmHg with S.D. of ±2.94 compared to the results of DBP in men test group, the average is 91.82 mmHg with S.D. of ±6.65. The increase in DBP in males is highly significant ($p < 0.001$)

Whereas the results of Systolic Blood Pressure (SBP) in women control group, the average is 118.53 mmHg with S.D. of ±4.87 compared to the results of SBP in women test group, the average is 137.33 mmHg with S.D. of ±9.61. The increase in SBP in females is highly significant ($p < 0.001$) and the results of Diastolic Blood Pressure (DBP) in women control group, the average is 79 mmHg with S.D. of ±3.87 compared to the results of DBP in women test group, the average is 90 mmHg with S.D. of ±5.34. The increase in DBP in females is highly significant ($p < 0.001$). The results of Left Ventricular Mass (LVM) in men control group, the average is 163.86 grams with S.D. of ±8.36 compared to the results of LVM in men test group, and the average is 294.5 grams with S.D. of ±75.32. The increase in LVM in males is highly significant ($p < 0.001$).

Whereas the results of LVM in women control group, the average is 161.27 grams with S.D. of ±9.41 compared to the results of LVM in women test group, the average is 309.53 grams with S.D. of ±63.19. The increase of LVM in female is highly significant ($p < 0.001$). The results of Fasting Plasma Glucose (FPG) in men control group, the average is 86.18 mg% with S.D. of ±10.41 compared to the results of FPG in men test group, and the average is 86.09 mg% with S.D. of ±7.86. The change in FPG in males is Not Significant ($p < 0.5$). Whereas the results of FPG in women control group, the average is 85.53 mg% with S.D. of ±8.59 compared to the results of FPG in women test group, the average is 91.6 mg% with S.D. of ±13.74. The increase in FPG in female is Not Significant ($p < 0.1$). The results of Total Triglycerides (TTG) in men control group, the average is 89 mg% with S.D. of ±42.74 compared to the results of TTG in men test group, and the average is 138.04 mg% with S.D. of ±58.6. The increase in TTG in males is significant ($p < 0.01$).

Whereas the results of TTG in women control group, the average is 96.27 mg% with S.D. of ±42.69 compared to the results of TTG in women test group, the average is 178.46 mg% with S.D. of ±80.95. The increase in TTG in female is significant ($p < 0.01$). The results of High Density Lipoprotein Cholesterol (HDLC) in men control group, the average is 42.23 mg% with S.D. of ±5.77 compared to the results of HDLC in men test group, the average is 39.18 mg% with S.D. of ±8.29. The decrease in HDLC in males is significant ($p < 0.01$).

Whereas the results of HDLC in women control group, the average is 49.2 mg% with S.D. of ±5.14 compared to the results of HDLC in women test group, the average is 44.33 mg% with S.D. of ±5.31. The decrease in HDLC in female is significant ($p < 0.01$).

The overall risk analysis for Metabolic Syndrome in the 22 (twenty two) men control group, 2 (Two) are with 3 risk factors which represents 9.09% male control group having Metabolic Syndrome. The overall risk for Metabolic Syndrome in the 22 (twenty two) men test group, 12 (Twelve) are with >3 risk factors which represents 54.55% male test group having Metabolic Syndrome. So, the increase in incidence is from 9.09% to 54.55% of Metabolic Syndrome in controls to hypertensive men of 40-60 year's age group.

Whereas the overall risk analysis for Metabolic Syndrome in the 15 (fifteen) women control group, 1 (One) is with 3 risk factors which represents 6.67% female control group having Metabolic Syndrome. The overall risk for Metabolic Syndrome in the 15 (fifteen) women test group, all15 (Fifteen) are with >3 risk factors which represents 100% female test group having Metabolic Syndrome. So, the increase in incidence is from 6.67% to 100% of Metabolic Syndrome in controls to hypertensive women of 40-60 years age group.

The comparative risk of CVD of Metabolic Syndrome is more in hypertensive middle aged women (100%) than that of middle aged men (54.55%).

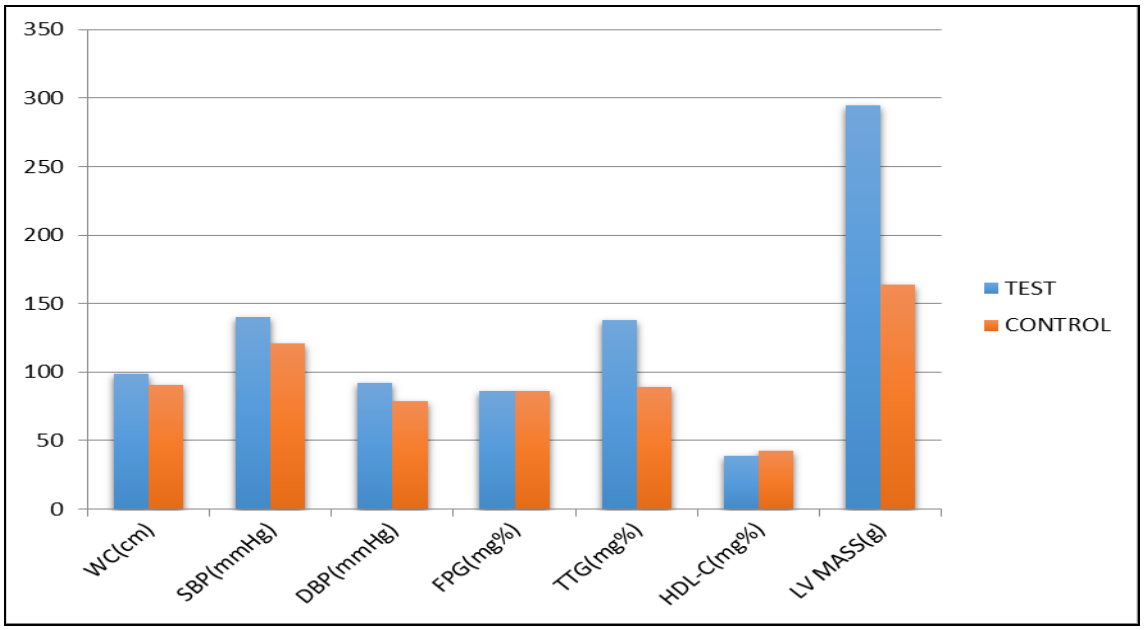

Figure 1: Showing relation of risk parameters in LVH to Controls in Males.

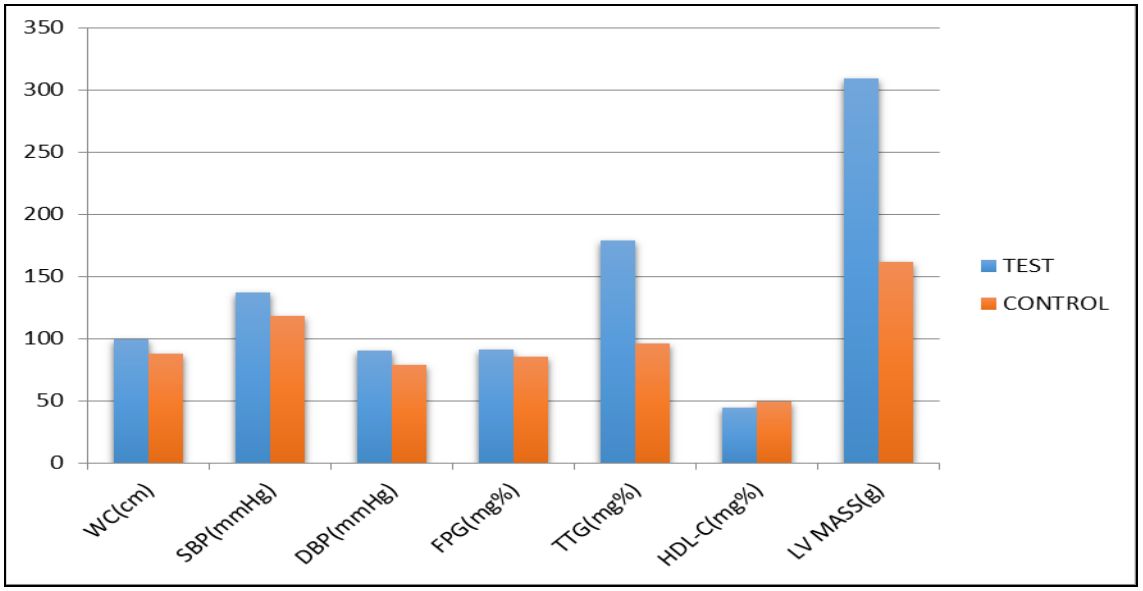

Figure 2: Showing relation of risk parameters in LVH to Controls in Females.

IV. Discussion

The Cardiovascular diseases (CVD) represent the major cause of death and disability in the world, involving not only the Western affluent societies but also the emerging low-middle income countries[39, 40] including India. Accordingly, the scientific community is expressing a growing effort to find new strategies capable of implementing successful primary prevention[41]. In this context, recent epidemiological studies indicate that early application of lifestyle changes should be preferable to drug only based management[42, 43]. This approach may be particularly appropriate in hypertension because of the well-recognized continuum of increased risk, even if blood pressure values are within the reference range[19, 44]. Hypertension, in addition, interacts with overweight and obesity to produce an additive rise of risk, which can be attenuated, if not normalized, by diet and exercise[43, 45, 46].

Echocardiography is more sensitive than electrocardiography in diagnosing left ventricular hypertrophy[47] and predicting cardiovascular risk[3]. The relation between left ventricular mass index and cardiovascular risk is continuous, thresholds of 125 g/sqm for men, and 110 g/sqm for women are widely used for conservative estimates of left ventricular hypertrophy. The concentric hypertrophy has been shown to be the condition which most markedly increases the risk[48, 49].

Metabolic Syndrome and Left Ventricular Hypertrophy

The metabolic syndrome (MetS) is characterized by the variable combination of visceral obesity and alterations in glucose metabolism, lipid metabolism and Blood Pressure. The most common features of MetS are: 1) The prevalence of MetS is directly related to age and increasing with age; 2) The Cardiovascular morbidity and mortality markedly higher in MetS[50–53] 3) A greater risk of new onset hypertension in MetS [54–56] 4) A 3- to 6-fold increase in the risk of developing diabetes[57,58] as well as 5) a frequent association with subclinical organ damage such as microalbuminuria and reduced glomerular filtration rate[59–61], arterial stiffening[62], left ventricular hypertrophy, diastolic dysfunction, atrial enlargement[50,59,60,63–65].

The cardiovascular risk is high in hypertensive patients with the metabolic syndrome it would appear advisable to pursue an effective blood pressure control, i.e. to lower blood pressure to values less than the high normal ones that are a common component of the syndrome[50]. Data from observational studies involving more than 1 million individuals have indicated that death from both ischemic heart disease and stroke increases progressively and linearly from BP levels as low as 115 mm Hg systolic and 75 mm Hg diastolic upward[66]. The increased risks are present in all age groups ranging from 40 to 89 years old. For every 20 mm Hg systolic or 10 mm Hg diastolic increase in BP, there is a doubling of mortality from both ischemic heart disease and stroke. In addition, longitudinal data obtained from the Framingham Heart Study have indicated that BP values in the 130 to 139 / 85 to 89 mm Hg range are associated with a more than 2-fold increase in relative risk from cardiovascular disease (CVD) compared with those with BP levels below 120 / 80 mm Hg[19]. The relationship between BP and risk of CVD events is continuous, consistent, and independent of other risk factors. The higher the BP, the greater is the chance of heart attack, HF, stroke, and kidney diseases. The presence of each additional risk factor compounds the risk from hypertension[67].

The common feature of all forms of LVH is increased left ventricular mass, although there are many different presentations and subtypes, each with different prognosis and therapy[68]. LVH subclasses can be characterized generally by the relative wall thickness, the presence or absence of reduced contractility, and the end-diastolic chamber size. LVH can occur in endurance athletes with normal or supranormal systolic function, large end-diastolic volumes, and elongation of myofibrils (eccentric hypertrophy). LVH due to hypertension is usually characterized by concentric hypertrophy with circumferential hypertrophy of myofibrils, normal or increased contractility, increased relative wall thickness, normal or low end-diastolic volumes, and at times impaired relaxation (diastolic dysfunction). In population-based samples, 30% to 50% of individuals with stage 1 and 2 hypertension have impaired LV relaxation, and in more severe forms of hypertension, about two-thirds have abnormal LV relaxation. In untreated or poorly treated individuals, LVH becomes a major risk factor for dilated cardiomyopathy and HF[3].

V. Conclusion

The physician can be benefited by detecting MetS to deal with the risk factors in his clinical management. All the patients who have the MetS should receive a thorough risk assessment and adopt effective therapeutic life style changes both physically by maintaining normal waist circumference and mentally by keeping peace of mind and positive attitude. In patients who have the MetS, long-term management of each risk factor is essential, because lifetime risk for CVD with MetS is higher than expected in untreated patients. Lifestyle intervention is fundamental and should be introduced, maintained, and reinforced in all individuals.

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